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USING SIMULATION MODELING TO EVALUATE THE IMPACT OF PROACTIVE TETHERING METHODOLOGIES ON GUINEA WORM INFECTIONS AMONG DOGS IN CHAD

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ABSTRACT

The detection of Guinea worm, or *dracunculiasis*, infections in animals, particularly dogs in Chad, has created challenges for related eradication efforts globally. Proactive tethering is a recent intervention employed to contain dogs and minimize potential exposure to water sources. Approximately 84% of 40,962 eligible dogs were reportedly tethered in Chad during 2023. However, household adherence to tethering intervention guidelines is not always uniform or ideal, with some dogs released from tethering at night and others tethered only intermittently. We adapt an agent-based simulation model to analyze various proactive tethering scenarios. Selecting dogs for tethering randomly each day results in up to 7 times fewer infections over time than tethering a fixed selection of dogs. Releasing dogs from tethering for part of the day results in up to 25 times more infections compared to full-day tethering. Understanding the impacts of proactive tethering practices can inform implementation strategies for interventions.

1 INTRODUCTION

The campaign to eradicate Guinea worm disease, or dracunculiasis, has made substantial progress since 1986 (The Carter Center 2024). Led by The Carter Center, in close collaboration with global ministries of health, the U.S. Centers for Disease Control and Prevention (CDC), the World Health Organization (WHO) and others, the campaign has seen a reduction from an estimated 3.5 million human cases annually in 1986 across 21 countries in Africa and Asia to only 14 human cases in 2023, a reduction of 99.99%. However, the disease also infects animals; since the detection of GW infections in dogs in 2012 and other domesticated and wild animals in subsequent years, animal infections have created challenges, inhibiting eradication and renewing risks to the human population. With recent updates to certification guidelines, Guinea worm eradication cannot be certified until the disease has been eliminated in both humans and non-human animal hosts (World Health Organization 2024).

Guinea worm (GW) is contracted when a human or animal consumes water containing freshwater copepods (microscopic crustaceans) that are carrying third-stage GW larvae or eats raw or undercooked aquatic paratenic or transport hosts (e.g., frogs, fish) with infective larvae (The Carter Center 2024). Approximately 10 to 14 months after infection with third-stage GW larvae, a gravid female worm(s) emerges from the infected host's skin, usually on a lower extremity (Eberhard et al. 2014). Submerging the affected body site in water can provide relief for the associated pain. Tens of thousands of first-stage GW larvae can be released from a single gravid female worm, and if the worm is submerged in water, these larvae can contaminate the water and may be ingested by copepods, thereby continuing the pathogen's life cycle (World Health Organization 2022).

Since there is currently no vaccine or treatment for humans or animals infected with GW (World Health Organization 2022), non-pharmaceutical interventions are promoted. Filtering drinking water and educating people on Guinea worm has helped to reduce infections in humans and animals (The Carter Center 2024), along with treating key water sources with Abate® larvicide (organophosophate larvicide temephos (Abate larvicide, BASF, or just "Abate")) to control copepod populations, burying of aquatic animal waste, distributing cash rewards for reporting Guinea worm infections, tethering infected dogs and cats with signs of GW, and proactive tethering where households tether dogs and cats without known GW infections.

The country of Chad has the highest number of dog infections in the world (407 across 277 villages in 2023), although the value decreased 22% from the previous year. The recent progress has been made due to the community-based interventions, especially increased tethering of animals. Chad's Guinea Worm Eradication Program (GWEP) reported that 53% of villages with at least one animal infection during 2022-2023 practiced proactive tethering in 2023. Additionally, approximately 84% of 40,962 eligible dogs were reportedly tethered in 2023 at least some of the time (WHO Collaborating Center for Dracunculiasis Eradication 2024). However, community adherence to tethering intervention guidelines is not always uniform or ideal. Field teams in Chad report that animals are often released from tethers at night and that some animals are tethered only intermittently. Because of the protracted prepatent period of GW, the impact of interventions will not be known until the following year. Understanding how variance in proactive tethering practices can impact future GW infections is important for evaluating the impact of the intervention and informing education interventions.

