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USE OF FLUMETHRIN-IMPREGNATED COLLARS TO MANAGE AN EPIDEMIC OF SARCOPTIC MANGE IN AN URBAN POPULATION OF ENDANGERED SAN JOAQUIN KIT FOXES (*VULPES MACROTIS MUTICA*)

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Abstract: Sarcoptic mange epidemics can have long-lasting impacts on susceptible wildlife populations, potentially contributing to local population declines and extirpation. Since 2013, there have been 460 reported cases of sarcoptic mange in an urban population of endangered San Joaquin kit foxes (*Vulpes macrotis mutica*) in Bakersfield, CA, with many of them resulting in fatality. As part of a multifaceted response to mitigate mange-caused mortalities and reduce this conservation threat, a 2-yr randomized field trial was conducted to assess the efficacy of long-acting flumethrin collars against sarcoptic mange in kit foxes. Thirty-five kit foxes living in a high-density population on a college campus were captured, examined, administered selamectin, and each fox randomly assigned to either receive a flumethrin collar placed within a VHF radio collar or a VHF radio collar without flumethrin. The survival and mange-infestation status of study animals was monitored via radio telemetry, remote cameras, and periodic recapture examinations and compared among treated and control kit foxes using a Cox proportional hazards model. The average time to onset of mange for treated kit foxes (176 days) was similar to controls (171 days) and treatment with flumethrin did not significantly reduce mange risk for all kit foxes. Kit foxes that had a mild mange infestation at the beginning of the study were four times more likely to develop mange again, regardless of flumethrin treatment, compared with kit foxes that had no signs at initial recruitment. This study demonstrates an approach to evaluating population-level protection and contributes to the limited literature on efficacy, safety, and practicality of acaricides in free-ranging wildlife.

INTRODUCTION

Disease poses a serious conservation threat to endangered species;[43,54] epidemics can significantly alter host behavior, reduce fitness, and cause population declines.[46] The San Joaquin kit fox (*Vulpes macrotis mutica*) is federally endangered[55] due to anthropogenic habitat degradation associated with agriculture and urban sprawl. San Joaquin kit foxes (kit fox hereafter) now occur only in a small metapopulation of 3 "core" and 13 "satellite" subpopulations in the southern San Joaquin Valley.[9,55] The subpopulation in the city of Bakersfield was the largest, most stable satellite, with highest survival and recruitment rates and occurring throughout the city despite the paucity of natural habitat.[8,10]

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In 2013, sarcoptic mange was first documented in a San Joaquin kit fox from Bakersfield,[11] with more than 460 cases confirmed within the city by October 2018 (Cypher, pers. comm.). As for other vulpids, mange in kit foxes has proven fatal without intervention.[3,11,12,32] Sarcoptic mange is caused by the mite *Sarcoptes scabiei* and infests a wide range of mammals including coyotes (*Canis latrans*), red foxes (*Vulpes vulpes*), and domestic dogs (*Canis lupus familiaris*),[37] although *S. scabiei* genetic strains can be highly host-specific.[60] Catastrophic population declines due to mange have been reported in Spanish ibex (*Capra pyrenaica*) in Spain;[21] red foxes in Sweden, United Kingdom, and Japan;[31,51,57] and bare-nosed wombats (*Vombatus ursinus*) in Australia.[24] Sarcoptic mange suspected to have originated from coyotes or red foxes caused 30% of the upper midwestern wolf (*Canis lupus*) population to decline, imperiling local re-introduction programs.[1,6,17,38] Mange may contribute to the extinction of Bakersfield San Joaquin kit foxes.[8,10,11]

Although treatment of disease in free-ranging wildlife populations is difficult, acaricides can protect individual kit foxes from mange. One such product, the topical selamectin (Revolution®, Zoetis, Florham Park, NJ 07932, USA) provides 28 days of protection from mange in dogs, cats, ferrets, rabbits, and mice.[15,36,47] Selamectin has

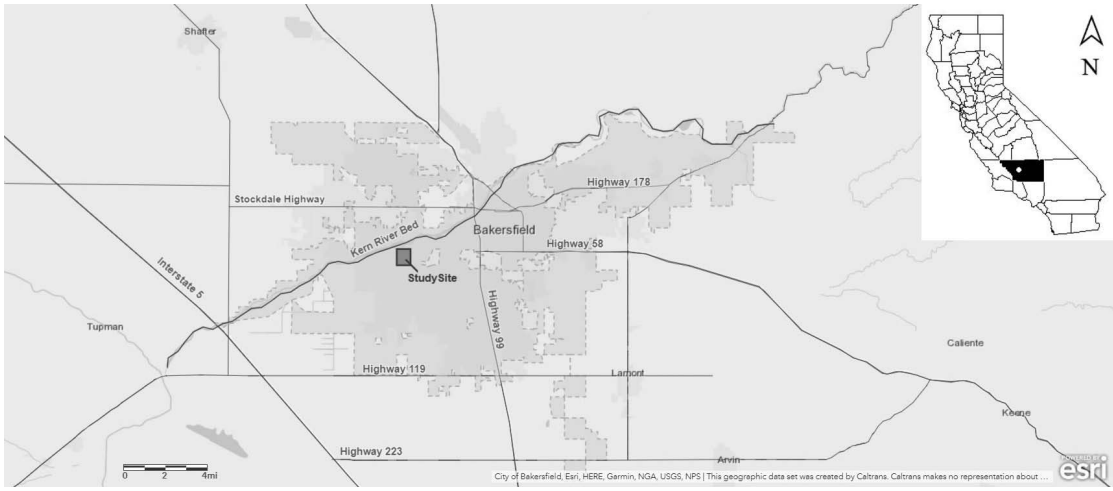

Figure 1. Location of study site, California State University, Bakersfield campus in Bakersfield, Kern County, CA.

been used to treat mange-infested kit foxes in rehabilitation but must be applied every 10–14 days for at least 4 wk.[7,15] Another product in the form of a collar, flumethrin (Seresto®, Bayer, Shawnee Mission, KS 66261, USA), was made commercially available in 2013. This product is labelled safe for dogs and cats (including sensitive breeds, pregnant, and lactating animals), and was reportedly effective for 8 mo of prevention against *S. scabiei*.[36] With its long duration of efficacy, flumethrin could have considerable population-level impacts on disease. Therefore, the objective of this study was to evaluate the efficacy of collar-based flumethrin on sarcoptic mange during a mange epidemic and the hypothesis that flumethrin collars would prolong the time to mange infestation in kit foxes when compared with a single application of selamectin. A randomized 2-yr field trial was conducted to compare time to infestation between kit foxes that received a single application of topical selamectin only and kit foxes that received selamectin and flumethrin.

