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Costs and effectiveness of alternative dog vaccination strategies to improve dog population coverage in rural and urban settings during a rabies outbreak

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ABSTRACT

Dog-rabies elimination programs have typically relied upon parenteral vaccination at central-point locations; however, dog-ownership practices, accessibility to hard-to-reach sub-populations, resource limitations, and logistics may impact a country's ability to reach the 70% coverage goal recommended by the World Organization for Animal Health (OIE) and World Health Organization (WHO). Here we report the cost-effectiveness of different dog-vaccination strategies during a dog-rabies outbreak in urban and *peri*-urban sections of Croix-des-Bouquets commune of the West Department, Haiti, in 2016. Three strategies, mobile static point (MSP), mobile static point with capture-vaccinate-release (MSP + CVR), and door-to-door vaccination with oral vaccination (DDV + ORV), were applied at five randomly assigned sites and assessed for free-roaming dog vaccination coverage and total population coverage. A total of 7065 dogs were vaccinated against rabies during the vaccination campaign. Overall, free-roaming dog vaccination coverage was estimated at 52% (47%-56%) for MSP, 53% (47%-60%) for DDV + ORV, and 65% (61%-69%) for MSP + CVR (differences with MSP and DDV + ORV significant at $p < 0.01$). Total dog vaccination coverage was 33% (95% CI: 26%-43%) for MSP, 49% (95% CI: 40%-61%) for MSP + CVR and 78% (77%-80%) for DDV + ORV (differences significant at $p < 0.001$). Overall, the least expensive campaign was MSP, with an estimated cost of about $2039 per day ($4078 total), and the most expensive was DDV + ORV with a cost of $3246 per day ($6492 total). Despite the relative high cost of an ORV bait, combining DDV and ORV was the most cost-effective strategy in our study ($1.97 per vaccinated dog), largely due to increased efficiency of the vaccinators to target less accessible dogs. Costs per vaccinated dog were $2.20 for MSP and $2.28 for MSP + CVR. We hope the results from this study will support the design and implementation of effective dog vaccination campaigns to achieve the goal of eliminating dog-mediated human rabies deaths by 2030.

1. Introduction

Rabies is among the most lethal infectious diseases with the highest case fatality rate of etiological agents. Worldwide, rabies is responsible for an estimated 59,000 human deaths annually, ~99% of which are due to a bite of an infected domestic dog [1–3]. Thus, controlling rabies in dog populations substantially reduces rabies exposures in humans [4]. Dog rabies has been suc-

Abbreviations: CDC, Centers for Disease Control and Prevention; CVR, Capture vaccinate release; DDV, Door to door vaccination; HDI, Human Development Index; LAC, Latin America and the Caribbean; MARNDR, Ministry of Agriculture, Natural Resources, and Rural Development; MSP, Mobile static point; OIE, World Organization for Animal Health; OLS, Ordinary Least Squares; ORV, Oral rabies vaccination; PEP, Post-exposure prophylaxis; RIG, Rabies immunoglobulin; SDI, Socio Demographic Index; SRS, Sight-resight; UNDP, United Nations Development Programme; WHO, World Health Organization; YLG, Years of life gained; YLL, Years of life lost.

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cessfully eliminated in most of the Western Hemisphere, Europe, and some countries in Asia. These success stories have been focused on routine, annual campaigns of mass dog vaccination as the primary intervention, requiring coordination and engagement at the national and community levels [4–9]. The World Health Organization (WHO) and World Organization for Animal Health (OIE) recommend dog-rabies endemic countries to conduct recurrent mass vaccination campaigns covering $\geq$ 70% of the dog population, sustained over three to seven years, to control and potentially eliminate dog rabies [1,10,11].

Dog-rabies elimination programs have typically relied upon parenteral vaccination at mobile static points (MSP); however, dog-ownership practices, ability to vaccinate hard-to-reach subpopulations, resource limitations, and logistics may impact a country's ability to reach the 70% goal in many settings [12,13]. Door-to-door vaccination (DDV) and capture-vaccinate-release (CVR) strategies have also been used in various settings to reach a larger dog population, including aggressive or overly shy dogs, but are more labor-intensive than MSP, and require special training [14,15]. Oral rabies vaccination (ORV) baits have been approved for use in wildlife as a compliment to parental vaccination of domestic animals [16–18], and have been used to vaccinate free-roaming dogs in various settings, but the technology is still under development [19,20] (Table 1). Dog-rabies endemic countries are at different stages of their rabies control capacity, and may face substantial challenges including, for example, a limited understanding of local epidemiology, inadequate financial and human resources, competing priorities of other diseases, and planning and logistic constraints [21–24]; one such country is the Republic of Haiti [22,25].

Haiti has the highest human rabies burden in the Western Hemisphere [22,25–27], though the true prevalence and incidence of rabies remain unknown. An annual average of four canine rabies cases and seven human rabies cases were reported in Haiti in 2010–2012 [26,28]. However, as in other countries [1-4,21,29–31], many human and dog rabies cases in Haiti are not recognized and/or reported to health authorities [22], limiting awareness, funding, and prevention efforts. For example, an 18-fold increase in case detection was reported following implementation of an animal rabies surveillance system in Haiti from 2013 to 2015 [22]. A modeling effort to assess the global burden of rabies estimated about 130 annual deaths from rabies in Haiti [2]. Resource limitations and competing health priorities have resulted in inadequate surveillance and laboratory capacity and few trained health professionals [22,28,32]. In collaboration with the US Centers for Disease Control and Prevention (CDC) and other agencies, the Haitian government has developed several initiatives to prevent and control dog rabies, including integrated bite case management, enhanced surveillance methods and expansion of mass dog vaccination campaigns [22,25,32–34]. Despite important improvements in rabies

Table 1
Summary and definition of alternative methods for mass dog vaccination, Haiti 2016.

Vaccination method	Characteristics and advantages	Limitations
Mobile Static Point vaccination (MSP)*	Community members are encouraged, through community engagement activities, to bring dogs to a centralized location where vaccinators have established a temporary vaccination clinic Owned dogs and dogs which are always or partially confined to an owner's control are typically favored by this vaccination strategy	Free roaming dogs† may not be readily handled by dog owners, thus are less likely to be reached. Potential risk of disease transmission between dogs. Community owned and stray dogs typically have no person or family which feels responsibility to bring these dogs to a MSP clinic Parenteral rabies vaccine, requires dog restraint with potential risk of bites Aggressive or overly shy dogs less likely to be brought to a MSP Depend on owner awareness of MSP clinic, and geographical accessibility
Capture vaccinate release vaccination (CVR)*‡	Vaccinators are required to capture the dog before vaccination	Requires a skilled workforce to capture and vaccinate dogs in a safe manner for the animal and vaccinator, may decrease effectiveness in time due to dogs running away from vaccinators.
	Strategy is aimed at reaching free roaming dogs†	Parenteral rabies vaccine, requires dog restraint with potential risk of bites
Door-to-door vaccination (DDV)*	Vaccinators visit each household to offer dog vaccination	More labor-intensive than MSP
	Do not require owner to bring dog to a MSP clinic	Free-roaming dogs and/or owner may not be at home when the vaccinators arrive
	Aggressive or overly shy dogs can be more easily reached	Parenteral rabies vaccine, requires dog restraint with potential risk of bites Unlikely to reach community owned and stray dogs
Oral rabies vaccination (ORV)§	Baits are handed to a dog or placed in the community for dogs to ingest	Technology still under development, limited field data on implementation
	Do not require dog restraint May more readily reach aggressive and shy dogs May reach free roaming†, community owned and stray dogs	Vaccines are more costly than parental vaccines Oral rabies vaccines are based on live replication competent viruses