In this study, we investigate various potential proactive tethering scenarios to determine the long-term impacts on dog infections over time. Using an agent-based simulation model, we consider proactive tethering practices as well as Abate® water treatments and tethering of dogs with emerging worms, and we forecast dog infections over multiple years. We quantify the effectiveness of proactive tethering practices, which vary by dog selection and tethering time each day, to inform priorities on how best to implement proactive tethering to reduce dog infections.

2 METHODS

We adapted the agent-based simulation for modeling dog infections in Chad that was developed by Perini et al. (2020) and revised for multiple water sources and for hypothetical diagnostics testing by Wang et al. (2023) and Smalley et al. (2024), respectively. Previous works considered limited scenarios with tethering of animals (e.g., only for animals with emerging worms). The current work is motivated by recent interventions with proactive tethering and field findings showing scale of interventions achieved in practice (WHO Collaborating Center for Dracunculiasis Eradication 2024).

From the Chad Guinea Worm Eradication Program, we obtained data that indicate the number of dogs exuding worms and the number of worms exuded by dogs during 2016-2022, reported by village and month. In our analysis, we considered villages in districts along the Chari River, which represent 93.3% of all dog infections in Chad for 2016-2022. Districts are grouped into clusters which we refer to as "West", "Central" and "East", indicating the position along the river (see Figure 1 showing the number of dogs with emerging worms). The simulation models dogs, worms, and water sources (1 per cluster) and simulates daily interactions and transmissions between dogs and water sources, considering the life cycle of GW.

The simulation tracks worms and larval cohorts released into the water sources (Perini et al. 2020; Wang et al. 2023; Smalley et al. 2024). GW larvae densities in water sources are impacted by treatments of the water sources with Abate® which is used to kill copepods which carry the Guinea worm larvae. Chad experiences a dry season and a rainy season which impact the water levels and quantities of water sources. We assume three water sources, with each water source primarily serving one cluster. In prior research, we have modeled one water source (Perini et al. 2020) and three water sources (Wang et al. 2023), with 10-40% of dogs having access to water sources serving other clusters during the dry season.

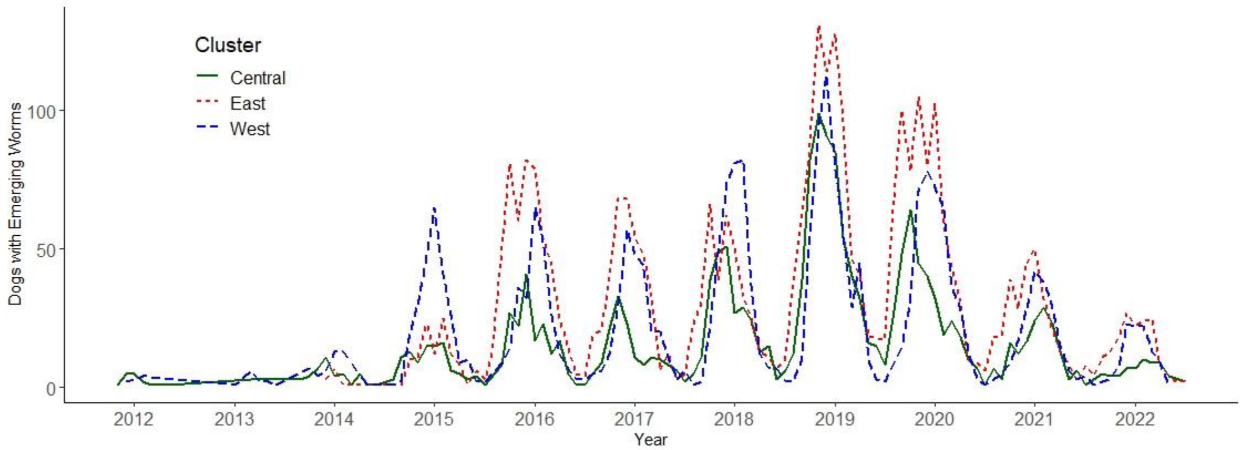


Figure 1: Reported dogs with emerging worms from 2012-2022 by cluster.

