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The Use of Trazodone Hydrochloride to Reduce Stress in Dogs During the Transition Period into a Municipal Animal Shelter: Impact on Incidence of Illness, Length of Stay, and Outcome

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The Use of Trazodone Hydrochloride to Reduce Stress in Dogs During the Transition Period into a Municipal Animal Shelter: Impact on Incidence of Illness, Length of Stay, and Outcome

by

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Abstract

Companion dogs housed in animal shelters are subject to a great number of uncontrollable and unalterable stressors. To combat these stressors and the associated immunosuppression that creates high contagious illness rates in sheltered dogs, a large open admission municipal animal shelter in New York City introduced trazodone hydrochloride as an anxiolytic to transitional stress. This pilot study had additional goals of reducing length of stay and increasing live outcome rates. Dogs were given low doses of trazodone at intake (5 mg/kg), one to two doses within 48 hours of arrival, and illness rates calculated for the months of November and December 2018 at the shelter's Brooklyn and Manhattan Care Center locations. These months were compared to the same months in 2017 and 2016, serving as a pre-trazodone baseline, using Pearson chi-square and independent samples t-tests. A statistically significant decrease was found between baseline 2016/2017 and trazodone pilot 2018, χ^2, (1, N = 1774) = 19.3, $p < .000$. Illness rate dropped from 41% in the baseline to 29% with trazodone. A statistically significant decrease in length of stay was found for 2018 (M = 7.44, SD = .25), $t(1772) = 2.75$, $p = .006$, compared to the 2016/2017 baseline (M = 10.48, SD = 1.22). Moreover, a significant difference was observed in adoption rates between 2016/2017 and 2018, χ^2, (1, N = 1774) = 18.7, $p < .000$, wherein average adoption rate increased from 30.5% in 2016/2017 to 42% in 2018. While correlational, the preliminary results of this study suggest that trazodone may be effective in decreasing transitional stress in dogs in a shelter setting and, thereby, decreasing illness rates and increasing adoption rates.

Domestic dogs have been humans' companions for thousands of years (Bradshaw, 2011), yet they have been historically underrepresented in scientific literature. There has been a recent increase in studies focusing on dog cognition and behavior but overall, very little consideration has been given from a welfare perspective (Beerda, Schilder, van Hooff, de Vries, & Mol, 1998; Hilby, Rooney, & Bradshaw, 2006). One reason for this may be that welfare is exceptionally difficult to study in a controlled setting, particularly in an animal shelter. Shelters are typically overpopulated, understaffed, and stretched for resources. Hours are limited and the overwhelming concern at all times is the welfare of the resident animals; ironically setting aside time to *study* welfare diminishes time that could be spent providing enrichment and working hands-on to improve individuals' quality of life. While improvements regarding the welfare of confined animals have been made during recent decades (Fraser, 2008), it is essential to evaluate interventions in real-world situations, within the hectic, perpetually over- or under-stimulated shelter environment.

Literature Review

A 2016 survey by the American Society for the Prevention of Cruelty to Animals found that about 4 million dogs enter a system of approximately 13,000 shelters nationwide (Protopopova & Gunter, 2017). On average, across the country, these shelters have a collective euthanasia rate of 30% (Gunter, Barber, & Wynne, 2016; Protopopova & Gunter, 2017). Efforts are being made to decrease euthanasia rates nationally through adoption promotions, focus on surrender prevention, and improving housing, care, and welfare in shelters. High stress levels in shelters can increase illness levels and negatively impact behavior, both of which increase the

risk of euthanasia. Thus, finding a way to reduce these stress levels is essential as shelters look to decrease euthanasia rates and increase placement rates.

Animal shelters are known to cause distress for all pets, even the most well-adjusted, due to the myriad new and typically uncomfortable situations they experience. Anxiety, phobias, heightened arousal, and distress are among the most commonly-reported behavior issues for dogs, and those are all exacerbated in a shelter setting (Gruen & Sherman, 2008). Anxious temperaments in combination with a stressful environment can lead to additional medical issues, including chronic idiopathic large-bowel disease (Hekman, Karas, & Sharp, 2014). Conflicts, stress, and frustration caused by the physical and social environment can lead to undesirable behaviors and stereotypies in the shelter, decreasing the likelihood of adoption (Hennessy, 2013; Kuhne, Hossler, & Struwe, 2014; Shiverdecker, Schiml, & Hennessy, 2013).

