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RESEARCH ARTICLE

Nalbuphine, medetomidine, and azaperone use in free-ranging American black bears and mountain lions in Wyoming

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Abstract

Safe and effective chemical immobilization is a necessary component of large carnivore management and research, but laws regulating controlled substances can limit the use of many drugs by non-veterinary personnel. NalMed-A (40 mg/mL nalbuphine HCl. 10 mg/mL medetomidine HCl. 10 mg/mL azaperone tartrate) is a non-controlled drug combination used to immobilize a number of free-ranging species, but there are limited published reports of its usage by non-veterinary personnel when immobilizing American black bears (Ursus americanus) and mountain lions (Puma concolor). Additionally, there are some safety concerns regarding anecdotal reports of spontaneous arousals occurring in large carnivores immobilized with NalMed-A. We performed a retrospective analysis of capture forms for free-ranging black bears (n = 34) and mountain lions (n = 7) immobilized with NalMed-A by non-veterinary personnel across Wyoming, USA, in 2017 and 2019-2024. Induction (x ± SE) was 10.74 ± 1.16 minutes for black bears (n = 34) and 7.14 ± 1.60 for mountain lions (n = 7). Reversal was 14.21 ± 1.51 minutes for black bears (n = 28) and 10.00 ± 1.26 minutes for mountain lions (n = 5). We used non-parametric tests (Kruskal-Wallis, Wilcoxon rank sum) and odds ratios to examine the effect of certain parameters on induction times, redoses, and spontaneous arousals in black bears. Median induction time for black bears injected in their hind leg or rump was greater than for black bears injected in their shoulder (n = 34, W = 79.5, P = 0.045). Six black bears (18%) experienced spontaneous arousals. We recommend avoiding the hind leg and rump for dart placement in bears, and using hobbles and a muzzle for large carnivores when using NalMed-A in a free-ranging setting because of the risk of spontaneous arousals.

KEYWORDS

American black bear, azaperone, chemical immobilization, medetomidine, mountain lion, nalbuphine, *Puma concolor*, spontaneous arousal, *Ursus americanus*

Chemical immobilization is an important tool when capturing and handling carnivores, such as American black bears (*Ursus americanus*) and mountain lions (*Puma concolor*), for management and research purposes. Drug combinations commonly used for immobilizing these large carnivores have focused on providing adequate levels of sedation and pain control. They typically contain dissociatives, alpha-two adrenergic agonists, and opioids; examples include ketamine-medetomidine (KM), tiletamine-zolazepam-medetomidine (TZM), and butorphanol-azaperone-medetomidine (BAM; ZooPharm, Laramie, WY, USA), which is a combination of 27.3 mg/mL butorphanol tartrate, 9.1 mg/mL azaperone tartrate, and 10.9 mg/mL medetomidine HCI (Jalanka and Roeken 1990, Bush et al. 2012, Kreeger and Arnemo 2018, Williamson et al. 2018). These drug combinations are effective in most cases, but there are some challenges when using them, including spontaneous arousal (Kreeger and Arnemo 2018), the inability to antagonize the combination (requiring longer downtime for the animals and longer monitoring periods for personnel), and the additional federal oversight because these combinations contain federally controlled substances in the United States (Drug Enforcement Administration 2020).

NalMed-A (40 mg/mL nalbuphine HCl, 10 mg/mL medetomidine HCl, 10 mg/mL azaperone tartrate; ZooPharm) is a drug combination that only includes unscheduled pharmaceuticals, of which 2 can be antagonized (i.e., nalbuphine, medetomidine). This relaxes some of the regulatory oversight, making it potentially more accessible to non-veterinary personnel (Wolfe et al. 2014, Sheldon et al. 2024). In addition, similar to BAM, NalMed-A's reversibility allows for a decrease in handling and monitoring time. This drug combination is already being used in the field, but there are limited published accounts on the success and safety of using NalMed-A in large carnivores (especially from a non-veterinary personnel point of view), and on any of the animal-specific variations (e.g., age, sex, body condition) or situational differences (e.g., season, capture method, injection site, injection type, number of attempts to inject) that could influence the capture outcome. There are 3 reports on the effectiveness of the drug combination when administered by veterinary personnel to immobilize captive (Wolfe et al. 2019, Sheldon et al. 2024) and free-ranging black bears (Wolfe et al. 2016) and 1 publication that mentions the successful immobilization of 1 mountain lion with either NalMed (40 mg/mL nalbuphine HCl, 10 mg/mL medetomidine HCl) or NalMed-A (Wolfe et al. 2014). None of these reports documented spontaneous arousals; however, there have been some anecdotal reports of spontaneous arousals occurring in large carnivores immobilized with NalMed-A by non-veterinary personnel in Wyoming, USA (T. P. Thomas, Wyoming Game and Fish Department, personal communication).