Infectivity parameters incorporated in the simulation were developed by Perini et al. (2020) and Wang et al. (2023). Perini et al. (2020) developed environmental factors to account for seasonality in transmission, e.g., driven by rainfall and temperature which affect GW densities. Other infectivity parameters and dog populations are distinct for each cluster. Parameter values are reported in Table 1. The basic infectivity of a water source given n infectious Guinea worm larvae in the water is calculated with equation (1), using the sigmoidal function (2). F_L, F_U, C and D represent the minimum and maximum rate of infection, the curvature, and the inflection point of the infectivity function, respectively (Perini et al. 2020). Incorporating the environmental factors (w_m for month m) and Abate® impact (a), the final infectivity function is given by equation (3).

$$F(n) = [f(n) - f(0)](F_U - F_L) + F_L \tag{1}$$

$$f(n) = \frac{1}{1+e^{-C(n-D)}} \tag{2}$$

$$F_{inf}(n, m) = w_m \cdot (1 - a) \cdot F(n) \tag{3}$$

Table 1: Parameters for calculation of water infectivity.

	Description	***Region*** West	Central	East
F_L	Minimum rate of infection	3.4e-04	1.55e-04	1.53e-04
F_U	Maximum rate of infection	4.265e-03	3.983e-03	2.472e-03
D	Inflection point	78	88	125
C	Curvature	0.0668	0.1210	0.1661
w_m	Environmental factor in month m: [0.0981, 0.2481, 0.2069, 0.9669, 0.9984, 1.00, 0.4977, 0.5968, 0.3446, 0.1808, 0.2520, 0.1018]			
n	Number of infectious guinea worms in the water source (worm burden)			
a	Abate level			

The simulation tracks dogs including tethering status and infection status (number of worms and exuding days per worm), worms (including exuding day per worm and larvae mature day and death day for exuded worms), and the number of GW larvae in the water sources. In the simulation, infected dogs exude a number of worms based on the worms per dog distribution, and each worm is assigned a day to emerge D_e, represented by equation (4), where d=current day, L and U represent the lower and upper bound of the prepatent period (i.e., 10-14 months * 30 days per month), and r represents a random value between 0 and 1. For each day d in the simulation, the number of infective L3 larvae in copepods living in the water source equals the previous number of L3 larvae, subtracting the L3 larvae that die on day d (GW larvae survive in water for up to 30 days), and adding L3 larvae reaching maturity on day d (10-15 days to maturity if consumed by copepods).

$$D_e = \lceil d + L + (U - L) * r \rceil \tag{4}$$

Each day, a random sample of GW larvae of size K in the water source is killed when Abate® is used, where K is a random number from a binomial distribution, with n equal to the number of Guinea worm larvae in the water and probability p equal to the Abate® coverage. An untethered dog is infected on a given day if the infectivity of the water on that day is greater than or equal to a random number r between 0 and 1; r is regenerated at each use.

We define parameters which allow some dogs to travel to other clusters during the dry season when water sources are less abundant (Wang et al. 2023; Smalley et al. 2024) based on an ecological study of GW infection in dogs (McDonald et al. 2020). The research found that a dog's mean range of travel during the dry season in Chad is 4.4km^2, and 80% of dogs visit water sources (e.g., ponds) within close proximity to the dog owner's home (i.e., 100 meters) (McDonald et al. 2020). Our travel assumptions are summarized below.

- From the west cluster, 60% use the west water source exclusively while 40% also visit the central water source with 20% probability.
- From the central cluster, 80% use the central water source exclusively while 40% may also visit the west water source with 20% probability and 10% may visit the east water source with 20% probability.
- From the east cluster, 90% of dogs use the east water source exclusively, while 10% of dogs may also visit the central water source with 20% probability.

The proactive tethering scenarios we considered are reported in Table 2. Scenarios vary in the following ways:

- Daily tethering time: either tether during the entire day or only half of the day.
- Dog selection: randomly select dogs for proactive tethering either at the start of the simulation (then fixed throughout) or repeat the random selection each day, week, month, or quarter. This variation can highlight the potential implications if some households decide not to tether dogs at all (i.e., fixed selection for whole simulation) or if an intervention is implemented everywhere but imperfectly. The fixed case with full day tethering provides a baseline for understanding the impact of completely removing access to community water sources for a subset of dogs.