METHODS

Study area

This study was conducted in the city of Bakersfield on and near the California State University Bakersfield (CSUB) campus, Kern County, CA (35°21′N, 119°06′W) (Fig. 1). Mange-infested and healthy kit foxes are often seen in the area, and kit foxes have been actively studied on the campus since 1997 (Endangered Species Recovery Program, unpubl. data). The 200-ha campus is surrounded by high-density urban development including homes to the east, commercial development to the north and south, and commercial development and open lots to the west. There are highways bounding north and south campus and an irrigation canal to the east. The climate features hot, dry summers, and cool, wet winters with average daily temperatures from 4.8 to 14.8°C in December and 21.8 to 37.8°C in July, and highly variable precipitation ranging from 14 to 26 cm/year.[35]

Capture methods

Humane capture and handling of kit foxes was performed following guidelines of the American Society of Mammalogists,[48] in accordance with approved permits for work under the federal Endangered Species Act from the United States Fish and Wildlife Service (TE25573-2), a Memorandum of Understanding with the California Department of Fish and Wildlife, and the University of California Davis Institutional Animal Care and Use Committee Protocol No. 18179.

Thirty-five kit foxes were captured between December 2015 and August 2017; although routine study trapping ceased during kit fox breeding and parturition seasons from 15 January to 1 May, trapping continued during that period to treat animals if they were seen with mange on camera. Wire-mesh box traps (25.4 × 25.4 × 121.9-cm, single-door noncollapsible traps; Tomahawk Live Trap, Hazelhurst, WI 54531, USA) were set approximately 1 hr before sunset and checked at sunrise the next morning. Traps were baited with various meats including wet cat food, bacon, and

beef hot dogs and were covered with canvas tarps or burlap to be less conspicuous to the public and to protect animals from harassment by other animals, inclement weather, and direct sunlight. Captured nontarget animals such as striped skunks (*Mephitis mephitis*), opossums (*Didelphis virginiana*), and domestic cats (*Felis catus*) were immediately released. Captured kit foxes were coaxed from traps into clean canvas bags and weighed using a 10-kg hanging scale (Pesola®, Schindellegi 8834, Switzerland). Kit foxes were muzzled and blindfolded (Quick Cat Muzzle®, Four Flags Over Aspen, Wabasha, MN 55981, USA) and manually restrained without anesthesia for physical examination and assessment for mange.

Data were collected including body mass, age, sex, body condition score (BCS) using a five-point scale, morphometric measurements, temperature, heart and respiration rate, and mange score. Early visible characteristics of mange-related lesions on kit foxes include bilateral scaling, scabbing, and alopecia on the ischial tuberosities and tail base progressive over 3 mo as mites proliferate to severe crusting; hyperkeratosis; and alopecia that spreads from the rear to the rest of the body.[11] A scoring system was used, adapted from published literature that identifies four mange scoring categories:[39] Class 0 (no mange) if no lesions were observed, Class I (mild) if lesions were present on $<25\%$ of the body, Class II (moderate) if lesions were present on 25–50% of the body, and Class III (severe) if lesions were present on $>50\%$ of the body. As there is no evidence that kit foxes can recover from sarcoptic mange without treatment, a recovered class (Class IV) was omitted from this scoring system. Kit foxes were assigned to age classes using dental wear patterns and reproductive status as: adults $\geq$1 yr of age, juveniles between 4 mo and 1 yr, and pups $\leq$4 mo of age. Kit foxes 4 mo of age and older were given metal ear tags with a unique four-or five-digit number (style 893, size 3, National Band and Tag Company, Newport, KY 41071, USA). Kit foxes were released at the site of capture after 10–30 min of handling.

Field trial design

Adult kit foxes in good body condition that had not been treated with selamectin within 45 days of capture and with a mange classification score of I or less were enrolled in the field trial. Kit foxes in advanced stages of mange (Class II or III) were not included in the field trial for animal welfare reasons but were instead transported to the California Living Museum, Bakersfield, CA for hospitalization and mange treatment. Kit foxes were returned to their original capture site once their mange infestation was resolved.

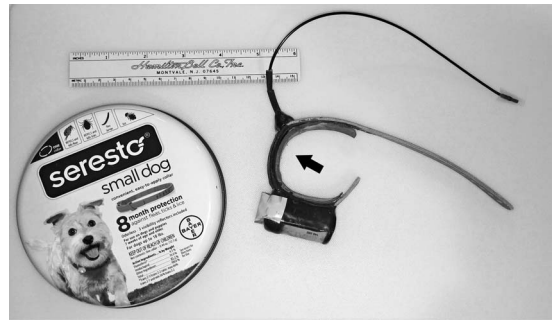

Figure 2. Flumethrin collar (Seresto®, Bayer) in the packaging and a flumethrin-impregnated VHF collar (black arrow).

Kit foxes were randomly assigned to the treatment (flumethrin collar) or control (no flumethrin collar) groups following a priori instructions to randomly assign the first fox to one of the groups and alternate group allocation thereafter. All kit foxes were administered topical selamectin (6 mg/kg) between the ears and fitted with a VHF radio collar (40–55 g; Advanced Telemetry Systems, Isanti, MN 55040, USA) containing a mortality sensor. For the treatment group, flumethrin small dog collars were secured to the inside of the VHF collars with E600 industrial adhesive (Eclectic Products, Eugene, OR 97402, USA; Fig. 2). Radio-collar antennae were labelled with reflective tape in unique patterns so that individuals could be visually identified (Fig. 3).

Mange-infestation status and survival of animals were monitored for 1 yr using radio telemetry, cameras, and visual observation. Radio telemetry was done 2–3 times a week. Cameras (Cuddeback Model E2, De Pere, WI 54115, USA) were deployed for 1 wk each month.[61] Because kit foxes are obligatory den users, cameras were placed near kit fox dens following published methods.[8,19,29,62] If a fox was not observed on camera, concerted efforts were made to obtain the location by telemetry. Trapping was done every 6 mo to enroll new foxes into the study and remove collars from animals that had been followed for a year.