Our objectives for this study were to collect more information on NalMed-A field usage in black bears and mountain lions by non-veterinary personnel. We were particularly interested in evaluating the capture outcome (i.e., induction and reversal times, redoses) and the safety for the non-veterinary personnel (i.e., spontaneous arousals).

STUDY AREA

Black bears and mountain lions occupy forested areas of all major mountain ranges in Wyoming; mountain lions also inhabit tall-shrub covered regions statewide (Wyoming Game and Fish Department 2006, 2007). Montane forests are dominated by lodgepole pine (*Pinus contorta*), while sagebrush (*Artemisia* spp.), and juniper (*Juniperus* spp.) are



FIGURE 1 Wyoming Game and Fish Department regions in Wyoming, USA, and the number of black bears and mountain lions immobilized with NalMed-A per region during 2017–2024. Image courtesy of Wyoming Game and Fish Department.

common in tall-shrub landscapes (Wyoming Game and Fish Department 2017*a*, *b*). Human land use in the described areas is variable; however, use in montane forests is primarily limited to forestry and recreation, while use in tall-shrub landscapes is mainly residential and agricultural (Wyoming Game and Fish Department 2017*a*, *b*). The mean elevation in Wyoming is 2,042 m, though mountain ranges have considerably higher elevations; the highest point, Gannett Peak, located in the west-central portion of the state, is 4,204 m. Due to its high elevation, Wyoming has a relatively cool climate, with mean maximum temperatures in July between 29°C and 35°C and mean minimum temperatures in January between -12° C and -15° C. Mountain ranges are considerably cooler, with average daily lows in the summer between -1° C and 4°C. The climate in Wyoming is semiarid, with the maximum precipitation period occurring in late-spring and early-summer. Annual precipitation averages vary across the state from 13-41 cm, with greater precipitation over the mountain ranges and at higher elevations (Western Regional Climate Center 2023). We used data from black bear immobilizations in the Casper, Green River, Lander, Laramie, and Sheridan regions and mountain lion immobilizations in the Casper, Cody, Green River, Lander, Laramie, and Sheridan regions (Figure 1).

METHODS

Data set development

We performed a retrospective analysis of field use of NalMed-A in black bears and mountain lions by Wyoming Game and Fish Department (WGFD) staff (i.e., biologists, wardens, technicians) that have received department

immobilization training, but the capture events occurred in the absence of a veterinarian. The dosage of NalMed-A for these species was recommended as 1 mL/45.5 kg, which equates to approximately 0.88 mg nalbuphine HCl/kg, 0.22 mg azaperone tartrate/kg, and 0.22 mg medetomidine HCI/kg. Staff were trained to administer a full redose if the animal showed no response to the drug within 15-20 minutes and to administer a half dose if the animal showed partial response to the drug within 15-20 minutes. Staff administered NalMed-A via pole syringes or remote delivery devices (i.e., darts) using various models of Pneu-Dart (Williamsport, PA, USA) CO₂-powered rifles, pistols, and darts with needles of various lengths. For black bears and mountain lions immobilized with NalMed-A for routine management purposes (e.g., relocations, incidental captures), staff recorded data for submission to a statewide drug tracking system, inclusion on a WGFD wildlife capture form, or both. Relevant data recorded for submission to the statewide drug tracking system included drug name, date used, amount used, vial number, injection type (e.g., dart, pole syringe, hand injection), location, species, and comments. Additional data recorded on capture forms included capture method (e.g., free-darted, trapped, treed), the number of attempts to inject, injection site (e.g., left shoulder, right hind), injection time(s), time animal immobile (i.e., sternal, head down, unresponsive to stimuli), time recovery complete (i.e., standing), and animal age, sex, mass (estimated or scale), and body condition. Staff emailed capture forms to state wildlife veterinarians; the body of these emails sometimes contained additional remarks regarding the immobilization event(s). Staff recorded body condition using either a 1-5 scoring system (BCS) or descriptive terminology (e.g., thin, good, excellent) and estimated age using parameters such as mass, tooth wear, and pelage. Comments recorded included descriptions of spontaneous arousals (e.g., nodding head, walking, running) and any stimuli (e.g., pulling out of trap, falling from tree). Staff antagonized the nalbuphine and medetomidine with intramuscular injections of naltrexone HCI and atipamezole HCI (Zoo Pharm), respectively (25 mg naltrexone/80 mg nalbuphine; 5 mg atipamezole/1 mg medetomidine). We calculated induction time in minutes by subtracting the first apparent injection time of NalMed-A from the time animal became immobile, and reversal time in minutes by subtracting the injection time of antagonists from the time recovery was complete. We defined spontaneous arousal as an animal that was deemed immobile suddenly exhibiting voluntary movement before the administration of antagonists.