Because of this, animal shelters are faced with constant welfare challenges as dogs experience a jarring loss of control over their situations (Hennessy, 2013; Shiverdecker et al., 2013). Dogs are separated from their attachment figures (familiar human and nonhuman animals) (Hennessy, Davis, Williams, Mellott, & Douglas, 1997; Hennessy, 2013; Protopopova, 2016; Shiverdecker et al., 2013). They experience severe social isolation, often housed in individual kennels with limited interaction (Beerda, Schilder, van Hooff, de Vries, & Mol, 1999b; Coppola, Grandin, & Enns, 2006; Hennessy et al., 1997; Hennessy, 2013; Protopopova, 2016; Wells, 2004). In addition to social isolation, dogs experience radical spatial restriction. Confined to small areas, their movement is limited and their new living spaces foreign and often austere (Beerda et al., 1999b; Protopopova, 2016; Shiverdecker et al., 2013). Social and spatial restriction has been found to change behavior (heightened excitability, increased aggressive

behaviors, withdrawal, lethargy) and to increase cortisol levels (Beerda et al., 1999b; Wells, 2004). Their routines are disrupted, and housetrained dogs are suddenly left with no alternative but to eliminate in their living areas (Hennessy, 2013). Many facets of their new environment are novel and unpredictable (Coppola et al., 2006; Hennessy et al., 1997; Hennessy, 2013; Shiverdecker et al., 2013). Noises and odors in the shelter are persistent, uncontrollable, and often threatening (Hennessy, 2013; Shiverdecker et al., 2013). All of these factors contribute to diminished welfare for dogs in a shelter environment (Beerda, Schilder, van Hooff, & de Vries, 1997; Protopopova, 2016).

The stressful shelter environment means dogs typically need time to adjust to their new surroundings in order to feel comfortable enough to behave in their normal manner (Bollen & Horowitz, 2008). However, shelter staff are tasked with making quick decisions about placement options, suitability for adoption, and medical conditions, sometimes with just a single interaction and long before there is an opportunity to get to know a dog's personality, temperament, and full behavioral repertoire. This situation is intensified in open admission shelters (typically municipal or animal control facilities), which must accept all animals regardless of available space, behavior, or medical concerns. For dogs brought into these shelters, there is additional urgency to limit length of stay both due to high daily intake numbers and in order to minimize environmental stress. This can be in conflict with allowing each individual dog sufficient adjustment time. Dogs and their shelter caretakers are also under pressure to make connections with potential adopters; however, individual housing and other shelter stressors can encourage behaviors adopters find undesirable, like sitting at the back of the kennel (Wells, 2004), barking, and disengaging. Adopters, on the contrary, are looking for dogs who are quiet, alert, and at the

front of the kennel (Wells, 2004). This pressure and conflict challenges both the welfare of the resident animals and the humans attending to them.

As shelters are rife with uncontrollable stressors upon a dog's arrival, dogs in animal shelters and in veterinary hospitals show behavioral and psychological signs of both acute and chronic psychogenic stress as a result of unpredictability, novelty, confinement, isolation, and invasive procedures (Gilbert-Gregory, Stull, Rice, & Herron, 2016; Hennessy, 2013). Therefore, one way to begin to combat the welfare challenges is to address animal stress within the shelter environment. Stress represents a sequence of events in which a stimulus causes a stress perception reaction in the brain. When triggered, the body's sympathetic (fight-or-flight) response and/or the hypothalamic-pituitary-adrenal (HPA) system is activated (Dhabhar, 2009; Glaser & Kiecolt-Glaser, 2005). The body enters a distressed state when homeostasis cannot be restored. This sequence has been found to have adverse effect(s) on health, specifically, physical and mental suffering (Hekman et al., 2014), as it represents a physical or psychological challenge to the body's homeostasis (Dhabhar, 2009; Hekman et al., 2014). Chronic stress can lead to a dysregulation of the HPA system and suppression of the immune system (Dhabhar, 2009; Hennessy, 2013; Shiverdecker et al., 2013). Psychogenic and physical stressors abound in a shelter setting: novelty, routine disruption, unpredictability, and loss of control (Hennessy et al., 1997; Hennessy, Williams, Miller, Douglas, & Voith, 1998; Hennessy, 2013; Protopopova, 2016). Psychogenic stress is recognized to negatively impact cardiovascular function in humans and in laboratory animals, while acute social stress has been found to elicit atrial fibrillation in humans and increase T-wave alternans (a sign of electrical instability) in dogs (Hekman, et al., 2014; Kovach, Nearing, & Verrier, 2001). The stress response increases susceptibility to and

severity of infection while decreasing vaccine immune response and slowing wound healing (Glaser & Kiecolt-Glaser, 2005). This response can also reactivate latent herpesvirus, cause gastrointestinal distress, and amplify production of pro-inflammatory cytokines associated with multiple age-related illnesses (Dhabhar, 2009; Glaser & Kiecolt-Glaser, 2005; Hekman et al., 2014).