Notes: The three vaccination strategies we assessed, combined the methods defined in the table: (1) MSP, (2) MSP + CVR, DDV + ORV. * Parenteral rabies vaccine. Parenteral vaccination is the standard vaccine type, globally, with many different vaccines being produced and approved by the World Organization for Animal Health (OIE) for use in dogs. Parenteral vaccines are produced by inactivating rabies virus constructs [37].
† Free roaming dogs constitute the highest rabies-risk population and largest contributors of enzootic rabies transmission.
‡ CVR should only be conducted under conditions which utilize humane methods and equipment that ensure the safety of both the animal and the vaccinator.
§Several ORV baits have been approved for use in wildlife in the United States and internationally, and have shown to be a successful compliment to parenteral vaccination programs in regards to domesticated animals [16–18]. Oral vaccines have also been used to vaccinate free-roaming dogs in various settings [19,20].

control, mass dog vaccination campaigns in Haiti have not yet reached the frequency and intensity required for rabies elimination [32,35].

Vaccination campaigns in Haiti frequently use a MSP strategy, but national coverage rates have never reached a 50% coverage and rabies cases continue to occur. To increase dog vaccination coverage, several community awareness events are conducted during the week before the vaccination campaign. On the day of the campaign, vaccinators set up fixed vaccination stations to which community members bring their dogs. Limited DDV may also occur if time allows and if not impeded by cultural norms. A recent evaluation of the 2015 campaign estimated that about 36%, 61%, and 50% of free-roaming dogs were vaccinated in urban, semi-urban, and rural communities, respectively [36]. The study found approximately 83% of Haitian dogs are allowed to roam freely in the community for at least part of their day, and up to 44% of dogs may be community owned.[1] Free roaming and community owned dogs are typically harder to reach for rabies vaccination through MSP, which require a person to physically bring the dog to the vaccination site [35]. These findings, and the fact that despite several years of animal rabies vaccination campaigns using MSP there has been no noticeable decrease in animal rabies cases [27], suggest that MSP vaccination alone may not be sufficient to achieve herd immunity for rabies control. In August 2016 a rabies outbreak was detected through Haiti's national rabies surveillance program, with seven dog rabies cases confirmed in the commune of Croix-des-Bouquet. In response, the Haitian government, CDC, and other organizations conducted an emergency vaccination program using three dog vaccination strategies in addition to MSP: DDV, CVR, and a modified live ORV [37].

Here we report the results from an evaluation of costs, effectiveness, and cost-effectiveness outcomes for three alternative combinations of dog vaccination strategies in urban and *peri*-urban sections of Croix-des-Bouquet commune, West Department, Haiti, in 2016, during a dog rabies outbreak. We present results as cost-per-dog-vaccinated, using a governmental perspective. Results are intended to help inform policy-makers about ways to improve dog vaccination coverage under budget constraints, and support the planning of more effective dog vaccination campaigns, with the ultimate goal of controlling and potentially eliminating dog-mediated human rabies deaths [23].

2. Materials and methods

2.1. Study area

The outbreak area of Croix-des-Bouquets was divided into five zones of approximately equivalent human population size (~20,000 people per zone), based on data from the Institut Haitien de Statistique et d'Informatique (IHSI) [38]. Zones were classified as *peri*-urban (human population density < 300 per km^2) or urban (>300 people per km^2). Each zone was further divided into three evaluation sites of equivalent human population (~6500 people). Using an estimated human-to-dog ratio of 10, each planning vaccination site had an estimated 650 dogs. We established a vaccination goal of at least 450 dogs per site, to achieve OIE/WHO's recommended goal of vaccinating $\geq$ 70% of the dog population [1,10,11]. The vaccination method was assigned randomly to three evaluation sites within each of the five zones (Fig. 1), and the campaign was conducted in August 2016. Further details about the campaign design and implementation are shown in the supplementary material.

2.2. Vaccination strategies

Table 1 describes each vaccination strategy. Vaccination was scheduled for working two days in each strategy, at the five vaccination sites. Sensitization of the community was conducted in the week prior to vaccination at all sites. All vaccination teams used a standardized paper form to track the number of dogs vaccinated per hour, hours worked per day, and other logistical data (supplementary material). We assigned a color to each vaccination strategy, and all vaccinated dogs received a temporary plastic collar and wax mark representing the strategy by which they were vaccinated [36]. Vaccination teams operated for two days in each site. The teams worked for up to six hours daily to vaccinate dogs at each evaluation site and were paid a fixed daily rate, even if there were no more dogs to be vaccinated at the assigned site. On days three and four (the two days after the vaccination site was completed) a sight-resight evaluation was conducted to determine the dog population, demography, and free-roaming dog vaccination coverage. The three vaccination strategies were:

(1) MSP. Four vaccinators with at least two years of experience and four assistants carried out routine parenteral vaccination. Vaccinators used a banner and megaphones to announce their presence, and used yellow collars and yellow wax to mark vaccinated dogs. Vaccinators remained at one location for one to two hours and moved another central location when community members were no longer bringing their dogs to vaccinate (Fig. 2A). MSP sites were pre-selected and exact locations for the MSP clinic were chosen by staff and local leaders on the morning of the campaign.

(2) MSP plus CVR. In addition to the MSP strategy, three teams of two trained health personnel (vaccinator and assistant), conducted CVR of free-roaming dogs. CVR vaccinators were members of Haiti's Animal Rabies Surveillance Program, which routinely captures suspected rabid dogs (Fig. 2B). Tools used included pole nets, control poles, Kevlar gloves, in addition to the supplies provided to MSP teams. MSP teams used blue collars and blue wax to identify vaccinated dogs and CVR teams used pink collars and pink wax to identify vaccinated dogs. CVR teams walked through pre-defined sites and announced their presence through megaphones as they walked through the community.

(3) DDV plus ORV. Five teams of two trained personnel (vaccinator and assistant), conducted DDV/ORV. These sites included no MSP. Vaccination teams walked through pre-defined sites and announced their presence through megaphones and by approaching domiciles. When possible, dogs were vaccinated parenterally; aggressive, scared, or dogs with no identifiable owner, were offered an ORV bait. Dogs were observed until they ate the ORV bait or lost interest in it. Every attempt was made to recover the foil/plastic vaccine capsule. Parenterally vaccinated dogs received white collars and white wax; dogs vaccinated by ORV received purple collars and purple wax or temporary purple paint sprayed from a 20 ml syringe, depending on how approachable the dog was. Almost no dogs with ORV received a collar, and it was not always possible to mark ORV dogs. We used boiled pig intestines as coating for the oral vaccines [37] (Fig. 2C).