Statistical analyses

We included immobilization events in our analyses if staff submitted a wildlife capture form and used NalMed-A prior to its beyond use date. We calculated mean induction time, reversal time, and standard error (SE) for black bears and mountain lions (R Core Team 2024). We did not perform additional analyses for mountain lions because of small sample sizes. To analyze the correlation between the time black bears were immobile before antagonists were administered and the time until recovery was complete, we used a Spearman's rank correlation test (R Core Team 2024). We used Kruskal-Wallis tests to analyze whether body condition, season, or capture method had an effect on induction time in black bears (R Core Team 2024). We pooled body condition into 3 classes: thin (e.g., BCS = 2, fair), healthy (e.g., BCS = 3, good), and overconditioned (e.g., BCS = 4, excellent). We classified summer as 21 June-20 September, autumn as 21 September-20 December, winter as 21 December-20 March, and spring as 21 March-20 June. We pooled capture methods into 3 classes: free-darted, trapped (e.g., foot snare, culvert trap, horse trailer), and treed. We included 1 black bear that was on the roof of an office building in the treed capture method class. We analyzed whether age, sex, injection site, injection type, or number of attempts to inject had an effect on induction time in black bears using Wilcoxon rank sum tests (R Core Team 2024). We categorized age as adult (\geq 3 yrs old) or juvenile (1–3 yrs old). We pooled injection site into 2 classes: 1) shoulder (including 1 black bear injected in the neck and 1 black bear injected in the flank) and 2) hind leg or rump. We categorized injection type as pole syringe or dart. We determined the number of attempts to inject by counting missed darts and equipment failures (e.g., broken needles, darts that did not discharge properly). To determine if certain injection sites or doses had higher odds of a receiving a

redose, and if certain capture methods had higher odds of a spontaneous arousal occurring, we used odds ratios (R Core Team 2024). We classified doses as 1) dosed appropriately or overdosed (i.e., $\geq 1 \text{ mL}/45.5 \text{ kg}$) and 2) underdosed (i.e., < 1 mL/45.5 kg) using actual mass (if known) or estimated mass. For spontaneous arousal odds ratio analysis, we further classified capture methods into either treed or not treed (e.g., free-darted, trapped). For all analyses, we used an alpha level of 0.05.

RESULTS

Staff immobilized 1 black bear with NalMed-A in 2017, 63 black bears with NalMed-A between 2019 and 2023, and 17 mountain lions with NalMed-A between 2019 and 2024. We included 34 black bears (male = 22, female = 10, undetermined = 2; Table 1) and 7 mountain lions (male = 3, female = 3, undetermined = 1) in our analyses (Table 2). Induction ($\bar{x} \pm SE$) was 10.74 ± 1.16 minutes for black bears (n = 34) and 7.14 ± 1.60 for mountain lions (n = 7). Staff euthanized 6 black bears because of poor condition or human conflicts and 2 mountain lions because of trapping-related injuries or human conflicts. Reversal was 14.21 ± 1.51 minutes for black bears (n = 28) and 10.00 ± 1.26 minutes for mountain lions (n = 5). There was no evidence of a correlation between the time black bears were immobile before antagonists were administered and the time until recovery was complete ($r_s = -0.14$, P = 0.49).

Body condition (n = 31, $H_2 = 3.33$, P = 0.19), season (n = 34, $H_2 = 0.38$, P = 0.83), and capture method (n = 34, $H_2 = 2.94$, P = 0.23) did not affect median induction time in black bears. Age (n = 34, W = 138.5, P = 0.83), sex (n = 32, W = 125.5, P = 0.54), injection type (n = 33, W = 77.5, P = 0.29), and number of attempts to inject (n = 34, W = 60.5, P = 1.00) also did not affect median induction time in black bears. Injection site did have an effect on median induction time in black bears injected in their hind leg or rump had longer median induction time (10 minutes) than black bears injected in their shoulder (6 minutes).