Table 2: Scenarios of proactive tethering.

Scenario		Fixed Dog Selection	Random Dog Selection				Daily Tethering	
			Daily (Y=1)	Weekly (Y=7)	Monthly (Y=30)	Quarterly (Y=90)	Full Day	Half Day
0	No proactive tethering	-	-	-	-	-	-	-
1	Randomly choose X% of dogs to tether all day, every day	✓	-	-	-	-	✓	-
2	Randomly choose X% of dogs to tether each day for half the day	✓	-	-	-	-	-	✓
3	Every Y days, randomly choose X% of dogs to tether for the whole day	-	✓	-	-	-	✓	-
4		-	-	✓	-	-	✓	-
5		-	-	-	✓	-	✓	-
6		-	-	-	-	✓	✓	-
7	Every Y days, randomly choose X% of dogs to tether for half the day	-	✓	-	-	-	-	✓
8		-	-	✓	-	-	-	✓
9		-	-	-	✓	-	-	✓
10		-	-	-	-	✓	-	✓

In the simulation, if a scenario is selected that includes proactive tethering for X% of dogs, then a random sample of X% of dogs is selected for proactive tethering (either during the initialization of the simulation or each day, week, month or quarter) and each dog is assigned a day or night proactive tethering probability depending on scenario (probability = 0 or 1); unselected dogs have proactive tethering probability equal to 0. Whether or not a dog is selected for proactive tethering, the model incorporates a probability of tethering when a worm is emerging which we vary between 50-90% (recent reports estimate 70% of dogs with emerging worms were tethered (WHO Collaborating Center for Dracunculiasis Eradication 2022; WHO Collaborating Center for Dracunculiasis Eradication 2023)). If a dog is tethered due to an emerging worm, then the simulation assumes 100% tethering of that dog for 30 days.

Worms in the revised simulation are assigned an emergence day and time of day (day or night). Then, on a given day and time of day, if a dog has an emerging worm and is selected for proactive tethering during that time of day, then we assume that dog will be tethered with 100% probability until the last worm emerges from that dog. Additionally, dogs that are proactively tethered at a specific time will not have contact with the water source(s) (or contract infections from other sources) at that time.

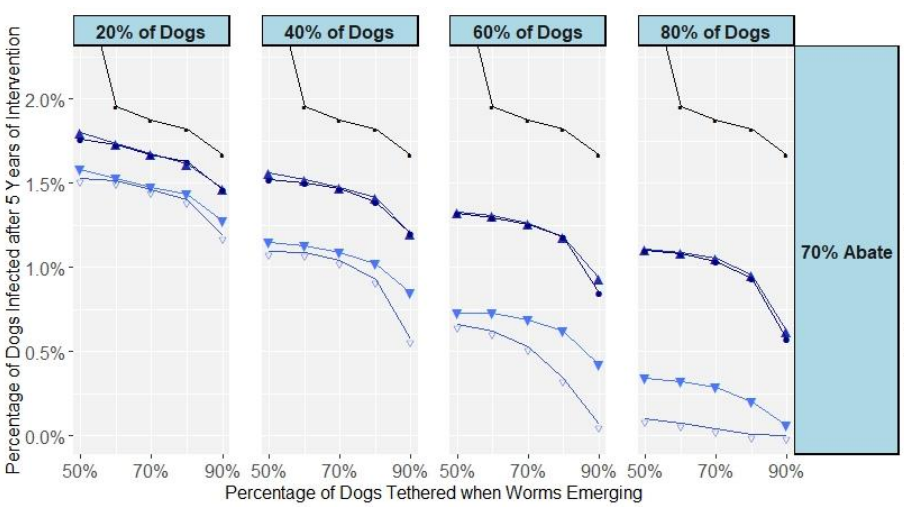
For each scenario, we ran 50 iterations, with the outcome reporting the average number (across iterations) of dog infections per year for each of the next 5 years. We estimate the number of tethering days required to prevent one infection for each scenario. Similar to a study (Oruc et al. 2021) in which the authors estimate the number of homebound days needed to prevent one COVID infection, we calculate the additional dog tethering days needed to prevent an infection under each scenario X relative to Scenario 0 (i.e., no proactive tethering) as follows:

$$g(X) = \frac{\text{Dog tethering days under Scenario X} - \text{Dog tethering days under Scenario 0}}{\text{Total dog infections under Scenario 0} - \text{Total dog infections under Scenario X}}.$$