Measuring animal welfare, specifically stress, is particularly challenging. No single parameter has yet been found to accurately gauge wellbeing (Hilby et al., 2006). Therefore, research evaluating shelter animal welfare has utilized both behavioral and physiological methods. Behavioral measures include those thought to be associated with anxiety, such as pacing and other locomotion, vocalization, fleeing, panting, lip licking, and shaking (Gilbert-Gregory et al., 2016). Physiologic measures include cortisol (plasma, salivary, and urinary), typically as a reflection of HPA axis hormones; salivary immunoglobulin A; neutrophil-to-lymphocyte ratio; and heart rate variability (Gilbert-Gregory et al., 2016; Hennessy, 2013). While neither measure is without its limitations, the findings from both behavioral and physiologic assessments suggest that intervention in the first few days within the new shelter environment is critical for a dog's success in a shelter (Hennessy et al., 1997).

Behavioral measures can be problematic as behaviors are non-specific and represent an indirect marker of distress (Hekman et al., 2014). In a shelter setting, where subjects have limited known history, behavioral measures can be unreliable as no behavioral baseline has been established for individual dogs. In situations where history is reported, the reports are subjective based on the individual making the observations. Thus, changes in behavior seen in the shelter may appear more subtle or magnified, and assessments may include some amount of guesswork.

Behavior in a shelter setting is notoriously capricious when compared to behavior in a stable, comfortable environment (Bollen & Horowitz, 2008; Haverbeke, Pluijmakers, & Diederich, 2015; Patronek & Bradley, 2016). Behavioral responses to stress can vary between dogs, and can be difficult for humans to interpret, suggesting that additional measures must be used to provide sufficient information (Beerda et al., 1998; Hekman et al., 2014). In addition, observational behavior studies often rely on feedback from owners. However, owner ratings have been shown to be susceptible to pre-existing beliefs and the placebo effect (Gruen, Roe, Griffith, & Sherman, 2017), thus clouding the ability to gauge true efficacy.

Glucocorticoid levels are a common welfare measure, but chronic stress causes dysregulation of the HPA axis, so glucocorticoid measures can become difficult to interpret (Hennessy et al., 1997; Hennessy, 2013). Social and spatial restriction has been shown to increase cortisol levels, increase HPA activity, and over time to decrease HPA responsiveness (Beerda, Schilder, Bernadina, van Hooff, de Vries, & Mol, 1999a; Hennessy et al., 1998). Cortisol levels are routinely found to be elevated in shelter settings, with plasma adrenocorticoid levels found to be raised after as little as 4 hours in a novel environment (Hennessy et al., 1997). Cortisol is increased over the first three days in a shelter setting, and this increase is three times higher than the cortisol level of a dog in their own home. Levels appear to begin to drop after day three (Coppola et al., 2006; Hennessy, 2013; Hennessy et al., 1997; Protopopova, 2016; Shiverdecker et al., 2013). While heavily represented in the studies reviewed here, cortisol poses problems as a measure of welfare (Beerda et al., 1999a; Coppola et al., 2006; Hekman et al., 2014; Hennessy, 2013; Hennessy et al., 1997; Hilby et al., 2006; Protopopova, 2016; Shiverdecker et al., 2013). Collection methods are often intrusive if not also invasive, and the

collection method itself can artificially influence the level. Cortisol is not specific to welfare or stress, but rather is produced during sustained physical and/or psychological arousal (Hekman et al., 2014; Hilby et al., 2006). Cortisol also shows a high level of variation both between individuals and within an individual (Hekman et al., 2014).

Despite millions of dogs entering shelters each year, canine welfare and stress studies tend toward case studies and small data sets. Five studies looking at anxiety levels as a result of specific stimuli and/or as a result of intervention between 1998 and 2017 had subject group sizes ranging from 10 to 120 dogs. Some studies looked at dogs in animal shelters, and others used owned dogs in veterinary hospitals (Beerda et al., 1998; Hilby et al., 2006; Gruen et al., 2017; Gruen & Sherman, 2008; Gilbert-Gregory et al., 2016). Frequently, dogs displaying the potential to aggress towards a human, dogs who were overtly fearful, and dogs from certain breeds with a reputation for aggression have been eliminated from study pools (Hennessy et al., 1997). While human safety is – and should always be – of utmost concern, removing dogs with these typically fear-based behaviors eliminates an important population within an average animal shelter, likely representing those with the poorest welfare.