No mountain lions received redoses or experienced spontaneous arousals, but 1 mountain lion had an incomplete immobilization; after 15 minutes, she was still not fully under and was responsive when approached. Six black bears (18%) received redoses. The odds of a black bear that was underdosed receiving a redose was less than a black bear that was dosed appropriately or overdosed receiving a redose, but the odds were not statistically significant (OR = 0.70, 95% CI = 0.07–7.20, P = 1.00). The odds of a black bear injected in its hind leg or rump receiving a redose was 3.75 times the odds of a black bear injected in its shoulder receiving a redose, but the odds were not statistically significant (95% CI = 0.39–36.43, P = 0.37; Figure 2). Six black bears (18%) experienced spontaneous arousals: 2 became alert after falling from trees, 2 stood up and walked short distances following initial handling, 1 exhibited head nodding during initial handling, and 1 climbed down a tree and walked away. The odds of a treed black bear experiencing a spontaneous arousal, but the odds were not statistically significant (95% CI = 0.58–23.03, P = 0.31; Figure 3).

DISCUSSION

Free-ranging black bears immobilized with NalMed-A by non-veterinary personnel in Wyoming had shorter induction and reversal times than published values for free-ranging black bears immobilized with NalMed-A by a wildlife veterinarian in Colorado, USA (Wolfe et al. 2016). Injection site affected median induction time in black bears, but no other situational differences (e.g., season, capture method, injection type, number of attempts to inject) or animal-specific variations (e.g., age, sex, body condition) that we evaluated had an effect. Injection site and initial dose did not affect the odds of a black bear receiving a redose. Wyoming Game and Fish Department staff considered sedation quality to be good for mountain lions and black bears immobilized with NalMed-A, with

Season ^a	Age (yrs)	Sex ^b	Capture method ^c	Injection site ^d	Injection type ^e	Dose ^f	Redose ^g	Induction ^h (minutes)	Reversal ⁱ (minutes)	Arousal ^j
Spring	4	М	т	S	U	DA/O	Ν	6	9	Ν
Autumn	3	М	т	S	D	DA/O	N	11	23	Ν
Spring	1	U	т	H/R	D	DA/O	Ν	5	23	Ν
Summer	2	М	Tr	S	D	DA/O	Y	26	33	Ν
Summer	2	М	т	S	D	DA/O	Ν	4	12	Ν
Summer	2	М	Fr	H/R	D	DA/O	Ν	8	5	Ν
Summer	2	М	Tr	H/R	D	DA/O	Ν	3	21	Ν
Summer	1	М	т	S	D	DA/O	Ν	5	11	Ν
Summer	≥15	F	Fr	H/R	D	DA/O	Ν	12	N/A	Ν
Spring	4	F	Tr	H/R	D	DA/O	Y	10	6	Y
Spring	2	М	Tr	H/R	D	DA/O	Ν	7	26	Ν
Summer	2	М	Fr	S	D	DA/O	Ν	11	8	Ν
Summer	2	М	Fr	S	D	DA/O	Ν	16	N/A	Ν
Summer	2-3	М	т	S	D	DA/O	Ν	4	20	Ν
Summer	≥5	F	Tr	H/R	D	Un	Y	9	N/A	Y
Summer	≥3	М	т	H/R	D	DA/O	Ν	11	13	Ν
Summer	2	М	Fr	H/R	D	DA/O	Y	18	6	Y
Autumn	4	М	т	H/R	D	Un	Ν	8	13	Y
Autumn	1.5	М	т	H/R	D	Un	N	36	N/A	Ν
Spring	2	М	Fr	S	D	DA/O	N	8	7	Ν
Spring	4-5	F	т	H/R	D	Un	N	11	29	Ν
Summer	3	F	т	S	PS	Un	Ν	6	8	Ν
Summer	2	М	Fr	H/R	D	DA/O	N	7	10	Ν
Summer	2	F	т	H/R	PS	DA/O	Ν	10	12	Ν
Summer	3	М	т	H/R	PS	Un	Ν	10	10	Ν
Summer	2	М	Fr	H/R	D	DA/O	Ν	12	N/A	Ν
Spring	4	F	Tr	H/R	D	U	Ν	14	9	Ν
Spring	1	F	Fr	H/R	D	DA/O	Y	10	5	Ν
Spring	1	U	Tr	H/R	D	DA/O	Y	12	13	Y
Summer	1	F	Tr	S	D	DA/O	Ν	5	26	Ν
Summer	1-2	М	Tr	H/R	D	DA/O	Ν	20	N/A	Ν
Summer	1	F	т	H/R	D	DA/O	N	18	10	N

TABLE 1 Summary of data recorded on Wyoming Game and Fish Department (WGFD) wildlife capture forms by WGFD staff during 34 immobilizations of black bears using NalMed-A in Wyoming, USA, in 2017 and 2019–2023.