2.3. Dog population

Three dog population categories were defined 1) owned, confined 2) owned, sometimes free-roaming 3) community owned, always free-roaming. We estimated the dog population for each site by adding the estimated number of owned, confined dogs from household surveys to our estimate of free-roaming dogs. To derive

[1] Community owned dogs typically receive food and other resources from multiple families. Community owned dogs are at a higher risk for rabies because they spend more time on the streets interacting with other dogs, and because there are typically few people who feel responsible for the community dogs' veterinary care.

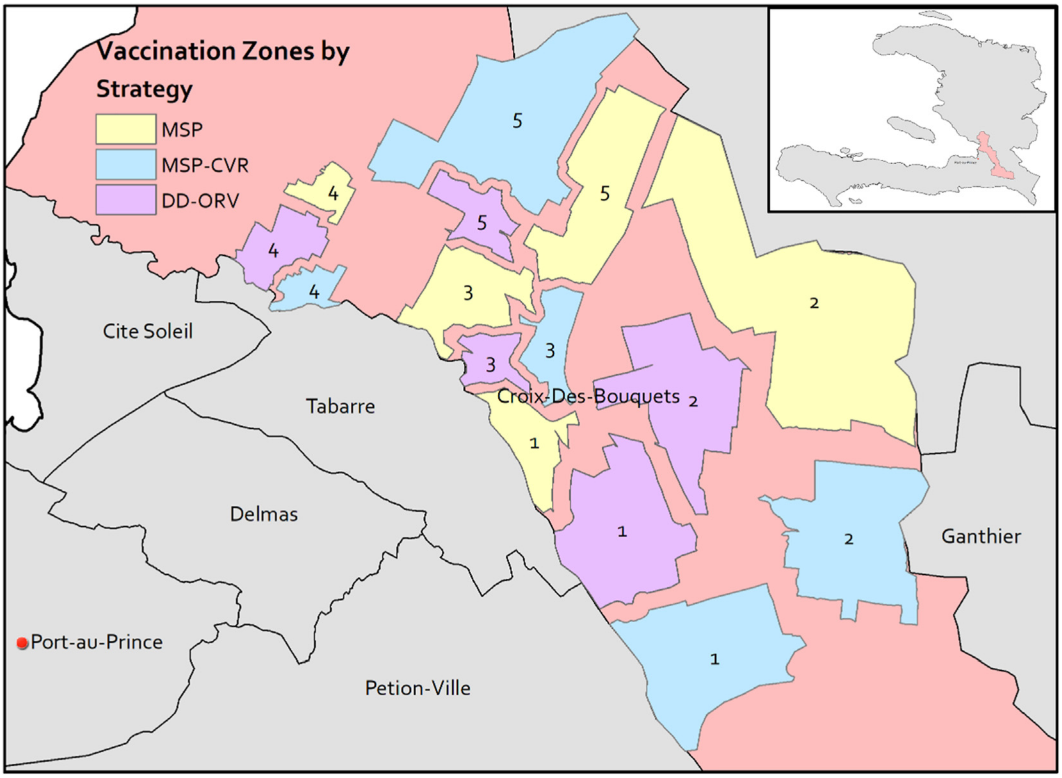

Fig. 1. Location of the dog rabies vaccination intervention and study design for the evaluation of alternative dog vaccination strategies to improve dog population coverage, Croix-des-Bouquets, West Department, Haiti 2016. **Notes.** MSP: mobile static point. CVR: capture, vaccinate, release. DDV: door to door vaccination. ORV: oral rabies vaccination. Study area in the West Department, Haiti. The focal outbreak area of Croix-des-Bouquets was divided into five zones of approximately equivalent human population size (~20,000 people per zone). One DDV-ORV site did not receive ORV and was excluded from analyses. Each of the five zones was divided into three sites, and we randomly assigned one vaccination strategy to each of these sites.

Fig. 2. Rabies vaccination strategies. **A.** In the mobile static point strategy, community members bring dogs to a centralized location where vaccinators have established a temporary vaccination clinic. **B.** A trained rabies control officer captures a free-roaming dog in the capture-vaccinate-release strategy, which requires dog restraint with potential risk of bites. **C.** Boiled pig intestines were used as coating for the oral vaccines, after piloting other alternatives. Dogs were observed until they ate the ORV bait or lost interest in it. Aggressive, scared, or dogs with no identifiable owner, were offered an ORV bait when parenteral vaccination was not possible.

the number of free roaming dogs, we used the largest of two estimates: the number of free-roaming dogs as determined by household surveys or as determined by field survey teams through sight-resight (SRS) count surveys using the Lincoln-Petersen estimator [36,39]. Because almost all dogs had received temporary laminated collars, wax marks, and/or spray paint (ORV) at the time of rabies vaccination, we could also estimate vaccination coverage based on the SRS survey. Detailed methods and results have been described elsewhere [36]. We used Fisher's exact mid-p test to obtain 95% confidence intervals (CI) for each dog ownership category.

2.4. Vaccination coverage and efficiency

We estimated dog vaccination coverage at each site for the free-roaming and total dog populations, by vaccination strategy. Free-roaming vaccination coverage was calculated directly from SRS data. All dogs received temporary laminated collars, wax marks, and/or spray paint at the time of rabies vaccination, and we used a standardized data collection tool to estimate the proportion of free roaming dogs with evidence of vaccination [36]. We evaluated vaccination efficiency as the number of dogs vaccinated per staff member per day. We used Fisher's exact mid-p to obtain the 95% CI; rates were compared by site, strategy, and urban and *peri*-urban communities.

2.5. Productivity of vaccinators

We defined vaccination productivity in two ways: (A) dogs vaccinated per hour and (B) dogs vaccinated per vaccinator per hour during the vaccination campaign. The relative vaccination productivity of each vaccination strategy varied throughout the day, with marginal productivity declining for most strategies (i.e., there are diminishing marginal returns over the hours). For example, for MSP vaccination, many owned dogs are brought for vaccination within the first several hours of vaccination clinic operations, but available dogs wane as time goes by. We thus tracked the number of vaccinated dogs per hour for each vaccination strategy.

To provide a measure of the productivity of each vaccination strategy, we used ordinary least square (OLS) regressions with robust standard errors. We used the two definitions of productivity as our dependent variables. We used vaccination hours (range: 1–5 h) and vaccination strategy (MSP; MSP + CVR, and DDV

Table 2
Cost data for the evaluation of alternative strategies for mass dog vaccination, West Department, Haiti 2016.