3 RESULTS

The percentage of dog infections after 5 years for proactive tethering scenarios considering fixed or random daily selection are reported in Figure 2 for an Abate® level of 70% and Figure 3 for Abate® levels of 50-70%. Results are reported by the percentages of dogs selected for proactive tethering, whether at the start of the time horizon (fixed selection) or daily (random selection), dependent on scenario, and by the percentage of dogs tethered when worms are emerging. As expected, tethering all day has better outcomes than tethering for only half of the day, regardless of dog selection method. In many cases, whether a dog is tethered all day or not has a greater impact on infections than how frequently dogs are chosen for proactive tethering. Scenarios with frequent random selection of dogs and full-day tethering result in fewer infections over time compared to fixing dog selection at the start of the time horizon (i.e., Scenario 1).

Realistically, when 70% of infected dogs are tethered when worms are emerging which aligns with recent reports (WHO Collaborating Center for Dracunculiasis Eradication 2022; WHO Collaborating Center for Dracunculiasis Eradication 2023) and 80% of dogs are proactively tethered which is close to the reported percentage for 2023 (WHO Collaborating Center for Dracunculiasis Eradication 2024), Scenarios 1 (fixed selection) and 3 (daily selection) result in 84.4% and 97.9% reductions in dog infections after 5 years of full-day intervention, respectively, when compared to no proactive tethering. Similarly, Scenarios 2 (fixed selection) and 7 (daily selection) each with half-day tethering result in 43.6% and 44.9% reductions in dog infections, respectively, compared to no proactive tethering.



Scenario	S0	S1	S2	S3	S7
	▪	▼	▲	▽	●
Fixed Selection	-	X	X	-	-
Daily Selection	-	-	-	X	X
Full Day Tether	-	X	-	X	-
Half Day Tether	-	-	X	-	X

Figure 2: Percentage of dog infections after 5 years of intervention for proactive tethering scenarios considering fixed or random daily dog selection, tethering time each day, tethering probability when worms are emerging, and percentage of dog population tethered, given 70% Abate® impact.