Statistical analysis

Data analyses were performed using Excel (Microsoft, Redmond, WA 98052, USA) and R;[40] *P*-values of <0.05 were considered signifi-

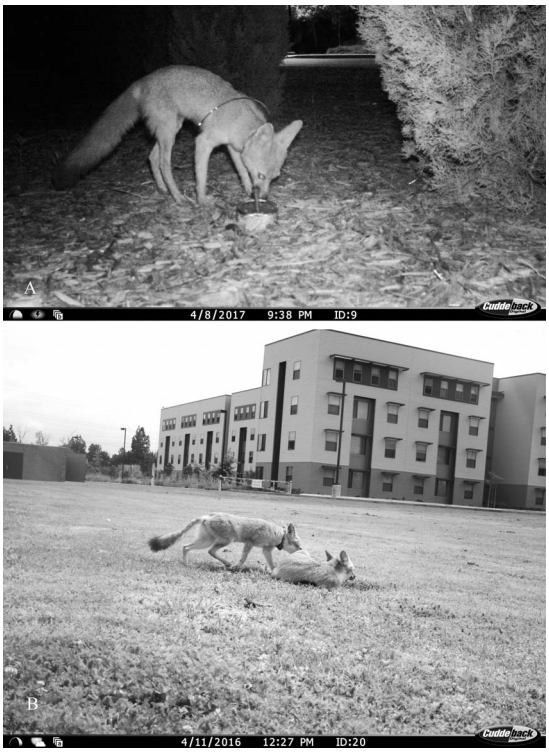

Figure 3. Camera trap images used to monitor the mange-infestation status at or near dens of radio-collared San Joaquin kit foxes (*Vulpes macrotis mutica*) wearing long-acting flumethrin-impregnated collars and untreated controls on the of California State University, Bakersfield. (**A**) female kit fox in the control group shows no signs of mange while visiting a camera station near her den; (**B**) female kit fox in the treatment group (wearing collar) is shown with her mate (not enrolled in study). The female has early signs of mange, demonstrated by hairless patches on the rump and thinning hair extending from the base of the tail (lion-tail appearance).

cant. Time to mange onset in days was the outcome variable of interest. Sex ratios and initial mange score of treatment and control kit foxes at the time of initial enrollment into the study (t_0) were compared using Pearson's chi-square tests with Yate's continuity correction. Mann–Whitney U test was used to determine whether mean number of days to the onset of mange was significantly different between treatment and control groups. Cox proportional hazards model was used to first estimate the baseline hazards ratio (HR) and 95% confidence interval for mange onset using the predictors of flumethrin treatment, sex, mange score of I (yes or no) at t_0, and whether or not the kit fox had a mate with mange. Multivariate Cox proportional hazards models with forward stepwise selection were then used to assess the association between sex, mange score at t_0, and mange-infested mates.

RESULTS

Thirty-five adult kit foxes were enrolled in the study: 17 kit foxes were assigned to the flumethrin treatment group (9 females and 8 males) and 18 kit foxes were assigned to the control group (8 females and 10 males; Table 1). At t_0, 11 treated and 7 control kit foxes had a Class I mange infestation limited to bilateral mild scaling and crusting on the ischial tuberosities. There were no significant differences in sex or mange score between treatment and control groups at t_0.

No adverse reactions to flumethrin collars were observed over the course of the study. During the year of monitoring, one control kit fox died from vehicular strike and 6 kit foxes (1 treated and 5 controls) were censored (removed from the study) due to collar failure and inability to recapture. Twenty-one study kit foxes developed mange (10 treated and 11 controls), while 8 (6 treated and 2 controls) did not (Fig. 4). Six kit foxes (1 treated and 5 controls) eventually died from mange despite efforts to capture and rehabilitate them.

Social groups

Based on direct observation, camera images, or co-localization of radio collars, a total of 25 study kit foxes (14 treated and 11 controls) were identified, having formed 11 known family groups consisting of a mate or a mate with offspring (Fig. 5). Six study kit foxes were paired with uncollared mates of unknown identity and whose fates remained unknown. Two mate re-pairings were observed during the study after the mate died. Two female study kit foxes that later developed mange were observed on camera and in the field co-rearing 6 pups, however their mates were never captured for inclusion in the study and the fates of these mates remained unknown as well as the fates of their pups. Two family groups had pups that were captured during a mange intervention. Four pups (2 from each family group) were later captured and included in the study. Ten study foxes (4 treated and 6 controls) were never observed with mates.

Of the 25 study kit foxes in the 11 known family groups, 6 foxes (5 treated and 1 control) did not develop mange, 17 (8 treated, 9 controls) developed mange, and 2 (1 treated and 1 control) were censored. Eight of the 11 family groups had pups with litter sizes ranging from 1 to 6. Among the