Item	Unit value (2016 US$)	Source
Variable costs of dog vaccination		
Vaccines		
Vaccination certificates	0.10	Administrative data
Tag: dog collar	0.09	Administrative data
Tag: wax ID mark	0.05	Administrative data
Parenteral vaccination$^{\chi}$	0.58	
Vaccine (parenteral vaccine) per dog	0.29	Boehringer-Ingleheim [37]
Material costs (needles, swabs, etc.)	0.04	
Wasted / spoiled vaccines	2%	
Oral vaccination$^{\chi}$ǂ	2.55	Wallace et al. [35]
Vaccine (oral vaccine)	2.00	
Material costs (bait, etc.) per vaccine	0.20	
Wasted / spoiled vaccines‡	5%	
Fixed costs of dog vaccination (per site)*		
Equipment/ supplies		
Cold-boxes	40.00	Administrative data
Protective clothing / equipment (site)	90.00	Administrative data
Squirt gun	50.00	Administrative data
Ice packs	2.50	Administrative data
Hazardous waste management	4.00	Administrative data
Animal capture / restraint equipment¶	250.00	Administrative data
Human resources (daily)		
Supervisor	25.00	Administrative data
Driver	6.00	Administrative data
Central point vaccinator †	9.00	Administrative data
Door-to-door vaccinator †	9.00	Administrative data
Capture-vaccinate-release vaccinator †	9.00	Administrative data
Lunch	2.00	Administrative data
Training	30.00	Administrative data
Transportation		
Vehicles (3 trucks for all sites) §	116.00	www.kayak.com
Gas (4 tanks per truck)	75.00	Administrative data
Awareness campaign		
Truck with speakers	75.00	Administrative data
Driver	25.00	Administrative data
Pamphlets / posters	1.00	Administrative data

Notes: ID: identifier.
‡ Estimated from fieldwork.
χ The unit costs for the parenteral and oral vaccination include the costs of the vaccination certificate, and tags (dog collar and wax ID). Parenteral vaccines were donated, so we used a reference cost.
ǂ Based on an estimate not on fixed prices.
* Fixed costs were apportioned to daily fixed costs on the basis of a potential three-week campaign (15 work-days).
¶Includes butterfly and throw nets, control supplies. We assumed that they would last for two years. Animal capture and restraint equipment was required for all three campaigns strategies, although each CVR team required one equipment kit
† Central point vaccination was made of 4 groups of 2 persons each (one walking around with a megaphone). Capture-vaccinate-release consisted in three groups with three members each: a vaccinator, a helper, and a data collector (excluded from costing estimates). Door to door had 5 teams of three members, a vaccinator, a helper, and a data collector (excluded from cost estimates).
§The trucks used were from MARNDR; to estimate daily costs per truck (including depreciation, maintenance, and insurance) we used the daily price for a truck rental in the study area.

+ ORV) as independent variables and added interaction terms between vaccination strategy and time (supplementary material).

2.6. Cost data

We estimated the costs of each vaccination strategy using a micro-costing approach, based on data from research budgets or field expenditure reports. The major items included costs per vaccines by type, shipping, storage, cold-chain materials, and vaccine transport, logistic support, personnel involved in each vaccination strategy (including personnel qualifications, e.g., supervisors, vaccinators, and drivers), transport and per diem expenses of vaccination personnel, security equipment, employee pre-exposure vaccinations, materials and supplies, hazardous waste management, awareness/social mobilization campaigns, time required to vaccinate each dog, marks/tags for vaccinated dogs, administration, and staff training. All costs are shown in 2016 US dollars. Table 2 shows a summary of cost data. We excluded the costs associated with data gathering and evaluation, including collection of blood samples, as these costs would not be typically included in a mass dog vaccination program.

We assumed that fixed costs of the vaccination campaign (i.e., costs that do not change as a function of the number of vaccinations) were equally distributed between the three vaccination strategies; daily fixed costs were apportioned on the basis of the duration of the typical vaccination campaign of three weeks. Animal capture and restraint equipment were required for all three campaigns strategies. MSP and DDV + ORV had one equipment kit for the entire site; in contrast, each CVR team required one kit. These differences were factored into the costs of each strategy.

2.7. Outcomes

We compared the three alternative dog vaccination strategies in a rabies endemic setting based on three complementary criteria. First, we estimated the cost-effectiveness of each strategy as the cost per dog vaccinated. Second, we compared the vaccination coverage of each vaccination strategy for free-roaming and total dog population. Third, we estimated the marginal productivity by hour for each dog vaccination strategy (i.e., vaccination coverage achieved per hour of operation). Based on the main results from the analysis, we suggest vaccination strategies under specific conditions, including target population (free-roaming dogs and total dog population), and by type of community (*peri*-urban and urban). Our goal was to achieve 70% vaccination coverage [1,10,11,40].

2.8. Ethics review

Sample collection activities were covered under CDC IACUC protocol #2498framulx-a5. All participants, including those taking blood samples, were members of CVM and MARNDR, and vaccination and surveillance activities were considered routine job duties. This evaluation was approved by the CDC's Human Research Office (CDC tracking number 062316RW). Since our aim was to evaluate the implementation of a public health intervention (mass dog vaccination), it was considered non-research public health program evaluation per CDC guidance.

3. Results

3.1. Intervention sites and vaccination coverage

Peri-urban sites ranged in size from 48 km^2 to 108 km^2 and urban sites ranged in size from 20.7 km^2 to 1.4 km^2. The average across MSP, MSP + CVR, DDV + ORV sites was 76 km^2, 128 km^2, and 75 km^2, respectively. Population densities across *peri*-urban sites ranged from 60 to 135 people/km^2 and from 314 to 4643 people/ km^2 in urban sites. MSP vaccination sites had the largest estimated dog population (n = 5687), followed by MSP + CVR sites (n = 5331). DDV + ORV sites had the smallest estimated dog population (n = 3474) (Table 3). The average proportion of confined dogs per vaccination site, as determined by combining survey and SRS, was 32% (n = 1820), 33% (n = 1759), and 41% (n = 1424) for MSP, MSP + CVR, and DDV + ORV, respectively. The remaining dogs were classified as free roaming, either individually or community-owned. Overall, urban sites had more owned-confined dogs than *peri*-urban vaccination sites.

A total of 7065 dogs (60.6% of the estimated total dog population, 95% CI: 55.3%-67.1%) were vaccinated against rabies during the vaccination campaign (Table 3). Overall, free-roaming dog vaccination coverage, determined by post-vaccination field surveys, was estimated at 52% (47–56) for MSP, 53% (47–60) for DDV + ORV, and 65% (61–69) for MSP + CVR (differences with MSP and MSP + CVR $p < 0.01$). The intervention showed the lowest free-

Table 3
Total vaccination coverage by dog vaccination strategy and evaluation method used.

	Dogs vaccinated	Estimated dog population	Estimated vaccinated coverage	95% Confidence interval
Free-roaming dog population				
MSP	229	443	51.7%	(47.1%–56.3%)
Peri-urban	86	143	60.1%	(52.0%–67.8%)
Urban	143	300	47.7%	(42.1%–53.3%)
MSP + CVR	326	502	64.9%	(60.7%–69.0%)
Peri-urban	112	172	65.1%	(57.7%–71.8%)
Urban	214	330	64.8%	(60.0%–69.8%)
DDV + ORV	119	224	53.1%	(46.6%–59.6%)
Peri-urban	90	139	64.7%	(56.5%–72.2%)
Urban	29	85	34.0%	(24.9%–44.7%)
Total dog population				
MSP	1854	5687	32.6%	(26.2%–43.1%)
Peri-urban	718	2337	30.7%	(25.0%–39.8%)
Urban	1136	3350	33.9%	(27.1%–45.4%)
MSP + CVR	2590	5332	48.6%	(40.3%–61.1%)
Peri-urban	856	2220	38.6%	(33.4%–45.7%)
Urban	1734	3112	55.7%	(45.0%–73.3%)
DDV + ORV	3300	4213	78.3%	(77.0%–80.0%)
Peri-urban	1451	2277	63.7%	(61.7%–65.7%)
Urban	1849	1936	95.5%	(94.4%–96.4%)