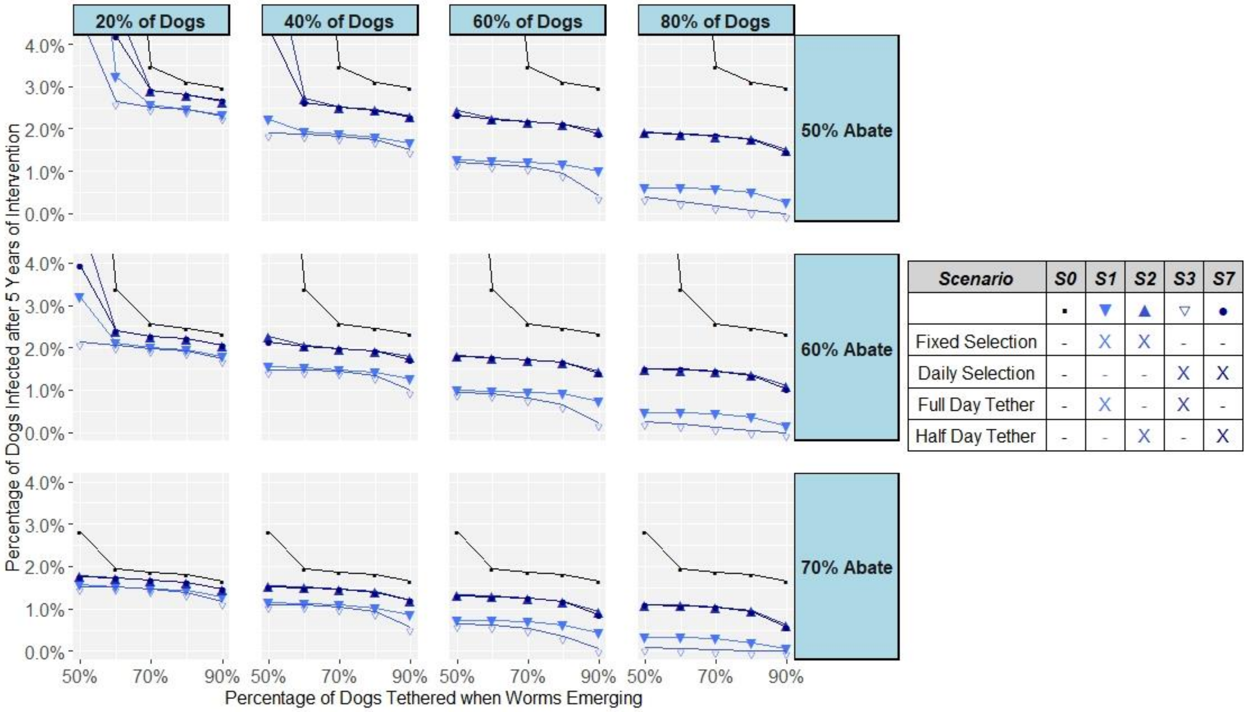


Figure 3: Percentage of dog infections after 5 years of intervention for proactive tethering scenarios considering fixed or random daily dog selection, tethering time each day, Abate® usage, tethering probability when worms are emerging, and percentage of dog population tethered.

Table 3 reports the simulated number of dog infections after 5 years of intervention for proactive tethering scenarios 3 through 10. These scenarios consider random daily, weekly, monthly and quarterly selection of dogs for proactive tethering either for full or half days. Results indicate large differences in infections when considering half vs. full day tethering but only minimal difference in infections between selection time period (i.e., daily, weekly, monthly, or quarterly). Likely due to the protracted prepatent period of GWD, randomly selecting dogs on a daily, weekly, monthly, or quarterly basis results in similar numbers of infections after 5 years, for full and half day tethering, respectively.

The largest numbers of prevented infections due to proactive tethering occur in the scenarios with 80% of dogs proactively tethered for full days and dogs selected for proactive tethering on a weekly, monthly, or quarterly basis. When compared to the base case of no proactive tethering, we see the greatest impact of proactive tethering among scenarios with low tethering probability due to emerging worms and low Abate® levels (Figure 4). If 80% of dogs were proactively tethered, dog infections could be reduced to under 1% of dogs after five years for all intervention levels tested (i.e., Abate® levels from 20%-70% and worm-emerging tethering levels from 50%-90%). Incrementally increasing Abate® levels creates more drastic reductions in infections than incrementally increasing tethering due to emerging worms.

When Abate® usage is low (e.g., 20%), the percentage of dogs tethered due to emerging worms is more impactful on total infections. Comparing other proactive tethering scenarios to this base case, Table 4 reports the additional number of tethered dog days (due to emerging worms and proactive tethering) required to prevent one infection for the proactive tethering scenarios which consider random dog selection. At higher abate levels, tethering dogs has less impact and more dogs need to be tethered to prevent a single infection.

Table 3: Simulated number of dog infections after 5 years of intervention for proactive tethering scenarios considering dog selection, Abate® usage and dog selection percentage, by full day and half day scenarios for random daily, weekly monthly, and quarterly dog selection. 70% probability of tethering when worms are emerging is assumed.

Scenario	Dog Selection Frequency	50% Abate				60% Abate				70% Abate			
		% of Dogs Tethered:				% of Dogs Tethered:				% of Dogs Tethered:			
		20%	40%	60%	80%	20%	40%	60%	80%	20%	40%	60%	80%
Full Day Tethering Scenarios													
3	daily	1112	805	487	82	873	634	362	50	644	459	234	18
4	weekly	1105	804	490	82	876	633	362	41	639	448	237	15
5	monthly	1106	804	487	75	873	630	358	41	642	461	235	15
6	quarterly	1107	804	480	76	872	632	359	40	639	456	227	15
Half Day Tethering Scenarios													
7	daily	1285	1112	959	810	998	875	754	633	734	645	552	455
8	weekly	1283	1102	963	809	994	878	760	630	733	643	552	456
9	monthly	1280	1105	953	806	998	872	748	639	731	645	546	455
10	quarterly	1281	1112	957	806	991	871	755	633	729	644	553	451