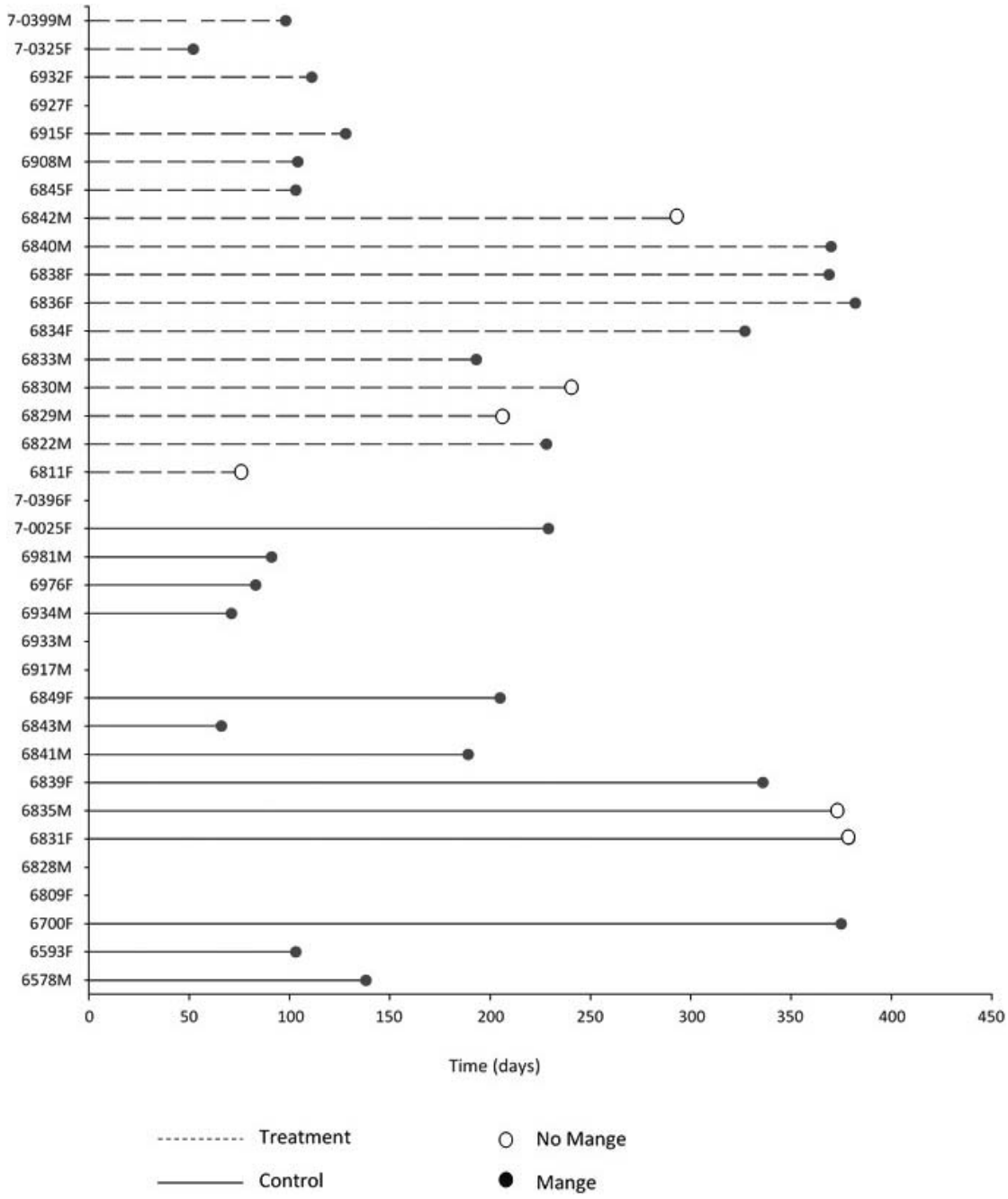

Figure 4. Mange-infestation status and time-to-mange development (in days) for flumethrin-treated (dashed line) and control (solid line) San Joaquin kit foxes (*Vulpes macrotis mutica*). Each line represents the fate of an individual kit fox tracked over time with their mange status denoted each time they were observed. Individuals with a closed circle developed mange during the follow-up period while individuals with open circles did not. Individuals without dashed or solid lines were censored from the study due to collar failure and subsequent loss to follow-up.

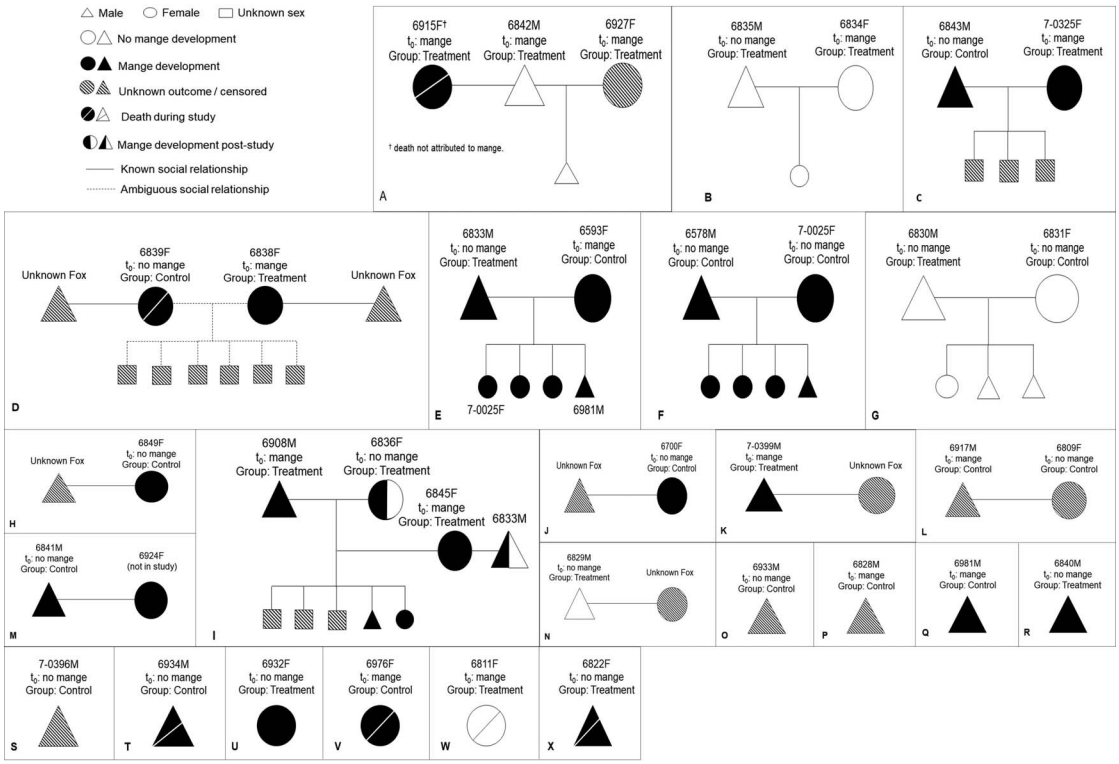

Figure 5. Familial relationships among San Joaquin kit foxes (*Vulpes macrotis mutica*) observed from December 2015 to August 2017 in Bakersfield, CA. The shapes—circle, triangle, and square—represent females, males, and unknown sex respectively. Large shapes represent adults (≥1 yr old) while small shapes represent pups and juveniles (<1 yr old). Shapes that are not colored represent foxes that did not develop mange, shapes that are solid-filled represent kit foxes that developed mange, shapes that are half-filled represent kit foxes that developed mange after they exited the study, and shapes that are striped represent a kit fox that was censored with an unknown outcome. The solid lines connecting shapes designate relationships while dotted lines represent ambiguity in the extent of the relationship. A solid slash represents a mortality. Kit fox ID, initial mange status at initial capture, and treatment group are noted.

known family groups with pups, 3 had at least one parent with mange and all pups in these groups developed mange. Mange was not observed in the 3 family groups with pups in which neither parent had mange at the time of parturition. A female study kit fox in the treatment group with Class I mange at t_0 was subsequently observed with advanced (Class III) mange on day 52 of follow-up. When she was recaptured for treatment, she had lost 300 g of body weight and her flumethrin-VHF collar was loose around her neck, no longer contacting her skin. Her mate (a control) had Class II mange on day 66. This pair was reported to have 3 pups observed by the public and were tracked to a natal den, however pups were not observed on camera or in the field and it is suspected that they perished. Overall, study kit foxes that developed mange during follow-up were more likely to have a mate with mange (x^2 = 13.4, $P < 0.01$) and two study kit foxes that did not develop mange during the 1-yr period did develop mange later while their mates were being monitored.

Survival analysis

Treated kit foxes developed mange by 176 days post treatment (SD = 113, median = 119 days, range = 52 to 382 days) compared with mange occurrence in control kit foxes of 171 days (SD = 107, median = 138 days, range = 66 to 375 days). These differences were not statistically significant (Fig. 6) and the curves of the Kaplan-Meier survival plot did not diverge greatly (Fig. 7). The HR of developing mange was not significantly lower in treated compared with control kit foxes ($\beta = -0.27$, HR = 0.77, 95% CI = 0.32 to 1.8, P = 0.55; Table 2; Fig. 7). The HR of mange onset did not differ by sex.