Notes. MSP: mobile static point. CVR: capture, vaccinate, release. DDV: door to door vaccination. ORV: oral rabies vaccination. The estimated vaccine coverage for the free-roaming dog population was estimated using a sight-resight survey count survey, based on the Lincoln-Petersen estimator [36,39].

roaming dog vaccination coverage for DDV + ORV in urban sites (34%, 95%CI: 25–45), and the highest free-roaming dog vaccination coverage for *peri*-urban communities with MSP + CVR (65%, 95%CI: 58–72) (Table 3). Total dog vaccination coverage was 33% (95%CI: 26–43) for MSP, 49% (95%CI: 40–61) for MSP + CVR and 78% (95% CI: 77–80) for DDV + ORV ($p < 0.001$). Vaccination coverage of free roaming dogs in individual sites ranged from 39% (DDV + ORV) to 88% (MSP + CVR), and for all dogs in individual sites ranged from 31% (MSP) to 94% (DDV + ORV) (Fig. 3). Results for DDV + ORV need to be interpreted with caution, however, because logistical challenges in the implementation of the campaign resulted in some teams running out of oral baits during parts of the day (mostly during the last 2hr. of vaccination). We completely ran out of ORV baits for one DDV + ORV team on the last day of campaign. Considering that caveat, overall, Fig. 3 and Table 3 suggest MSP + CVR reached the largest free-roaming dog coverage in *peri*-urban and urban sites, and DDV + ORV strategy was the most successful strategy when considering total dog vaccination coverage (Fig. 3).

A total of 590 ORV baits were procured for this evaluation, limiting their use to about 15 baits per team per day. On average, teams used two ORV baits/hour. A total of 1999 dogs were parenterally vaccinated by DDV + ORV teams; an additional 590 dogs were vaccinated by ORV, 29.5% increase in the number of vaccinated dogs due to inclusion of ORV. The vaccination strategy included both DDV and ORV; if dogs were aggressive or overly shy, vaccinators used ORV, otherwise, they used a parenteral vaccine. About 2% of the dogs offered a bait did not accept it, either because the dog was not interested or because it was afraid of vaccinators. When analyzing hourly use of ORV, over half of vaccination teams had exhausted the oral vaccine by the fourth hour of daily operation; suggesting the potential impact of ORV may be underestimated.

3.2. Costs to vaccinate a dog by vaccination strategy

Table 4 shows a summary of the overall cost per day and the cost-effectiveness (cost/dog vaccinated) of three alternative strategies. Overall, the least expensive campaign was MSP, with an estimate cost of ~$2039 per day, and the most expensive was DDV + ORV, with a cost of ~$3246 per day. DDV + ORV was the most cost-effective of the three strategies considered, with an estimated cost of $1.97 per dog vaccinated ($2.20 for MSP). The cost per dog vaccinated in *peri*-urban communities was higher than in urban communities for MSP and MSP + CVR, most probably due to the lower density of dog populations. The cost per dog vaccinated in *peri*-urban and urban communities for DDV + ORV was comparable, which reflects the ability to vaccinate dogs that would be otherwise difficult to reach, thereby increasing the total number of dogs reached through vaccination efforts.

3.3. Vaccination productivity and efficiency

We found substantial variation in the average number of dogs vaccinated per staff member per day of campaign operation (vaccinator efficiency). The MSP + CVR was the least efficient strategy, ranging from 12.6 to 20.1 dogs vaccinated per staff member per day. The most efficient strategy was DDV + ORV, which had efficiency rates ranging from 26.6 to 39.0 dogs vaccinated per staff member per day.

We used OLS regressions to provide a systematic way of measuring productivity measured as (A) the number of dogs vaccinated per hour by strategy (strategy productivity) and (B) as the number of dogs vaccinated per vaccinator per hour (vaccinator productivity). We used regression results (supplementary material), to characterize the relation between time and strategy productivity and

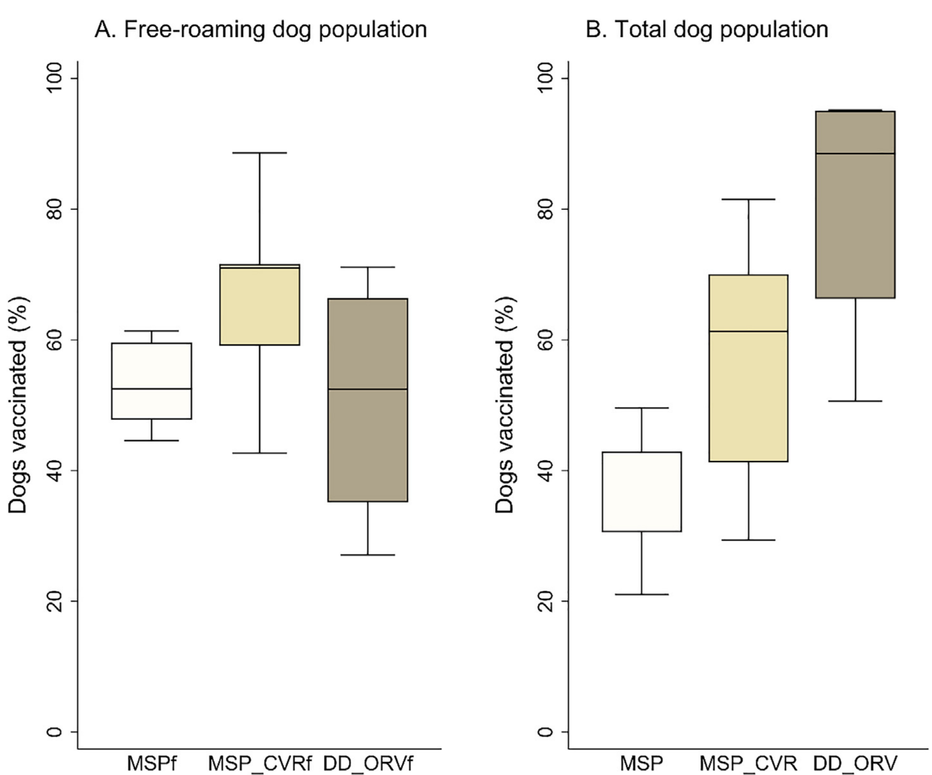

Fig. 3. Variation in the effectiveness of dog vaccination strategies across *peri*-urban and urban study sites in Croix-des-Bouquets, Haiti, 2016. **Notes.** MSP: mobile static point; CVR: capture vaccinate release; DDV: door-to-door vaccination; ORV: oral rabies vaccine. The subscript *f* denotes free-roaming dogs. (A) Distribution in the proportion of free-roaming dog population that was vaccinated across sites by dog vaccination strategy. (B) Distribution of the proportion of the total dog population that was vaccinated across sites by dog vaccination strategy. The figure shows large variations in the effectiveness of dog vaccinations. These results underscore that there is no "one-size-fits-all" approach, even within a department in Haiti.

Table 4
Main daily outcomes of the evaluation of three alternative strategies for mass dog vaccination, West Department, Haiti 2016: (i) Mobile static point vaccination (MSP), (ii) MSP + Capture, vaccinate, and release (CVR), (iii) Door-to-door (DDV) + Oral rabies (ORV).