TABLE 1 (Continued)

Season ^a	Age (yrs)	Sex ^b	Capture method ^c	Injection site ^d	Injection type ^e	Dose ^f	Redose ^g	Induction ^h (minutes)	Reversal ⁱ (minutes)	Arousal
Summer	2	М	Т	S	PS	DA/O	Ν	5	21	Y
Autumn	4	М	т	S	D	Un	N	7	9	Ν

^aSpring (21 Mar-20 June), summer (21 Jun-20 Sep), autumn (21 Sep-20 Dec).

^bFemale (F), male (M), unknown (U).

^cFree-darted (Fr), trapped, such as in a culvert trap or in foot snare (T), treed (Tr).

^dHind leg or rump (H/R), shoulder (S).

^eDart (D), pole syringe (PS), unknown (U).

^fDosed appropriately or overdosed with $\ge 1 \text{ mL}/45.5 \text{ kg}$ (DA/O), unknown (U), underdosed with < 1 mL/45.5 kg (Un). ^gNo (N), yes (Y).

^hTime from when the animal was immobile minus the injection time of NalMed-A.

ⁱTime from when the animal was recovered minus the injection time of antagonists; N/A indicates it is not applicable. ^jAn animal that was deemed immobile suddenly exhibiting voluntary movement before the administration of antagonists; no (N), yes (Y).

TABLE 2Summary of data recorded on Wyoming Game and Fish Department (WGFD) wildlife capture formsby WGFD staff during 7 immobilizations of mountain lions using NalMed-A in Wyoming, USA, 2019–2024.

Season ^a	Age (yrs)	Sex ^b	Capture method ^c	Injection site ^d	Injection type ^e	Dose ^f	Redose ^g	Induction ^h (minutes)	Reversal ⁱ (minutes)	Arousal ^j
Autumn	4-5	F	т	H/R	D	DA/O	Ν	3	8	Ν
Autumn	8+	F	т	H/R	D	DA/O	Ν	15	8	Ν
Spring	U	М	Fr	S	D	U	Ν	8	14	Ν
Winter	3	F	т	H/R	D	DA/O	Ν	10	N/A	Ν
Autumn	2	М	т	H/R	D	DA/O	Ν	4	12	Ν
Winter	0.25	U	т	H/R	D	DA/O	Ν	5	N/A	Ν
Winter	2	М	т	H/R	D	DA/O	Ν	5	8	Ν

^aSpring (21 Mar-20 June), autumn (21 Sep-20 Dec), winter (21 Dec-20 Mar).

^bFemale (F), male (M), unknown (U).

^cFree-darted (Fr), trapped, such as in a culvert trap or in foot snare (T).

^dHind leg or rump (H/R), shoulder (S).

^eDart (D).

^fDosed appropriately or overdosed with \geq 1 mL/45.5 kg (DA/O), unknown (U).

^gNo (N).

^hTime from when the animal was immobile minus the injection time of NalMed-A.

ⁱTime from when the animal was completely recovered minus the injection time of antagonists;

N/A indicates it is not applicable.

ⁱAn animal that was deemed immobile suddenly exhibiting voluntary movement before the administration of antagonists; no (N).

the exception of 1 mountain lion that had an incomplete immobilization and 6 black bears that experienced spontaneous arousals.

Free-ranging black bears immobilized by a wildlife veterinarian in Colorado had induction (n = 25) and reversal (n = 24) times of 16.2 ± 0.9 minutes and 19.0 ± 1.6 minutes, respectively (Wolfe et al. 2016). Comparative induction

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FIGURE 2 Frequencies of black bears receiving redoses by dose (A) and injection site (B) in Wyoming, USA, 2017–2023. We used a recommended dose of 1 mL NalMed-A/45.5 kg body mass.



FIGURE 3 Frequencies of black bears immobilized in Wyoming, USA, 2017–2023, that experienced spontaneous arousals by capture method class. Not treed includes free-darted and trapped black bears.

and reversal times for mountain lions immobilized with NalMed-A have not been published. The mean induction time for free-ranging mountain lions immobilized with NalMed-A in our study was similar to mean induction times reported for free-ranging mountain lions immobilized with ketamine-xylazine (KX; 120 mg ketamine HCl/mL, 20 mg xylazine HCl/mL) in Wyoming (male: 5.0 ± 1.9 minutes, n = 5; female: 6.0 ± 1.9 minutes, n = 9; Logan et al. 1986) and for captive mountain lions immobilized with tiletamine-zolazepam (2 mg/kg), ketamine (1.6 mg/kg), and xylazine (0.4 mg/kg) in lquitos, Peru (10.4 ± 6.4 minutes, n = 5; Lescano et al. 2014). Of these 3 drug combinations, NalMed-A is the only one that contains no controlled substances; NalMed-A also has the advantage of reversibility (with the exception of azaperone). An evaluation of the effect of situational differences or animal-specific variations on induction time in black bears immobilized with NalMed-A has not been reported.