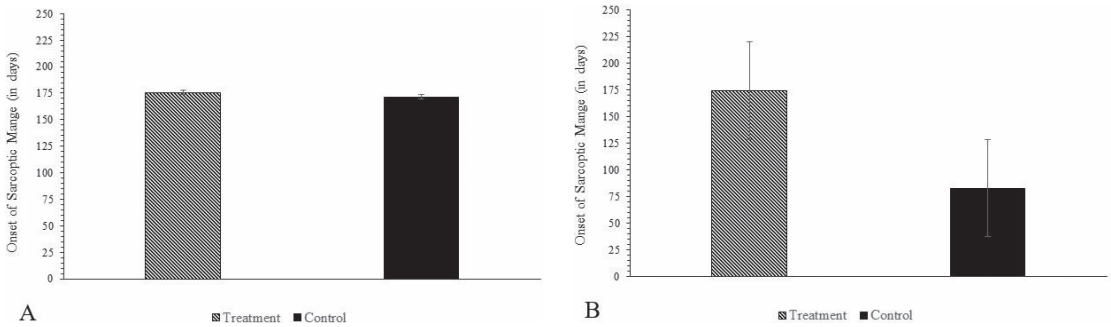

Figure 6. Average duration of time (in days) for San Joaquin kit foxes (*Vulpes macrotis mutica*) treated with a long-acting acaricide collar ($n = 17$) and control ($n = 18$) to become infested with mange at the California State University, Bakersfield campus in Bakersfield, CA. (**A**) Entire study population and (**B**) kit foxes that had Class I mange at initial capture.

Regardless of treatment group, kit foxes that had no signs of mange at the beginning of the study tended to be less likely to develop mange overall compared with a fox that originally experienced infestation but for which our treatment cleared the primary presenting mange. Specifically, study kit foxes with mange at t_0 ($n = 18$) were four times more likely to develop mange during follow-up compared with study foxes without mange at t_0 ($\beta = 1.4$, HR = 3.9, 95% CI = 1.5 to 10, $P = 0.0051$; Table 2; Fig. 7). Among the 18 study kit foxes treated for Class I mange at initial capture, those with flumethrin collars ($n = 11$) had significantly ($\beta = -1.38$, HR = 0.25, $P = 0.02$, 95% CI = 0.08 to 0.81) delayed time to reinfestation of mange (SD = 108 days, median = 116 days, range = 52 to 369 days) compared with control foxes that also had Class I mange at t_0 ($n = 7$, SD = 13 days, median = 83 days, range = 66 to 103 days; Table 2).

DISCUSSION

The sarcoptic mange epidemic in San Joaquin kit foxes has the potential to contribute to local extinction of this unique, urban-adapted Bakersfield population and tools with population-level efficacy are urgently needed. This study found long-acting flumethrin to be safe but unfortunately it did not provide overall statistically longer duration of protection compared with a single dose of selamectin. Flumethrin collars have been marketed for nearly 20 yr against ectoparasites including *S. scabiei* for up to 8 mo in cats and dogs.[52] Kit foxes experienced approximately 5 mo of protection against mange, with the earliest onset of mange detected at 52 days post treatment in a kit fox that had lost considerable body mass

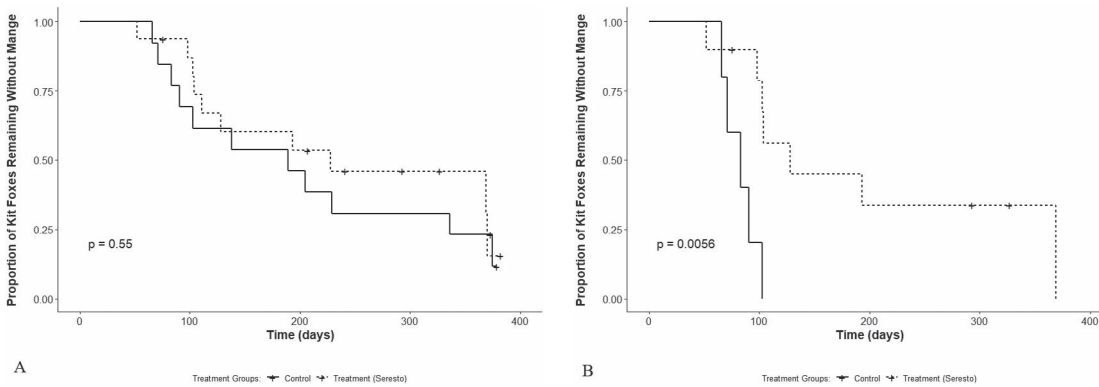

Figure 7. Kaplan–Meier plot of probability of mange infestation in San Joaquin kit foxes (*Vulpes macrotis mutica*) over time (in days). Vertical lines (+) indicate individual censored data and the corresponding time at which their censoring occurred. The shaded regions indicate confidence intervals—dark gray for control kit foxes and light gray for treated kit foxes. (**A**) Entire study population and (**B**) stratified by kit foxes that had Class I mange (mange-associated lesions that are <25% of the body) at initial capture.

Table 1. Sex, mange-infestation status at initial capture (t_0), and follow-up outcomes of mange occurrence and time-to-mange onset in days for San Joaquin kit foxes (*Vulpes macrotis mutica*) enrolled into a flumethrin treatment study from December 2015 to August 2017 in Bakersfield, CA. A mange scoring system (Class 0–III) was used to classify mange-associated lesions.[39] Only kit foxes with a mange score of 0 (no mange) or I (lesions covering <25% of the body) were included in the study. Kit foxes that could not be tracked throughout the year-long follow-up period were censored and are designated with an "NA."

Fox ID	Sex	Class I mange observed at t_0	Treatment group	Development of mange	Number of days until mange onset
6593F	Female	Yes	Control	Yes	103
6700F	Female	No	Control	Yes	375
6809F	Female	No	Control	NA	NA
6831F	Female	No	Control	No	No mange
6839F	Female	No	Control	Yes	336
6849F	Female	No	Control	Yes	205
6976F	Female	Yes	Control	Yes	83
7-0025F	Female	No	Control	Yes	229
6578M	Male	No	Control	Yes	138
6828M	Male	Yes	Control	NA	NA
6835M	Male	No	Control	No	No mange
6841M	Male	No	Control	Yes	189
6843M	Male	Yes	Control	Yes	66
6917M	Male	Yes	Control	NA	NA
6933M	Male	No	Control	NA	NA
6934M	Male	Yes	Control	Yes	71
6981M	Male	Yes	Control	Yes	91
7-0396F	Male	No	Control	NA	NA
6811F	Female	Yes	Treatment	No	No mange
6834F	Female	Yes	Treatment	No	No mange
6836F	Female	No	Treatment	No	No mange
6838F	Female	Yes	Treatment	Yes	369
6845F	Female	Yes	Treatment	Yes	103
6915F	Female	Yes	Treatment	Yes	128
6927F	Female	Yes	Treatment	NA	NA
6932F	Female	No	Treatment	Yes	111
7-0325F	Female	Yes	Treatment	Yes	52
6822M	Male	No	Treatment	Yes	228
6829M	Male	No	Treatment	No	No mange
6830M	Male	No	Treatment	No	No mange
6833M	Male	Yes	Treatment	Yes	193
6840M	Male	No	Treatment	Yes	370
6842M	Male	Yes	Treatment	No	No mange
6908M	Male	Yes	Treatment	Yes	104
7-0399M	Male	Yes	Treatment	Yes	98

such that her collar was no longer contacting her skin, likely preventing the collar from working effectively. Moreover, because kit foxes seasonally shed their winter coats, differences in coat thickness could also change collar contact with skin, necessitating seasonal adjustment of collars.