Vaccination strategy	Urban	Peri-urban	Total
Intervention			
Sites	9	6	15
Average costs of the intervention*			
Shared costs (by sector)			
Awareness campaigns	$360	$240	$600
Mobile Static Point (MSP)			
Vaccines	$655	$414	$1069
Human resources	$910	$607	$1517
Transport	$374	$250	$624
Equipment / supplies	$161	$107	$268
Sub-total costs MSP	$2,460	$1,618	$4078
MSP + Capture, vaccinate, release (CVR)			
Vaccines	$1,000	$494	$1493
Human resources	$1,378	$919	$2297
Transport	$655	$437	$1092
Equipment / supplies	$261	$174	$435
Sub-total costs MSP + CVR	$3,654	$2,263	$5917
Door to Door (DDV) + Oral rabies (ORV)			
Vaccines	$1,587	$1,480	$3067
Human resources	$1,066	$711	$1777
Transport	$468	$312	$780
Equipment / supplies	$161	$107	$268
Sub-total costs DDV + ORV	$3,642	$2,850	$6492
Cost-per dog vaccinated			
Cost per dog vaccinated MSP	$2.17	$2.25	$2.20
Cost per dog vaccinated MSP + CVR	$2.11	$2.64	$2.28
Cost per dog vaccinated DDV + ORV	$1.97	$1.96	$1.97

Notes. * Costs correspond to the average by vaccination strategy of two days of work in each study site. Please note some sums do not exactly add up due to rounding of cents.

vaccinator productivity. Fig. 4 shows predicted results, with 95%CI, for the number of dogs vaccinated/hour, for all strategies combined, MSP, MSP + CVR, and DDV + ORV. Recall that the number of vaccinators in each vaccination strategy was different, so Fig. 4 should be interpreted with caution. Fig. 5 in contrast, shows the rate of vaccinated dogs per hour per vaccinator, for all sites, and for each vaccination strategy. Two results stand out. First, MSP + CVR (Fig. 5, panel C) showed less average productivity, but had a more stable productivity during the day than the other strategies. The larger negative slope of the productivity curve for MSP (Fig. 5, panel B), suggests that the addition of CVR to the MSP strategy helped maintain a more constant productivity rate. Second, DDV + ORV proved to be, on average, the most productive strategy throughout the day (albeit with larger confidence intervals).

We last examined trends in dog vaccination coverage, for each vaccination strategy implemented. Fig. 6 shows estimated coverage rates by hour (i.e., number of dogs vaccinated at hour "t"/total dog population), and trends were estimated using locally weighted scatter plot smoothing (LOWESS). Results suggest that MSP and MSP + CVR, in the conditions that our vaccination program was implemented in Haiti, would not be enough to achieve 70% vaccination or would require additional resources. In contrast, DDV + ORV tended to reach the expected target, most likely because the strategy provides a means to access hard-to-reach, aggressive, or fearful dogs that otherwise would not have been vaccinated.

4. Discussion

We assessed the costs, effectiveness, and cost-effectiveness outcomes for three mass dog vaccination strategies, MSP, MSP + CVR, and DDV + ORV, in urban and *peri*-urban sections of Croix-des-Bouquets (2016). DDV + ORV was the most successful strategy when considering vaccination coverage for all dog population. MSP + CVR was the most effective strategy to reach free-roaming dogs, probably because some teams ran out of baits during parts of the day. The least expensive campaign was MSP, with an estimate cost of about $2039 per day of operation, and the most expensive was DDV + ORV, with a cost of $3246 per day. However, DDV + ORV was the most cost-effective vaccination strategy and MSP did not achieve the desired coverage in any of the sites. We also saw a substantial decrease in dogs vaccinated per vaccinator per hour throughout the day across all strategies. Our results suggest MSP and MSP + CVR may not be enough to achieve the goal of 70% of the dog population vaccinated or would require substantial additional efforts to reach this objective. The goal of dog vaccination programs is to reach a level of herd immunity to cease enzootic transmission of the virus; practical experience has shown this is achieved with ~ 70% vaccination coverage among the susceptible dogs in most settings [1,10,11]. Vaccination coverage for all dogs nearly doubled when DDV was used in lieu of MSP.

Dog population estimation is important for planning and evaluating vaccinations campaigns, but estimation methods are time consuming, costly, and prone to measurement error. Our estimated dog vaccination coverage reflects these limitations showing wide confidence intervals. Estimated dog population always included confined dogs. In theory, confined dogs are not necessarily susceptible to rabies infection, as they may not interact with susceptible dogs and thus could have only a limited or null role in viral transmission. In Haiti community members' interpretations of a "confined dog" may have included dogs that occasionally roam or remain in the yard where community dogs have access to. Field teams suggested that even self-reported confined dogs had some risk of interaction with susceptible free-roaming dogs. Because the share of confined dogs varies between communities, our estimates of dog vaccination coverage from SRS surveys are possibly better indicators of campaign success than estimates of immunity among susceptible dog populations.

When vaccinating a relatively low number of dogs, the fixed costs of a vaccination campaign are relatively high. However, as the number of vaccinated dogs increase, the average cost per dog vaccinated decreases. This fact may partially explain the wide range of costs to vaccinate a dog reported in the literature, particularly those "sweet spot" estimates for vaccinations in the range of 30–50% of the dog population [40]. A large proportion of dog vaccination campaign costs correspond to human resources, mostly vaccination staff [23,31,41–43]. Therefore, increasing the number of dogs vaccinated per day for a team can have a large impact on reducing overall program costs. Campaign costs should consider the end-coverage achieved and the efficiency of the vaccinators conducting the program to better evaluate if the strategy was successful.

When considering efficiency, costs, vaccination coverage, and vaccinators' productivity, no single strategy was clearly favorable in all conditions or across all sites, even within a department in Haiti. Our results for Haiti suggest that in *peri*-urban settings the DDV + ORV method would be the most successful to maximize vaccination coverage levels. In urban settings, a combination of methods may be required; a potentially successful combination of methods may include MSP for several hours, followed by two or more days of DDV + ORV or CVR to ensure free roaming dogs are adequately vaccinated. A study in India [44] described the strategy of vaccination-assessment-move, in which the number and distribution of dog vaccinations is tracked in near-real-time, and decisions on completeness of a vaccination site are based on feedback from field operators and geo-spatial evaluation. This method does not limit the number of days in a vaccination site to an a priori protocol decision; the duration is based on field information. If applied in Haiti, this strategy may improve coverage,