Our study identified that for black bears in Wyoming, injection site affected induction time. Dart placement can affect drug absorption, as drug absorption from areas of large fat deposits is slow and unpredictable; therefore, the

fat deposits around the rump in bears should be avoided (Caulkett and Arnemo 2015, Kreeger and Arnemo 2018). While not statistically significant, the higher odds of black bears injected in their hind leg or rump receiving a redose than black bears injected in their shoulder was also likely due to NalMed-A being deposited in fat stores. Although we did not find a difference in median induction times across seasons, black bears have larger rear fat stores in the autumn than in the spring (Caulkett and Arnemo 2015). One study has reported that mean induction time in captive black bears immobilized with NalMed-A was 2 minutes longer in autumn than in spring (8 minutes and 6 minutes, respectively; Wolfe et al. 2019). Injection type can also affect induction time; injections via pole syringe almost always result in faster inductions than injections via darts, although we did not find evidence of a difference (Kreeger and Arnemo 2018). The impact of darts can also cause tissue injury, including hemorrhage, which reduces drug absorption (Arnemo and Kreeger 2017, Kreeger and Arnemo 2018). We may not have noted a difference in induction times across injection type, in part, because staff used CO₂-powered darts, which inflict less tissue trauma than powder-charged darts (Bush et al. 2012). We were unable to examine the influence of needle length on induction time across injection type, as staff did not record needle length. A study on free-ranging fallow deer (Dama dama) reported faster retrieval times and deeper levels of sedation for fallow deer darted with 40-mm needles than with 30-mm needles (Bergvall et al. 2015). The psychological condition of the animal can also influence induction time, and highly excited animals require higher drug dosages (Kreeger and Arnemo 2018). We had hypothesized that black bears that were free-darted or treed may be more highly excited than those that were trapped; similarly, we thought that black bears that took multiple attempts to inject may be more highly excited than those that were injected successfully on the first attempt because of increased overall pursuit time; however, we did not find evidence of an effect of capture method and number of attempts on induction time.

Other animal-specific variations can also change responses to immobilization. Juvenile animals require more drug for immobilization than do prime-age adults, as do animals in late-stage pregnancy, whereas malnourished animals usually require less drug (Kreeger and Arnemo 2018). All of the black bears we included in our analysis were at least 1 year old, and none were reported to be in late-stage pregnancy or emaciated, which could account for the lack of a difference in induction times across age, sex, and body condition. All black bears were effectively immobilized, but 6 received redoses.

The odds of a black bear that was underdosed receiving a redose was less than a black bear that was dosed appropriately or overdosed receiving a redose, but these odds were not statistically significant. This might suggest that our initial dosage does not need to be increased, and that there are other factors at play for black bears requiring redoses, such as injection type. Of the 6 black bears that received redoses, 3 were injected via pole syringe. Six black bears experienced spontaneous arousals, including 4 that received redoses.

Spontaneous arousal in black bears immobilized with NalMed-A did occur, but otherwise, overall sedation quality in black bears was thought to be good. This is slightly different from previous studies, in that while they considered sedation quality to be good in black bears immobilized with NalMed-A, they also did not publish any arousal events in black bears, and felt it safe to handle and collect samples (e.g., blood) for the duration of the processing period (Wolfe et al. 2016, 2019, Sheldon et al. 2024). There had been no published reports of spontaneous arousals in large carnivores immobilized with NalMed-A, but all previously published work was conducted by wildlife veterinarians with considerable chemical immobilization experience (Wolfe et al. 2016, 2019, Sheldon et al. 2024). When injecting NalMed-A, fat deposits were avoided to ensure consistent drug absorption (Wolfe et al. 2016, Sheldon et al. 2024), and levels of sedation were subjectively monitored and scored throughout the processing period (Wolfe et al. 2016, 2019, Sheldon et al. 2024). The varying levels of chemical immobilization experience and experience with this drug combination, in particular, can vary by WGFD staff and this could have contributed to the differences noted in sedation guality from previous studies. Situational differences may have also played a role, as previous studies used captive black bears (Wolfe et al. 2019, Sheldon et al. 2024), and captive animals generally require lower dosages than free-ranging animals (Kreegar and Arnemo 2018), or free-ranging black bears, in which the majority were trapped and injected via pole syringe, and none of which were specified to have been treed prior to immobilization (Wolfe et al. 2016).