Although kit foxes treated with flumethrin experienced multiple mange-free months, some control kit foxes also experienced a longer than expected time-to-mange development, whereas others—typically in particular social groups—all succumbed. A single application of selamectin can clear early stage mange[47] but the drug must be reapplied every 21 to 28 days to prevent re-infestation.[2,47] Thus the delay of mange onset beyond 28 days in the control group suggests that these individuals were not exposed to *S. scabiei* mites, likely influenced by their social group structure. Kit foxes generally form small social groups consisting of a mated pair and their offspring;[13,14] the largely monogamous male may participate in extra-pair copulation during breeding season. Adult females have overlapping home ranges with their female relatives.[34,41,42,63] Related females may co-rear pups and share dens.[34,41,42] Kit foxes from different social groups avoid one

Table 2. Univariate and multivariate β coefficients, hazard ratios, *P*-value, and 95% confidence intervals (CI) associated with mange development in flumethrin-treated and control San Joaquin kit foxes (*Vulpes macrotis mutica*) between December 2015 and August 2017 using Cox proportional hazards models. A dash indicates a reference value. Mange at t_o refers to the initial time point at which the animal was treated and recruited into the study.

Univariate models	No. of individuals that developed mange	β	HR	*P*-value	95% CI interval
Treatment group					
Control (no flumethrin collar)	11	—	—	—	—
Treated (flumethrin collar)	10	−0.27	0.77	0.55	0.32–1.8
Sex					
Female	11	—	—	—	—
Male	10	0.19	1.2	0.67	0.55–2.9
Mange at t_0					
No	9	—	—	—	—
Yes	12	1.4	3.9	0.0051	1.5–10
Multivariable models	**β**	**HR**	***P*-value**	**95% CI interval**	**AIC**
Treatment + sex					116.9
Flumethrin collar	−0.32	0.72	0.47	0.30–1.8	
Male	0.27	1.3	0.46	0.52–3.2	
Treatment + mange at t_0					103.6
Flumethrin collar	−1.3	0.26	0.02	0.08–0.81	
Class I mange at initial recruitment	2.2	9.3	0.0007	2.5–34	
Treatment + sex + Mange at t_0					104.5
Flumethrin collar	−1.5	0.23	0.02	0.61–2.4	
Male	0.49	1.6	0.29	0.46–1.1	
Class I mange at initial recruitment	2.3	9.9	0.0051	0.66–3.5	

another.[34,41] Thus accurate identification of social groups and the groups' mange status could be very useful in population management. Because once mange was observed in a kit fox that had a known mate or a mate and pups, eventually that entire social group developed mange, and more impactful mange intervention should include synchronous treatment of all in-contact animals.[3]

Besides the lack of overall significant treatment effect of flumethrin across all groups, kit foxes with flumethrin collars that had Class I mange at initial enrollment—and were treated for their infection with selamectin—became reinfested 35 days later than control kit foxes that had only received selamectin. Even so, the most important result in this study was that flumethrin-treated kit foxes who had mange on enrollment had significantly fewer mange-free days than those who appeared initially uninfested. The initial selamectin and flumethrin treatment would have provided a window of at least one or a few months of protection from reinfestation. However, those individuals presenting with clinical mange were highly likely to be members of social groups in which there were other infested kit foxes, most of which were not treated for mange. Study kit foxes could be re-exposed to mange through direct contact and by contact with mites in dens.[23,30] The early return to mange infestation in these flumethrin-treated kit foxes suggests considerably less than 8 mo of protection.

Large and uncontrolled disease epidemics that imperil wildlife populations and increase the vulnerability of small populations to demographic and environmental stochasticity are of great conservation importance. Practical management approaches are needed to help prevent extinction and evaluating the effectiveness of attempted management strategies contributes to the understanding of the ecology of diseases.[20,50,64] However, extra-label use of medications designed for domestic animals must be critically evaluated for use in wildlife, as performance of these medications may vary by species and under controlled vs field conditions. For example, the use of vaccines in wild populations has a controversial history because of problems with safety and efficacy in certain species.[5,26,65] Treatment application of properly dosed medications need also be considered and will vary by host species. In Australia, successful delivery of moxidectin onto wombats via treated door-flaps on burrow entrances was identified as the single most important factor in population-level control of *S. scabiei* mites.[25]

Attempted medical treatment at a population level must also consider risks to nontarget species, as well as the margin of safety and possible side effects of the medication in the target species. Macrocyclic lactones such as ivermectin, moxidectin, and selamectin are popularly used parasiticides worldwide.[59] Although ivermectin has been used to treat sarcoptic mange,[4] it is toxic in certain dog breeds and has a lower margin of safety in cats compared with dogs.[18,27,28,33] Secondary exposure to ivermectin and subsequent toxicosis has been documented in soil fauna and fish after the drug is excreted by animals undergoing treatment.[16] Ivermectin toxicity is also a greater risk for sick or debilitated animals.[28,49] In addition to considering impacts on wildlife of medication per se, other aspects of the management program must be considered. For example, repeated use of oral medication on attractive bait may result in habituation of the animal with negative consequences for the individual.

While this study provided some evidence that selamectin with flumethrin may have a role in population management for mange in highly vulnerable species such as kit foxes, more efficacious medication would be a tremendous benefit. Isoxazolines, such as sarolaner, afoxolaner, and fluralaner, represent a newer class of medications for flea and tick infestations in cats, dogs, and other animals. They have been used extra-label against mange and may be effective in mild infestations with only a single oral or topical dose.[44,53] A single oral administration of fluralaner successfully treated sarcoptic mange in a black bear (*Ursus americanus*) from Virginia.[58] But data on the safety of isoxazolines for cats and dogs younger than 6 mo old, and pregnant or lactating domestic animals, is lacking. In 2018, the United States Food and Drug Administration responded to increasing reports of neurologic adverse events following the use of isoxazolines by requesting that manufacturers include new label information highlighting this risk.[56]

Sarcoptic mange is highly infectious, causes severe morbidity and mortality, and is responsible for population declines in numerous wildlife species. Many vulnerable host individuals cannot be protected through immunity as for vulpids in which sarcoptic mange is routinely fatal. Even successfully treated animals fail to develop immunity against re-infestation[22] and there is limited literature on sarcoptic mange treatment in field settings.[45] Although flumethrin showed promise as being safe, long-lasting, and efficacious, its extra-label use in the field was not as effective as it is for treatment of mange in domestic animals. Additional studies focusing on mange transmission, novel medications, and kit fox sociology should be conducted to determine what refinements could improve individual animal protection and reduce the impacts of this disease in the Bakersfield population.