Shelters have been actively trying to ameliorate this stress over recent decades. Following in the footsteps of zoological societies by recognizing the need for confined animals to have enriched environments and the ability to practice natural behaviors (Wells, 2004), shelters have been implementing enrichment that appeals to the different senses – food items, toys, conspecific social time, exciting and relaxing smells, music, and human interaction (Wells, 2004). While these enhancements have improved welfare overall, studies have not always found a robust response to these enrichment types. Toys are a common addition to the kennel, thought to

encourage curiosity, comfort, and play behavior. However, studies are, at best, split on the effect. Some indicate that toys can positively influence behavior and increase activity but others find that dogs in shelter settings show limited interest in toys, having no impact aside from possibly making the kennel appear more inviting to human visitors (Protopopova & Gunter, 2017; Wells, 2004; Wells & Hepper, 2000). Adult dogs have also been found to habituate quickly to toys. To be effective they require continuous rotation (Wells, 2004). Therefore, auditory and olfactory forms of enrichment hold promise. Lavender, chamomile, and synthetic dog-appeasing pheromone (DAP) have been found to have a positive effect on behavior in shelter, as has classical music (Wells, 2004). However, additional research is needed to address the impact of these types of enrichments (Hennessy, 2013). Overall, environmental enrichment appears to be of value, but a value that is not yet reliably or consistently quantifiable. An enrichment program also requires significant human effort, time, and attention, and is at the mercy of a shelter's available resources.

Pharmacologic interventions have been suggested as a way to improve wellbeing and decrease stress, particularly when other enrichment and socialization programs have already been instituted. Studies have pointed out the need for a fast-acting oral anxiolytic that can alleviate the stress itself and protect mental wellbeing, rather than just diminishing the physical signs of stress, when dogs are hospitalized or otherwise confined (Gilbert-Gregory et al., 2016; Hekman et al., 2014). Moderating the initial stress response may help prevent the risk of chronic stress activation and system dysregulation (Hennessy 2013). Further exploration is needed to determine how viable this intervention may be and which medications may fill the role, but one that is appearing with some frequency in veterinary settings is trazodone hydrochloride (trazodone).

Trazodone is an atypical antidepressant that has been used in human medicine since 1966 (Gruen et al., 2017; Gruen & Sherman, 2008). Atypical antidepressants are multi-modal, showing multiple mechanisms of action (Betti, Palego, & Giannaccini, 2018). Classified as a serotonin receptor antagonist and reuptake inhibitor (SARI), trazodone is primarily a serotonin 2A postsynaptic receptor antagonist, and secondarily a presynaptic serotonin reuptake inhibitor (Ciribassi & Ballantyne, 2014; Gruen & Sherman, 2008). At lower doses it acts with its primary mechanism of action only; at higher doses, the secondary mechanism is added (Gruen et al., 2017). The exact dosage breakpoint for this mechanism change in dogs is not yet precisely known (Gruen et al., 2017). In humans, trazodone is used to treat major depressive disorder (MDD), which has symptoms including depression, lethargy, disturbed sleep or appetite, and reduced concentration (Fagiolini, Comandini, Dell'Osso, & Kasper, 2012; Zhang et al., 2014). Trazodone is also used in veterinary medicine, indicated to treat anxiety and stress and to induce calm behavior in dogs and cats (Gruen et al., 2017). Trazodone has a high bioavailability with oral dosing, a wide dose range, is well tolerated, and has few side effects (Gruen et al., 2017; Gruen & Sherman, 2008). Published dosage ranges for oral administration are 1.7 to 19.5 mg/kg daily, dosed every 8 to 24 hours, or 2 to 10 mg/kg up to every 8 hours when dosed 'as needed' (Ciribassi & Ballantyne, 2014; Gilbert-Gregory et al., 2016). Daily trazodone is commonly used in dogs diagnosed with generalized anxiety disorders, while 'as needed' usage is for dogs experiencing intermittent anxiety or who have a clear anxiety trigger (ex. thunderstorm phobia) (Gruen & Sherman, 2008).

There are no studies known to this researcher that have been published or even planned on the effect of trazodone administration at the time of intake to a shelter to mitigate stress and

decrease illness rates. There is considerable support for such investigation thanks to anecdotal success stories, yet only two scientific studies on the effect of trazodone as a single agent have been conducted and thus far, results are inconclusive at best. A 2016 study of dogs, also in a veterinary hospital setting, found a reduction in some frenetic stress-related behaviors (lip licking, panting, and whining), but not in freeze or fractious behaviors (Gilbert-Gregory et al., 2016). A 2017 study looked at trazodone's ability to maintain calm behavior in dogs postoperatively; no significant difference was found in its efficacy against a placebo (Gruen et al., 2017).