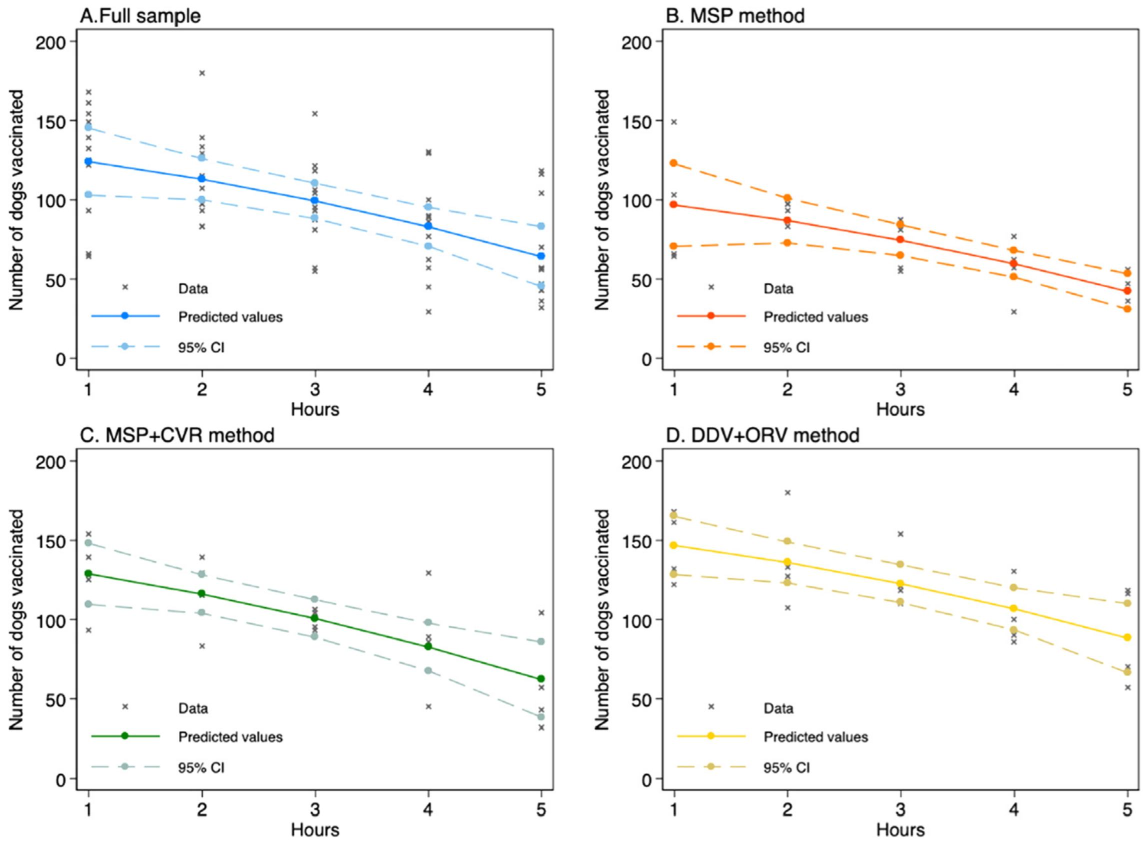

Fig. 4. Predicted results from OLS regressions of the number of dogs vaccinated by hour, for (A) all vaccination strategies combined, (B) mobile static point (MSP), (C), MSP + capture vaccinate release (CVR), and (D) door-to-door vaccination (DDV) and oral rabies vaccine (ORV). **Notes.** Predicted values of the number of dogs vaccinated by hour obtained from OLS regressions (supplementary material, Table S1). Sample size = 60. MSP stands for Mobile Static Point. CVR stands for Capture Vaccinate Release. ORV stands for Oral Rabies Vaccination. DDV stands for Door to Door Vaccination (see Supplementary material for specific coefficients and equations).

particularly for strategies that involve more active vaccination methods (MSP + CVR and DDV + ORV).

In August 2016 a rabies outbreak was detected in Croix-des-Bouquets commune, West Department, through Haiti's national rabies surveillance program [22] after seven dog rabies cases were confirmed in the preceding six months. During the six months following this emergency vaccination program there were no further human rabies cases in the study area, but an additional four dog rabies cases were reported. While rabies cases declined, the campaign did not halt transmission. Synthesis of these results, and reformulation of the national vaccination strategy may help develop more cost-effective approaches to national dog vaccination in Haiti, and increased probability of complying with OIE/WHO dog vaccination guidance.

Of the three vaccination strategies used, DDV + ORV resulted in the lowest costs per dog vaccinated ($1.97). Despite the relatively higher costs of ORV compared to parenteral vaccines, ORV allowed vaccinators to more rapidly vaccinate dogs that were not readily accessible due to aggressive or shy behavior. MSP was a relatively costly vaccination strategy, on average, when considering cost per dog vaccinated ($2.20). MSP operations showed high vaccination productivity during the first two hours of operation; but the marginal productivity of vaccinators decreased substantially during the day, resulting in higher overall costs compared to other strategies. In contrast, hourly productivity for DDV + ORV and MSP + CVR were more uniformly distributed along the day, and DDV + ORV showed consistent high productivity throughout the day (Figs. 4 and 5). MSP typically attracts motivated owners with controllable dogs [13]; when this subpopulation reaches saturation the campaign decreases efficiency.

Many lessons and practices that were successful in the elimination of dog rabies in Latin America and the Caribbean (LAC) [28] may be applicable to Haiti. But conditions in Haiti suggest that novel strategies of rabies control, which require a more skilled workforce, need to be assessed to achieve the goal of zero dog-rabies-mediated human deaths by 2030 [23]. MSP vaccination strategies in Haiti have not resulted in vaccination coverage required for rabies elimination. Considering commonly used indicators of human development, education, economic growth, and health, Haiti is similar to rabies endemic countries in Sub-Saharan Africa. To illustrate, in 2015, Haiti had a sociodemographic index (SDI) [45], an index combining income, health, and education used by the Global Burden of Disease studies, of 0.401, comparable to 0.391 for Sub-Saharan Africa (SSA) and substantially lower than 0.678 for LAC. Human Development Index for Haiti is 0.493, comparable to 0.523 in SSA and much lower than 0.751 for LAC. About 38% of the population has access to electricity in Haiti, compared to 43% in SSA and 98% in LAC [46] (further comparisons in supplementary material). Considering rabies epidemiology, logistical challenges, and resource limitations, lessons learned in Haiti may be more relevant to low-income countries with endemic dog-transmitted human rabies, such as those in SSA, than to countries with sporadic or controlled [47] dog transmitted rabies.

Our evaluation is not without limitations. First, the dog vaccination strategies assessed were implemented in five sections of Croix-des-Bouquets Commune of the West Department, Haiti. We found substantial variability in the effectiveness of vaccination in the evaluation sites, and they may not necessarily be representative of all Haiti or other countries. We partially addressed this limitation by randomly assigning each vaccination strategy to sec-