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LITERATURE CITED

1. Arlian LG, Morgan MS, Rapp CM, Vyszenski-Moher DL. The development of protective immunity in canine scabies. Vet Parasitol. 1996;62(1):133–142.

2. Bishop B, Bruce C, Evans N, Goudie A, Gration K, Gibson S, Pacey M, Perry D, Walshe N, Witty M. Selamectin: a novel broad-spectrum endectocide for dogs and cats. Vet Parasitol. 2000;91(3–4):163–176.

3. Bornstein S, Mörner T, Samuel WM. *Sarcoptes scabiei* and sarcoptic mange. 2nd ed. Ames (IA): Iowa State University Press; 2001.

4. Campbell W, Benz G. Ivermectin: a review of efficacy and safety. J Vet Pharmacol Ther. 1984;7(1):1–16.

5. Carpenter JW, Appel M, Erickson RC, Novilla MN. Fatal vaccine-induced canine distemper virus infection in black-footed ferrets. J Am Vet Med Assoc. 1976;169(9):961–964.

6. Chronert JM, Jenks JA, Roddy DE, Wild MA, Powers J. Effects of sarcoptic mange on coyotes at

Wind Cave National Park. J Wildl Manage. 2007;71(6): 1987–1992.

7. Curtis CF. Current trends in the treatment of *Sarcoptes, Cheyletiella* and *Otodectes* mite infestations in dogs and cats. Vet Dermatol. 2004;15(2):108–114.

8. Cypher B. Kit Foxes. In: Gehrt S, Riley S, Cypher B, (eds.). Urban carnivores: ecology, conflict, and conservation. Baltimore (MD): Johns Hopkins University Press; 2010. p. 49–60.

9. Cypher B, Phillips S, Kelly P. Quantity and distribution of suitable habitat for endangered San Joaquin kit foxes: conservation implications. Canid Biol and Conserv. 2013;16:25–31.

10. Cypher BL, Frost N. Condition of San Joaquin kit foxes in urban and exurban habitats. J Wildl Manage. 1999;63(3):930–938.

11. Cypher BL, Rudd JL, Westall TL, Woods LW, Stephenson N, Foley JE, Richardson D, Clifford DL. Sarcoptic mange in endangered kit foxes (*Vulpes macrotis mutica*): case histories, diagnoses, and implications for conservation. J Wildl Dis. 2017;53(1):46–53.

12. Devenish-Nelson ES, Richards SA, Harris S, Soulsbury C, Stephens PA. Demonstrating frequency-dependent transmission of sarcoptic mange in red foxes. Biol Lett. 2014;10(10):20140524.

13. Egoscue HJ. Ecology and life history of the kit fox in Tooele County, Utah. Ecology. 1962:481–497.

14. Egoscue HJ. Population dynamics of the kit fox in western Utah. Bull South Calif Acad Sci. 1975;74(3): 122–127.

15. Fisher M, Beck W, Hutchinson MJ. Efficacy and safety of selamectin (Stronghold®/Revolution™) used off-label in exotic pets. Int J Appl Res Vet Med. 2007; 5(3):87–96.

16. Halley BA, Jacob TA, Lu AY. The environmental impact of the use of ivermectin: environmental effects and fate. Chemosphere. 1989;18(7–8):1543–1563.

17. Jimenez MD, Bangs EE, Sime C, Asher VJ. Sarcoptic mange found in wolves in the Rocky Mountains in western United States. J Wildl Dis. 2010;46(4):1120–1125.

18. Jourdan G, Boyer G, Raymond-Letron I, Bouhsira E, Bedel B, Verwaerde P. Intravenous lipid emulsion therapy in 20 cats accidentally overdosed with ivermectin. J Vet Emerg Crit Care. 2015;25(5): 667–671.

19. Koopman ME, Scrivner JH, Kato TT. Patterns of den use by San Joaquin kit foxes. J Wildl Manage. 1998:373–379.

20. Lafferty KD, Gerber LR. Good medicine for conservation biology: the intersection of epidemiology and conservation theory. Conserv Biol. 2002;16(3): 593–604.

21. León-Vizcaíno L, Ruíz de Ybáñez MR, Cubero MJ, Ortíz JM, Espinosa J, Pérez L, Simón MA, Alonso F. Sarcoptic mange in Spanish ibex from Spain. J Wildl Dis. 1999;35(4):647–659.

22. Little SE, Davidson WR, Rakich PM, Nixon TL, Bounous DI, Nettles VF. Responses of red foxes to first and second infection with *Sarcoptes scabiei*. J Wildl Dis. 1998;34(3):600–611.

23. Loredo AI, Rudd JL, Foley JE, Clifford DL, Cypher BL. Climatic suitability of San Joaquin kit fox (*Vulpes macrotis mutica*) dens for sarcoptic mange (*Sarcoptes scabiei*) transmission. J Wildl Dis. 2020; 56(1):126–133.

24. Martin AM, Burridge CP, Ingram J, Fraser TA, Carver S. Invasive pathogen drives host population collapse: effects of a travelling wave of sarcoptic mange on bare-nosed wombats. J Appl Ecol. 2018;55(1):331–341.

25. Martin AM, Richards SA, Fraser TA, Polkinghorne A, Burridge CP, Carver S. Population-scale treatment informs solutions for control of environmentally transmitted wildlife disease. J Appl Ecol. 2019; 56(10):2363–2375.

26. McCormick A. Canine distemper in African cape hunting dogs (*Lycaon pictus*): possibly vaccine induced. J Zoo Anim Med. 1983;14(2):66–71.

27. Merola VA, Khan S, Gwaltney-Brant S. Ivermectin toxicosis in dogs: a retrospective study. J Am Anim Hosp Assoc. 2009;45(3):106–111.

28. Merola VM, Eubig PA. Toxicology of avermectins and milbemycins (macrocylic lactones) and the role of P-glycoprotein in dogs and cats. Vet Clin North Am Small Anim Pract. 2012;42(2):313–333.

29. Moehrenschlager A, Cypher BL, Ralls K, List R, Sovada ME. Comparative ecology and conservation priorities of swift and kit foxes. In D.W. Macdonald and C. Sillero-Zubiri, eds. The biology and conservation of wild canids. Oxford (UK): Oxford University Press; 2004. p. 185–189.

30. Montecino-Latorre D, Cypher BL, Rudd JL, Clifford DL, Mazet JA, Foley JE. Assessing the role of dens in the spread, establishment and persistence of sarcoptic mange in an endangered canid. Epidemics. 2019;27:28–40.