In 2018, Animal Care Centers of NYC (ACC), a New York City animal shelter, embarked on a pilot study utilizing trazodone as an anti-anxiety medication to ease the transition period into the shelter environment. This is a jarring transition for most dogs where everything they were comfortable with and in control of is removed and novelty is ubiquitous. Careful review of medical and shelter operations policies and procedures have taken place over recent years to reduce illness levels and increase adoption rates at ACC. Dogs diagnosed with a contagious respiratory illness, categorized at ACC as canine infectious respiratory disease complex (CIRDC) and commonly referred to as "kennel cough," are given a veterinary examination and antibiotics, and moved to an isolated room away from apparently healthy dogs, where handlers wear personal protective equipment (disposable gowns, gloves, and shoe covers) during interactions. All kennels for all dogs are cleaned daily with Rescue® disinfectant cleaner (https://rescuedisinfectants.com/), healthy dogs cleaned before sick dogs. In spite of these careful steps, contagious illness remains high, likely due to increased stressors on the immune system in combination with the presence of an increased viral load and exposure to novel germs.

ACC has a large staff behavior team focused on providing in-kennel enrichment and out-of-kennel socialization and playgroup sessions to keep dogs as engaged as possible during their time in care. The enrichment program includes walks, conspecific playgroups, individual socialization sessions, basic cue training, clicker training, classical music playing throughout the kennel rooms, quiet lights out time overnight, scent enrichment (lavender, DAP, predator and prey urine), food enrichment (food puzzles, ice blocks, hollow items stuffed with food and frozen), long lasting chews (bones, cow and pigs' ears, bully sticks, rawhides), and toys.

In their continued mission to further increase placement rates and reduce illness, having already addressed the simpler and more obvious obstacles, ACC began looking to pharmacological interventions. In 2018, ACC's Senior Director of Veterinary Services, after discussion with other prominent shelter veterinarians and researchers, decided to pilot the administration of trazodone doses at the time of intake. Trazodone is commonly used in shelter settings for stress relief, though its typical use is long-term for dogs who begin showing signs of kennel stress and behavioral deterioration after being housed in a kennel environment for a period of time.

The objective behind the current study is to evaluate the impact of trazodone hydrochloride administered over the first 48 hours of a dog's arrival at a large municipal animal shelter in New York City. For shelters like ACC who have made great strides in addressing overall welfare practices and have attended to the clearest, easiest, and most direct sources of contagion in a shelter, pharmacological intervention is a logical next step to reduce illness rates and stress levels.

Hypotheses

Based upon ACC's designed and conducted pilot study, it was hypothesized that:

1. The administration of trazodone to dogs during the transition period would result in a decreased number of dogs diagnosed with CIRDC during their stays.
2. The administration of trazodone to dogs during the transition period would result in a decreased average length of stay.
3. The administration of trazodone to dogs during the transition period would result in increased placement and decreased euthanasia outcomes.

Method

Participants: Species. Domestic dogs, *Canis lupus familiaris*. The sample was determined by the population of dogs in the shelter during the designated months. All breeds and breed mixes, ages, and sexes were included. A total of 2,734 dogs' records were reviewed, and 1,774 dogs' records were included in the final analysis. Of these 1,774 records, the 2016/2017 baseline includes 1,364 total dogs and 560 sick dogs, and the 2018 trial of dogs receiving trazodone includes 410 total dogs and 119 sick dogs.

Facilities: Animal Care Centers of NYC (ACC). ACC is New York City's only open admission animal shelter, a combination municipal shelter with a city contract and 501(c)(3) non-profit that offers a range of community services including pet intake, stray intake, bite quarantine, legal hold, surrender prevention, owner requested euthanasia, community pet clinics, field pickups and emergency calls, and adoption, along with foster and volunteer programs. ACC has two large full-service care centers (in Manhattan and Brooklyn), one small full-service care

center (Staten Island), two resource centers (Bronx and Queens), and an administrative headquarters in downtown Manhattan. Each full-service care center has a medical team to care for all resident animals, and all dogs are given veterinary examinations, parasite control, vaccinations, microchips, and spay or neuter surgery during their stay. ACC houses and adopts out dogs, cats, and rabbits, but accepts any animal of any species, behavior, and medical condition. ACC is contracted to take in animals from all five boroughs. ACC's 2018 total intake was 23,095 animals; 2017 intake was 23,501 and in 2016 intake was 29,536. ACC's 2018 placement rate (sometimes referred to as "live release rate") was 92.5% (from ACC's January 23, 2019 Board Meeting Presentation, https://www.nycacc.org/sites/default/files/pdfs/boardmeetings/ACC%20Board%20Presentation%20Jan%2023%202019.pdf). ACC has a stated mission of ending animal homelessness in NYC.

All dogs were housed per ACC practices and policies. Dogs are housed individually in metal Shor-Line kennels of varying sizes. When space allows, all dogs are given double kennel housing by opening transfer doors between kennels. In this arrangement, dogs are given their beds (typically Kuranda beds with a blanket on top) and their food and water bowls on one side, with the other side left open for moving around and eliminating. When space does not allow, transfer doors are closed as needed and dogs given only a single kennel side with a bed and food/water bowls. Meals are fed twice daily, at 6am and 6pm. Toys and other in-kennel enrichment are provided. Dogs are walked throughout the day by staff and volunteers; frequency and duration of walks is based on each dog's individual needs and behaviors. This study did not request any changes made to any dog's housing, treatments, enrichment, or movements through the shelter.