In our study, 2 black bears experienced spontaneous arousals after falling from a tree, likely due to the stimulus caused by impacting the ground, despite attempts to break their fall (e.g., tarps). Aside from the 1 mountain lion that had an incomplete immobilization, WGFD staff reported good sedation quality in mountain lions and felt the animals were safe to handle.

Human safety is the primary consideration when chemically immobilizing animals, particularly large carnivores, and spontaneous arousals can be very dangerous for handlers (Kreeger and Arnemo 2018). Animals immobilized with KM were found to experience spontaneous arousals and be capable of directed attack (Kreeger 2023). A wild adult male European brown bear (Ursus arctos) attacked handlers 78 minutes after being darted with medetomidine (48 μg/kg), ketamine (1.0 mg/kg), and an additional dose of ketamine (1.0 mg/kg) without exhibiting previous signs of arousal (Jalanka and Roeken 1990). One study reported spontaneous arousals in 50% of bobcats (Lynx rufus; n = 12) immobilized with BAM (Jacques et al. 2024). Restraint guidelines have recommended using hobbles for immobilized bears in case of spontaneous arousal. For immobilizations of large felids, the same guidelines have recommended restraining feet with snare pools or by strapping them to a flat surface (e.g., stretcher) as a backup mechanism if the animal should spontaneously arouse (Shury 2014). Wedgewood Pharmacy, owner of ZooPharm, has issued dosage guides for both BAM and NalMed-A. The BAM dosage guide includes a disclaimer to use extreme caution when anesthetizing carnivores as immobilization can be dangerous for handlers and certain species have feigned a response to anesthesia; the NalMed-A dosage guide does not include such a disclaimer in package inserts (Wedgewood Pharmacy, Swedesboro, NJ, USA). When possible, black bears that experienced spontaneous arousals were redosed and physically immobilized further (with hobbles and a muzzle). If a redose was not possible, animals were physically immobilized further, reversed, and released.

Because 18% of black bears immobilized with NalMed-A experienced spontaneous arousals, including 3 out of 9 treed black bears, we recommend certain considerations when using this drug combination. Limitations of our study included small sample sizes, which required that we run less powerful statistical analyses for black bears, and a biased sex ratio for black bears. Because of our small sample sizes for mountain lions, additional research into the safety and effectivity of NalMed-A in this species is recommended. As a retrospective study, we were also limited to the data recorded by field personnel, which did not include needle length.

MANAGEMENT IMPLICATIONS

Our findings support previous recommendations to avoid fat deposits around the rump of bears during chemical immobilization, as drug absorption from these sites is slow and unpredictable. Due to the risk of spontaneous arousals, we recommend using hobbles and a muzzle for large carnivores immobilized with NalMed-A. We also recommend minimizing the potential for stimulation of treed black bears by trying to gently lower them from a tree versus allowing them to fall from any distance. Wildlife managers should also take into consideration the potential for spontaneous arousals in large carnivores in public settings where there are additional human safety concerns.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

ETHICS STATEMENT

Data used in this study were obtained from existing records of routine management actions by Wyoming Game and Fish Department staff. This study did not involve handling or observation of animals by the authors, and we did not require animal care protocols.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