31. Mörner T. Sarcoptic mange in Swedish wildlife. Rev Sci Tech. 1992;11(4):1115–1121.

32. Mörner T, Christensson D. Experimental infection of red foxes (*Vulpes vulpes*) with *Sarcoptes scabiei* var. *vulpes*. Vet Parasitol. 1984;15(2):159–164.

33. Muhammad G, Abdul J, Khan M, Saqib M. Use of neostigmine in massive ivermectin toxicity in cats. Vet Hum Toxicol. 2004;46(1):28–29.

34. Murdoch JD, Ralls K, Cypher B, Reading R. Social interactions among San Joaquin kit foxes before, during, and after the mating season. J Mammal. 2008; 89(5):1087–1093.

35. National Ocean and Atmospheric Administration. Local climatological data, 2010: annual summary with comparative data, Bakersfield, California. National Oceanic and Atmospheric Administration Report. 2010.

36. Novotny M, Krautmann M, Ehrhart J, Godin C, Evans E, McCall J, Sun F, Rowan T, Jernigan A. Safety of selamectin in dogs. Vet Parasitol. 2000;91(3):377–391.

37. Pence D, Ueckermann E. Sarcoptic manage in wildlife. Rev Sci Tech. 2002;21(2):385–398.

38. Pence DB, Windberg LA. Impact of a sarcoptic mange epizootic on a coyote population. J Wildl Manage. 1994:624–633.

39. Pence DB, Windberg LA, Pence BC, Sprowls R. The epizootiology and pathology of sarcoptic mange in coyotes, *Canis latrans*, from south Texas. J Parasitol. 1983;69(6):1100–1115.

40. R Core Team. R: A language and environment for statistical computing. Vienna, Austria. [Internet]. 2018. Available from http://www.R-project.org/.

41. Ralls K, Cypher B, Spiegel LK. Social monogamy in kit foxes: formation, association, duration, and dissolution of mated pairs. J Mammal. 2007;88(6): 1439–1446.

42. Ralls K, Pilgrim KL, White P, Paxinos EE, Schwartz MK, Fleischer RC. Kinship, social relationships, and den sharing in kit foxes. J Mammal. 2001; 82(3):858–866.

43. Roelke-Parker M, Munson L, Packer C, Kock R, Cleaveland S, Carpenter M, O'Brien S, Pospischil A, Hofmann-Lehmann R, Lutz H. A canine distemper virus epidemic in Serengeti lions (*Panthera leo*). Nature. 1996;379:441–445.

44. Romero C, Heredia R, Pineda J, Serrano JA, Mendoza GD, Trapala P, Cordero AM. Efficacy of fluralaner in 17 dogs with sarcoptic mange. Vet Dermatol. 2016;27(5):e353–388.

45. Rowe ML, Whiteley PL, Carver S. The treatment of sarcoptic mange in wildlife: a systematic review. Parasit Vectors. 2019;12(1):99.

46. Scott ME. The impact of infection and disease on animal populations: implications for conservation biology. Conserv Biol. 1988;2(1):40–56.

47. Shanks D, McTier T, Behan S, Pengo G, Genchi C, Bowman D, Holbert M, Smith D, Jernigan A, Rowan T. The efficacy of selamectin in the treatment of naturally acquired infestations of *Sarcoptes scabiei* on dogs. Vet Parasitol. 2000;91(3):269–281.

48. Sikes RS, Gannon WL. Guidelines of the American Society of Mammalogists for the use of wild mammals in research. J Mammal. 2011;92(1):235–253.

49. Skerratt L, Martin R, Handasyde K. Sarcoptic mange in wombats. Aust Vet J. 1998;76(6):408–410.

50. Soule ME. Conservation biology: the science of scarcity and diversity. Sunderland (MA): Sinauer Associates, Inc; 1986.

51. Soulsbury CD, Iossa G, Baker PJ, Cole NIKC, Funk SM, Harris S. The impact of sarcoptic mange *Sarcoptes scabiei* on the British fox *Vulpes vulpes* population. Mammal Review. 2007;37(4):278–296.

52. Stanneck D, Kruedewagen EM, Fourie JJ, Horak IG, Davis W, Krieger KJ. Efficacy of an imidacloprid/flumethrin collar against fleas, ticks, mites and lice on dogs. Parasit Vectors. 2012;5(1):102.

53. Taenzler J, Liebenberg J, Roepke RK, Frénais R, Heckeroth AR. Efficacy of fluralaner administered either orally or topically for the treatment of naturally acquired *Sarcoptes scabiei* var. *canis* infestation in dogs. Parasit Vectors. 2016;9(1):392.

54. Thorne ET, Williams ES. Disease and endangered species: the black-footed ferret as a recent example. Conserv Biol. 1988;2(1):66–74.

55. United States Fish and Wildlife Service. San Joaquin kit fox (*Vulpes macrotis mutica*) 5-year review: summary and evaluation. Sacramento (CA); 2010.

56. United States Food and Drug Administration. Animal drug safety communication: FDA alerts pet owners and veterinarians about potential for neurologic adverse events associated with certain flea and tick products [Internet]. 2018. Available from https://www.fda.gov/animal-veterinary/cvm-updates/animal-drug-safety-communication-fda-alerts-pet-owners-and-veterinarians-about-potential-neurologic

57. Uraguchi K, Ueno M, Iijima H, Saitoh T. Demographic analyses of a fox population suffering from sarcoptic mange. J Wildl Manage. 2014;78(8): 1356–1371.

58. Van Wick M, Hashem B. Treatment of sarcoptic mange in an American black bear (*Ursus americanus*) with a single oral dose of fluralaner. J Wildl Dis. 2019; 55(1):250–253.

59. Vercruysse J, Rew RS. Macrocyclic lactones in antiparasitic therapy. Wallingford (UK): CABI Publishing: 2002.

60. Walton S, Dougall A, Pizzutto S, Holt D, Taplin D, Arlian L, Morgan M, Currie B, Kemp D. Genetic epidemiology of *Sarcoptes scabiei* (Acari: Sarcoptidae) in northern Australia. Int J Parasitol. 2004;34(7):839–849.

61. Westall TL, Cypher BL. Latency to first detection of kit foxes during camera surveys. Canid Biol Conserv. 2017;20(8):32–37.

62. Westall TL, Cypher BL, Ralls K. Efficacy of three methods for collecting behavioral data on urban San Joaquin kit foxes, *Vulpes macrotis mutica*. West Wildl. 2016;3:1–7.

63. White PJ, Ralls K. Reproduction and spacing patterns of kit foxes relative to changing prey availability. J Wildl Manage. 1993:861–867.

64. Wilson EO. The diversity of life. 2nd ed. Cambridge (MA): W.W. Norton Company; 1999.

65. Woodroffe R. Assessing the risks of intervention: immobilization, radio-collaring and vaccination of African wild dogs. Oryx. 2001;35(3):234–244.

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