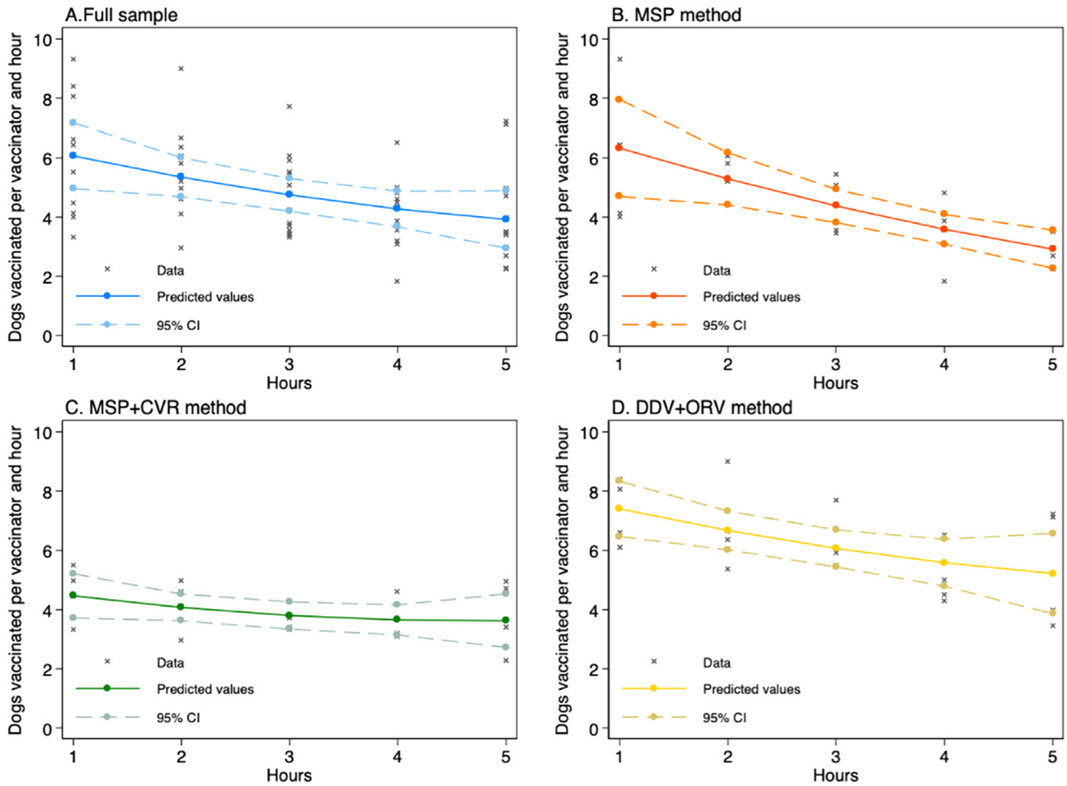

Fig. 5. Predicted results from OLS regressions of the number of dogs vaccinated by vaccinator per hour, for (A) all vaccination strategies combined, (B) mobile static point (MSP), (C), MSP + capture vaccinate release (CVR), and (D) door-to-door vaccination (DDV) and oral rabies vaccine (ORV). **Notes.** Predicted values of the number of dogs vaccinated per vaccinator per hour obtained from OLS regressions (Supplementary material, Table S1). Sample size = 60. MSP stands for Mobile Static Point. CVR stands for Capture Vaccinate Release. ORV stands for Oral Rabies Vaccination. DDV stands for Door to Door Vaccination. (see Supplementary material for specific coefficients and equations).

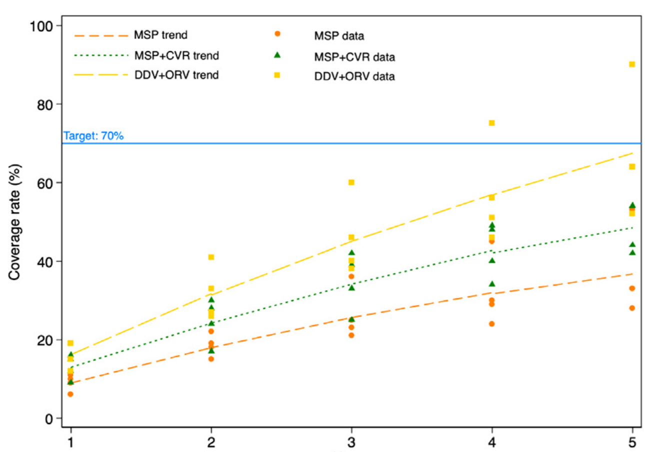

Fig. 6. Estimated coverage rates for dog vaccination by mass vaccination strategy for the total dog population. ***Notes***. Coverage rates are calculated as total number of dogs vaccinated at hour "t" / total dog population. trends were estimated using locally weighted scatterplot smoothing (LOWESS). MSP stands for Mobile Static Point. CVR stands for Capture Vaccinate Release. ORV stands for Oral Rabies Vaccination. DDV stands for Door to Door Vaccination.

tors within municipalities; but effectiveness of dog vaccination varies by a wide range of factors, including distance and topography, dog density, dog owner reception to vaccination, vaccinator experience, trust in government officials, dog ownership practices, public infrastructure [13,41,48,49]; our results need to be interpreted accordingly. Second, the project was implemented in the West Department and carried out by workers from the government of Haiti in collaboration with international partners. Implementing the program at the national level may not necessarily lead to the same results, due to differences in trained vaccinators, public infrastructure, and dog population, among other characteristics. For example, our estimated costs per dog vaccinated were less expensive (in 2016 dollars) than estimates in other rabies-endemic countries, such as Indonesia (~US$2.63) [50] or Chad (~US$2.40) [49], probably because of implementation in a limited geographical area.

Third, there are field challenges that could affect dog vaccination coverage, including dog ownership practices, trust in the government, accessibility, availability of vaccinators, cold chains, and even specific features of the vaccination campaign. For instance, we piloted several alternatives of coating for ORV vaccines, some of which had much lower uptake than boiled pig intestines. We also had a relatively limited procurement of ORV baits, which limited the ability of some vaccination teams to use them when needed; results of the DDV + ORV likely represent the lowest expected coverage by this strategy and could probably have been higher had ample ORV been made available, as found elsewhere [51]. Daily vaccination data also showed that rabies vaccination teams used substantially less ORV baits during the first day of vaccination, probably because of vaccinators' lack of experience with ORV, and during the last three days of vaccination, due to dwindling ORV bait supplies and rationing of ORV allocated to the teams by vaccination program managers. Last, no ORV dog received a collar and the use of paint sprayed from a syringe may have not been as visible as collar and wax, which may have resulted in an underestimate of vaccinated ORV dogs.

5. Conclusion

Our results suggest that strategies beyond MSP can be potentially cost-effective, depending on implementation settings. DDV + ORV seemed to give the best overall vaccination coverage results in our study. Unfortunately, ORV is not currently readily available or a common tool in the design and implementation of dog vaccination campaigns, and may require some extra labor to make baits. Recently, Smith et al. [37] showed that the ORV construct used in this vaccination campaign was highly effective at vaccinating inaccessible dogs in Haiti, with seroconversion rates of 59–78%. Despite the relative high cost of an ORV bait (more than four times the costs of a parenteral vaccination), combining DDV and ORV was the most cost-effective strategy in our comparison, largely due to increased efficiency of the vaccinators. MSP was an effective strategy during the first hours of operation, but marginal productivity of vaccinators declined during the day. In contrast, DDV + ORV maintained high productivity throughout the day. Hourly productivity for MSP + CVR and DDV + ORV were more uniformly distributed. Combining various vaccination strategies is probably required to achieve the goal of 70% vaccination. We hope the results from this study will support the design and implementation of more effective dog vaccination campaigns to achieve the goal of dog-mediated human rabies elimination by 2030 [23,52].

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7. Disclaimer

The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the U.S. Centers for Disease Control and Prevention.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Ceva Biologics, which has been developing an oral rabies virus vaccine, employs Vos. All other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Author contributions

Conceptualization, methods, and design of the study: EU, JC, JB, RW; data acquisition, resources, implementation: MM, ME, VET, JC, RW; data curation, analysis, visualization: EU, KA, JC, YR, RW; article draft, revision for intellectual content, data interpretation: EU, MM, KA, ME, JC, YR, VET, RW; all authors attest they meet the ICMJE criteria for authorship, and have approved the final article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2020.06.006.

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