Procedures

The trazodone pilot began in June 2018, during which time the experimental group received the pharmacological intervention of trazodone. In years 2016 and 2017 no trazodone was administered and thus served as a pre-trazodone baseline. All dogs received two doses of trazodone during their transition period into the shelter, determined to be the first 48 hours in the new location. All trazodone doses used during this trial were prescribed by licensed veterinarians at 5mg/kg by mouth, the first dose given by the medical team as close to a dog's arrival as possible, and a second dose given the following morning (*source: ACC Internal Memorandum).* The decision was made to include only dogs with lengths of stay of four or more days in the final data set. Analyzing exclusively the data of dogs in the shelter for more than three days allowed us to focus on the period immediately following that transition period to evaluate effect. We did not feel we could adequately evaluate effect on dogs who were in care for a shorter period, so their inclusion would have distracted from the focus of the study by impacting average lengths of stay and illness rates.

Data on the pilot's procedural success (dates trazodone given, illness and outcome rates) were collected in June, July, and August 2018 when the trazodone was initially introduced, but no data from these months are included in this study because this time was used to streamline the implementation of the trazodone policy and to evaluate the data collection process. November and December were selected as the months to be evaluated each year.

Intake spreadsheets were created by running intake reports in either the Chameleon (2016) or the Shelter Buddy (2017 and 2018) database. The databases contained the same essential information for each animal, but in October 2017 ACC changed its record-keeping

system from the former to the latter. Reports included all dogs who came directly into the Brooklyn and the Manhattan Care Centers from November 1 through December 31 for each of the three years, live intakes only, from all sources, all intake reasons, and all jurisdictions. Each list was exported to Excel and the data sorted by intake date. For situations involving repeated stays in the care center, first stays were included and subsequent stays excluded if the dog was out of the care center for less than 20 full days. This amount of time allowed for the development and treatment of CIRDC should it appear and/or reappear post-adoption. Dogs diagnosed with CIRDC in-shelter remained available for adoption per ACC protocols, and after diagnosis sick dogs were often added to ACC's "at risk list," which may or may not facilitate a more urgent placement.

For all dogs meeting the inclusion criteria, each dog's name, unique identification number, intake date, behavior assessment determination, CIRDC diagnosis date, outcome type, and exit date was pulled from the database and recorded on the Excel spreadsheet. Outcome types include public adoption ("adopted"), placement with a rescue group partner ("placed"), movement into an ACC foster home ("foster"), reunification with the owner ("reclaimed"), and euthanasia for medical and/or behavioral reasons ("euthanized"). Additionally, for November and December 2018, the dates of the first and second trazodone doses were recorded for each dog. Cleaning the collected data produced the final data sets (see Table 1). The data from these final data sets were used to calculate the total number of dogs tracked for each month in each location, total number diagnosed with CIRDC, average length of stay, and outcome.

Table 1

Final Group Sizes

Year	Month	Shelter location	Total records reviewed	Final sample size (all)	Final sample size (sick)
2016	November	Brooklyn Care Center	186	133	65
2016	November	Manhattan Care Center	289	197	81
2016	December	Brooklyn Care Center	261	204	98
2016	December	Manhattan Care Center	296	217	80
2017	November	Brooklyn Care Center	210	147	51
2017	November	Manhattan Care Center	206	145	65
2017	December	Brooklyn Care Center	224	159	50
2017	December	Manhattan Care Center	224	162	70
2018	November	Brooklyn Care Center	216	91	30
2018	November	Manhattan Care Center	223	111	33
2018	December	Brooklyn Care Center	170	86	22
2018	December	Manhattan Care Center	229	122	34

Data Analysis

Data sets were created using Microsoft Excel and data were analyzed with IBM *SPSS* 25. Pearson chi-square tests were run for the count data and an independent samples t-test (two-tailed) was run for the data looking at averages. The assumptions of independent observations, normality, and homogeneity were met for the parametric t-test. The alpha level was .05, but in

cases of multiple comparisons a Bonferroni correction was used to reduce the risk of type 1 error. This correction decreased the alpha level to .01.