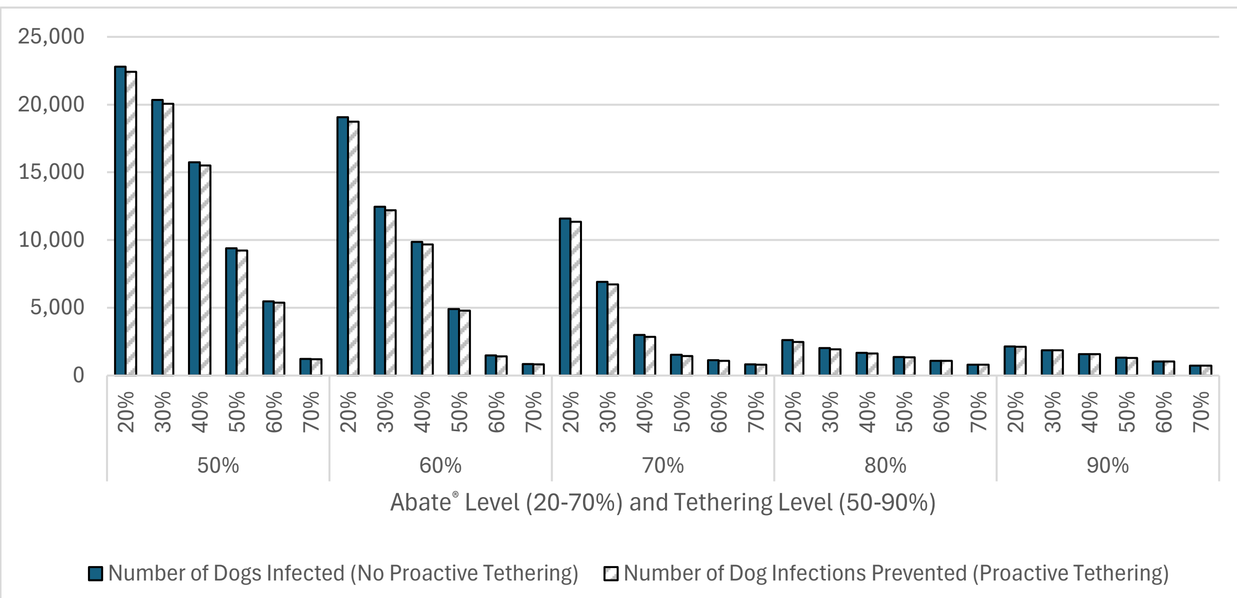


Figure 4: Number of dog infections after 5 years of intervention for the base case with no proactive tethering and the maximum number of dog infections prevented among proactive tethering scenarios for varied Abate® and tethering levels. Scenarios achieving the maximum prevented infections include random selection of dogs weekly, monthly, or quarterly and 80% of dogs proactively tethered.

Table 4: Additional tethered dog days required to prevent one infection for proactive tethering scenarios (considering random dog selection) compared to Scenario 0 (no proactive tethering), reported by Abate® usage, percentage of dogs selected for proactive tethering, and assuming 70% probability of tethering due to emerging worms.