- Arnemo, J. M., and T. J. Kreeger. 2017. Commentary on Costa et al.: "Influence of ambient temperature and confinement on the chemical immobilization of fallow deer (*Dama dama*)". Journal of Wildlife Diseases 53:699-700.
- Bergvall, U. A., P. Kjellander, P. Ahlqvist, Ö. Johansson, K. Sköld, and J. M. Arnemo. 2015. Chemical immobilization of free-ranging fallow deer (*Dama dama*): effect of needle length on induction time. Journal of Wildlife Diseases 51: 484-487.
- Bush, M., S. B. Citino, and W. R. Lance. 2012. The use of butorphanol in anesthesia protocols for zoo and wild mammals. Pages 596–603 in R. E. Miller and M. E. Fowler, editors. Fowler's zoo and wild animal medicine, volume 7. Elsevier, St. Louis, Missouri, USA.
- Caulkett, N. A., and J. M. Arnemo. 2015. Comparative anesthesia and analgesia of zoo animals and wildlife. Pages 764–776 in K. A. Grimm, L. A. Lamont, W. J. Tranquilli, S. A. Green, and S. A. Robertson, editors. Veterinary anesthesia and analgesia, fifth edition. Wiley Blackwell, Ames, Iowa, USA.
- Drug Enforcement Administration. 2020. Drugs of abuse: a DEA resource guide. 2020 edition. U.S. Department of Justice, Washington, D.C., USA.
- Jacques, C. N., R. W. Klaver, C. S. DePerno, and A. P. Rockhill. 2024. Comparing the efficacy of two immobilization drug combinations for the chemical restraint of bobcats (*Lynx rufus*). Journal of Wildlife Diseases 60:86-94.
- Jalanka, H. H., and B. O. Roeken. 1990. The use of medetomidine, medetomidine-ketamine combinations, and atipamezole in nondomestic mammals: a review. Journal of Zoo and Wildlife Medicine 21:259-282.
- Kreeger, T. J., and J. M. Arnemo. 2018. Handbook of wildlife chemical immobilization. Fifth edition. Published by authors.
- Kreeger, T. J. 2023. Chemical immobilization of furbearers. Pages 17.1–17.24 in T. L. Hiller, R. D. Applegate, R. D. Bluett, S. N. Frey, E. M. Gese, and J. F. Organ, editors. Wild furbearer management and conservation in North America. Wildlife Ecology Institute, Helena, Montana, USA.
- Lescano, J., M. Quevedo, L. Baselly, A. Crespo, and V. Fernández. 2014. Chemical immobilization of captive cougars *Puma concolor* (Linnaeus, 1771) (Carnivora: Felidae) using a combination of tiletamine-zolazepam, ketamine, and xylazine. Journal of Threatened Taxa 6:6659-6667.
- Logan, K. A., E. T. Thorne, L. L. Irwin, and R. Skinner. 1986. Immobilizing wild mountain lions (*Felis concolor*) with ketamine hydrochloride and xylazine hydrochloride. Journal of Wildlife Diseases 22:97-103.
- R Core Team. 2024. R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.
- Sheldon, J.D., Z. Xiaojuan, R. Williamson, and C. Blair. 2024. Butorphanol-azaperone-medetomidine is as safe and effective as nalbuphine-azaperone-medetomidine for immobilization of juvenile American black bears (Ursus americanus). Journal of Wildlife Diseases 60:188-192.
- Shury, T. 2014. Physical capture and restraint. Pages 109–124 *in* G. West, D. Heard, and N. Caulkett, editors. Zoo animal and wildlife immobilization and anesthesia, second edition. John Wiley and Sons, Ames, Iowa, USA.
- Western Regional Climate Center. 2023. Climate of Wyoming. https://wrcc.dri.edu/Climate/narrative_wy.php. Accessed 21 Dec 2023.
- Williamson, R. H., L. I. Muller, and C. D. Blair. 2018. The use of ketamine-xylazine or butorphanol-azaperone-medetomidine to immobilize American black bears (Ursus americanus). Journal of Wildlife Diseases 54:503-510.
- Wolfe, L. L., W. R. Lance, D. K. Smith, and M. W. Miller. 2014. Novel combinations of nalbuphine and medetomidine for wildlife immobilization. Journal of Wildlife Diseases 50:951-956.
- Wolfe, L. L., H. E. Johnson, M. C. Fisher, W. R. Lance, D. K. Smith, and M. W. Miller. 2016. Chemical immobilization in American black bears using a combination of nalbuphine, medetomidine, and azaperone. Ursus 27(1):1-4.

- Wolfe, L. L., M. E. Wood, M. C. Fisher, and M. A. Sirochman. 2019. Evaluation of chemical immobilization in captive black bears (*Ursus americanus*) receiving a combination of nalbuphine, medetomidine, and azaperone. Journal of Wildlife Diseases 55:84-90.
- Wyoming Game and Fish Department. 2006. Mountain lion management plan. Wyoming Game and Fish Department, Trophy Game Section, Lander, USA.
- Wyoming Game and Fish Department. 2007. Wyoming black bear management plan. Wyoming Game and Fish Department, Trophy Game Section, Lander, USA.
- Wyoming Game and Fish Department. 2017*a*. Wyoming state wildlife action plan: III. Montane and subalpine forest. Wyoming Game and Fish Department, Habitat Section, Cheyenne, USA.
- Wyoming Game and Fish Department. 2017b. Wyoming state wildlife action plan: III. Xeric and lower montane forest. Wyoming Game and Fish Department, Habitat Section, Cheyenne, USA.

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