Results

Trazodone Dosing

For the trazodone pilot months of November and December 2018, the ideal scenario followed the protocol as determined by the senior medical director: first dose on the day of intake, second dose the following morning. However, due to the real world constraints of an active shelter, not all dogs coming into the care center received doses on this schedule. Exam delays caused some dogs to receive their first doses on their second or even third day in the care center. Additionally, some dogs did not receive or consume a second trazodone dose. Multiple types of high-value treats and foods were used to encourage consumption, but if the dog did not eat their second dose this was recorded as a missed dose. Ultimately the decision was made to consider three different dosing scenarios: ideal (as per protocol); dogs with a delayed first dose but who still received two doses within 48 hours of arriving at the shelter; and dogs who received one dose on day one in the shelter but did not receive or refused to eat a second dose. See Table 2 for the descriptive data. A Pearson chi-square test run to compare the three schedules found no significant difference amongst the different methods of dosing, χ^2, (2, N = 410) = .49, p = .784. Therefore, all three of these schedules were included in the trazodone pilot data set.

Table 2

Final Descriptive Data for Trazodone Dosing Schedules

2018	Sick	Not sick	Total	Percent sick
Ideal, 2 doses	69	158	227	30.40
Delayed, 2 doses	16	41	57	28.07
1 dose on day 1	34	92	126	26.98

Illness Rate

To evaluate whether a significant difference in illness rate existed between the Manhattan and Brooklyn shelters in the baseline years (2016/2017) compared to 2018, a Pearson chi-square test was conducted. No significant difference was observed, χ^2 (1, N = 1774) = 2.0, p = .16. Therefore, data for the two shelters were combined as a baseline.

To evaluate whether a significant change in illness rate occurred in the baseline years (2016/2017) compared to the trazodone pilot (2018), a Pearson chi-square test was conducted. Table 3 includes group sizes for the baseline and trazodone years. A significant drop in illness rates during the trazodone trial was observed, χ^2 (1, N = 1774) = 19.3, p < .000. The average rate of illness in the baseline years was 41.1%; during 2018, when the trazodone administration was introduced, illness rate dropped to 29%.

Table 3

Group Sizes for Baseline and Pilot

Years	Number Sick	Number Not sick	Total	Percentage Sick
Baseline 2016/2017	560	804	1364	41.1
Trazodone pilot 2018	119	291	410	29.02

Length of Stay

To evaluate changes in length of stay, the baseline years were compared to 2018 (using the descriptive data presented in Table 2). An independent samples t-test (two-tailed) was conducted. Equal variances could be assumed. Results indicate that dogs in the shelter during the baseline years had a longer average length of stay (M = 10.47, SD =8.52) than did those in the shelter during the trazodone pilot year (M = 9.22, SD = 6.56). Therefore, dogs receiving trazodone had a significantly shorter average length of stay, $t(1772) = 2.75$, $p = .006$. Further analysis was done by looking at the sick and non-sick samples individually. A t-test was conducted using the samples of dogs not diagnosed with CIRDC (non-sick) during the baseline years and trazodone year, and found no significant difference between the baseline year (M = 8.29, SD = 8.13) and the trazodone year (M = 7.75, SD = 6.00), $t(1093) = 1.037$, $p = .300$. For the sample of sick dogs only, a t-test could not be run because the data violated the equal variance assumption. Therefore a non-parametric Mann-Whitney test was run. This test also found no

significant difference between baseline 2016/2017 and trazodone 2018 (U = 31325.5, Z = -1.028, p = .304).

Outcome

To evaluate differences in outcome between the baseline and trazodone pilot years, a Pearson chi-square was conducted. A statistically significant difference was observed within the five outcome groups between 2016/2017 and 2018, χ^2, (4, N = 1774) = 24.2, p < .000 (see Table 4 for descriptive data). In order to determine where the significant difference occurred, the three years were compared individually by Pearson chi-square using a Bonferroni correction (p = .01) to reduce the risk of type 1 error.

Table 4

Outcome Data for Baseline and Pilot

Outcome	Baseline 2016/2017		Trazodone pilot 2018		Total number	
	Number	Percent	Number	Percent	Number	Percent
Adopted	416	30.5	172	42.0	588	33.1
Placed	648	47.5	175	42.7	823	46.4
Reclaimed	122	8.9	27	6.6	149	8.4
Foster	35	2.6	2	0.5	37	2.1
Euthanized	143	10.5	34	8.3	177	10.0
Total	1364		410		1774	

A statistically significant difference was observed in adoption outcomes between the baseline years 2016/2017 and trazodone pilot 2018, χ^2, (1, N = 1774) = 18.7, p < .000. The

average adoption rate for 2016/2017 was 30.5%, which increased to 42% in 2018. No significant difference was observed in average rates of euthanasia χ^2, (1, N = 1774) = 1.7, p = .19, placement χ^2, (1, N = 1774) = 2.6, p = .07, reclaim χ^2, (1, N = 1774) = 2.3, p = .13, and foster outcomes χ^2, (1, N = 1774) = 6.7, p = .010.