Scenario	Dog Selection Frequency	50% Abate				60% Abate				70% Abate			
		% of Dogs Tethered:				% of Dogs Tethered:				% of Dogs Tethered:			
		20%	40%	60%	80%	20%	40%	60%	80%	20%	40%	60%	80%
Full Day Tethering Scenarios													
3	daily	2.90E+04	1.64E+04	1.17E+04	9.06E+03	4.68E+04	2.40E+04	1.63E+04	1.23E+04	6.54E+04	3.32E+04	2.21E+04	1.66E+04
4	weekly	2.79E+04	1.60E+04	1.11E+04	8.00E+03	4.52E+04	2.33E+04	1.51E+04	1.07E+04	6.37E+04	3.16E+04	1.95E+04	1.43E+04
5	monthly	2.75E+04	1.60E+04	1.11E+04	7.96E+03	4.53E+04	2.32E+04	1.50E+04	1.06E+04	6.29E+04	3.18E+04	1.96E+04	1.43E+04
6	quarterly	2.76E+04	1.60E+04	1.10E+04	7.96E+03	4.50E+04	2.32E+04	1.50E+04	1.06E+04	6.20E+04	3.13E+04	1.93E+04	1.42E+04
Half Day Tethering Scenarios													
7	daily	4.84E+04	2.77E+04	2.04E+04	1.61E+04	8.81E+04	4.55E+04	3.07E+04	2.34E+04	1.29E+05	6.50E+04	4.25E+04	3.21E+04
8	weekly	4.78E+04	2.73E+04	2.05E+04	1.61E+04	8.59E+04	4.60E+04	3.13E+04	2.32E+04	1.26E+05	6.34E+04	4.22E+04	3.13E+04
9	monthly	4.71E+04	2.75E+04	2.02E+04	1.60E+04	8.83E+04	4.50E+04	3.03E+04	2.36E+04	1.22E+05	6.41E+04	4.14E+04	3.12E+04
10	quarterly	4.73E+04	2.80E+04	2.03E+04	1.61E+04	8.38E+04	4.49E+04	3.09E+04	2.33E+04	1.20E+05	6.38E+04	4.25E+04	3.08E+04

4 DISCUSSION

Tethering interventions require resources and education across communities. Moreover, we have heard public health practitioners who have asked whether proactive tethering is working and how much impact it has. By estimating the impacts of different proactive tethering scenarios that might be implemented in practice (or are currently being practiced), we can help inform the implementation of interventions to have the maximum impact.

Our results indicate that randomly selecting dogs for proactive tethering results in fewer dog infections over time as opposed to choosing a fixed group of dogs to tether from the beginning of the time horizon. Choosing a fixed group of dogs might happen if an intervention prioritized educating a portion of households repeatedly (which can increase adoption) rather than educating all communities. One factor that leads to this result is that dogs with emerging worms have a chance of being tethered regardless of whether they are selected for proactive tethering or not. Effectively, when dogs are selected annually for proactive tethering, the total number of dogs tethered may be smaller than when they are selected daily (where we may not need to consider whether to proactively tether a dog if they are already tethered because of an emerging worm). Most importantly, the message is that proactive tethering is less effective when applied for a subset of households than when dogs across all households have a chance to be chosen.

Proactively tethering dogs for only half of each day produces better outcomes than the scenario with no proactive tethering. Releasing dogs for part of the day results in substantial increases in dog infections over time compared to full day tethering. Our results provide evidence that can be used by public health practitioners and field implementers as they are educating communities about the importance of full proactive tethering.

Clearly, continuing to apply Abate® to water sources is important. Indeed, we find that increasing Abate® within the ranges tested may be more important than incremental increases in tethering due to emerging worms. This may also be because of how many dogs are already tethered while worms are emerging, and the interactivity of dogs across water sources.

If GW is to be eradicated, we find that the interventions should include use of Abate® at high levels (e.g., 70% or higher), along with tethering of dogs while worms are emerging, and proactive tethering. At high Abate® levels and realistic levels of dogs tethered with emerging worms, it will be necessary to tether 14,000 or more additional dogs to prevent a single infection. This quantification will help practitioners understand the level of implementation needed, as the marginal rate of return decreases closer to eradication.

4.1 Limitations

The simulation model assumes that dogs randomly selected for tethering due to emerging worms are tethered 100% of the time until the last worms emerge from the host, thus preventing the worms from emerging into water sources. However, in reality, some dogs tethered for this purpose are released occasionally from tethering and interaction with water sources is possible in these situations. We assume that dogs that are tethered (whether proactively or due to emerging worms) will be fed food and water that is not contaminated with infective GW larvae. However, infections are possible if dogs are provided GW-contaminated water or eat raw or undercooked aquatic animals that carry infective GW larvae (Eberhard et al. 2014; Richards and Holian 2022). We do not consider water source infection from human infections or other animals such as cats (although both have much lower infections than dogs).

4.2 Conclusion

In conclusion, combined with Abate® and tethering of dogs with emerging worms, proactive tethering is an impactful intervention that helps to reduce dog infections over time. Simulation modeling of interventions for reducing GW infections can help to inform decision making and assist the effort to achieve elimination of the disease among dogs in Chad.

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