Discussion

All three hypotheses put forth at the start of this study were supported by the data (although the third hypothesis was only partially supported). The first hypothesis suggested that *the administration of trazodone to dogs during the transition period would result in a decreased number of dogs diagnosed with CIRDC during their stays*. The data supported this hypothesis, finding a statistically significant decrease in the number of dogs diagnosed in 2018 during trazodone administration versus 2016 and 2017. This means that dogs receiving trazodone had a lower incidence of contagious illness than did dogs not receiving the pharmacological intervention. As this one was one of main goals of the pilot from the veterinary perspective, this is a welcome and meaningful result.

Hypothesis two stated that *the administration of trazodone to dogs during the transition period would result in a decreased average length of stay*. This was also supported by the finding that there was a statistically decreased length of stay from the baseline years to the trazodone pilot year, meaning dogs left the shelter more quickly, on average, in 2018 than they had in 2016 and 2017. Strangely, we did not see significant differences in length of stay when we look at the sick and non-sick populations individually. Practically speaking, becoming sick may increase LOS for dogs if adopters are wary of taking in a sick dog, while decreasing LOS in

other cases through placement on ACC's at risk list with its new venue of visibility. However, it is possible that these results, specifically the different in LOS, further represent the successful effects of the trazodone administration. Since all dogs were given trazodone in 2018, it may be the case that LOS was shortened for this group overall because dogs were less likely to become sick. Length of stay for dogs with CIRDC is likely to remain consistent across the conditions, regardless of the use of trazodone, given that it is not an antibiotic. Thus, this non-significant difference within the sick and non-sick populations may not be so surprising. These results, however, require additional exploration and further study.

Finally, the third hypothesis predicted that *the administration of trazodone to dogs during the transition period would result in increased placement and decreased euthanasia outcomes.* Of the five outcome types studied, a significant difference between baseline and pilot years was found in only one: adoption. Therefore the hypothesis was partially supported: this one outcome (adoption) is related to increased placement, so the dogs receiving trazodone experienced an increased rate of adoption; however, the pilot appeared to have no measurable effect on overall euthanasia rates, so the prediction of decreased euthanasia outcomes was not found. This does not mean that euthanasia remained consistent in all categories. Euthanasia at ACC occurs for a number of reasons, both medical and behavioral, and it is possible that euthanasia of dogs for contagious medical illness (CIRDC) decreased while euthanasia for behavioral reasons increased, keeping overall numbers fairly consistent but reducing euthanasia in behaviorally sound, medically treatable animals. This study is unable to evaluate the data in such a way, but perhaps future research can look more deeply at specific outcomes to consider such a possibility.

As this is the first known exploration of trazodone administration at the time of intake into an animal shelter, these results open a door for future exploration. The primary goal of ACC's pilot program was to decrease the incidence of contagious illness in the shelter, and while the results here certainly do not indicate causation, they do suggest that a trazodone intervention during this difficult transition period can be an asset in accomplishing this goal. This study is also distinguished from many other canine studies in the sheer number of dogs included (1,774) as compared to the 120 or fewer included in similar studies. This study involved the full population of the shelter during the months evaluated, with no dogs excluded for breed, age, behavior, or medical reasons, making the sample representative of the true, complete shelter population in New York City. This study also required no changes to be made to the dogs' schedules and quality of care during their stay, so we were able to evaluate dogs as they experienced typical shelter life.

While trazodone has a history of being used long-term for management of generalized anxiety disorders (Ciribassi & Ballantyne, 2014), the results of this study indicate a possible practical new use. Previous studies have acknowledged that intervention within the first days in a shelter is critical for a dog's success (Hennessy et al., 1997). Therefore, the more options available for trial during this time may ultimately result in increased observable success. The hope (and expectation) was that trazodone would moderate stress, thereby preventing the suppression of the immune system and decreasing rates of illness. The results of this study support the possibility that trazodone can assist in this way. In light of this promising first study, these results should encourage further study in the area of trazodone as a short-term moderator of transitional stress.

Limitations. This real-world study took place in an active, full-service shelter and, therefore, is subject to the restrictions and challenges of being one small piece of a great number of activities and focuses throughout the day. While the aim was to give all dogs a first dose immediately following intake and a second dose eight to 24 hours later, this schedule was not always practical. Delayed intake exams resulted in delayed first doses in some cases, and a considerable number of dogs refused to eat a second dose the following morning. However, this ended up allowing for an additional comparison that was not initially planned: looking at differences amongst different trazodone administration schedules. Ultimately, we included dogs who had received two doses within the 48-hour transition period, comprising a group that followed the ideal schedule and a group with a delayed first dose; and dogs who had received their first dose at intake but who, for any number of reasons, did not receive a second dose. A comparison of these schedules revealed no significant differences, so it is possible that the same effect may be found from a single trazodone dose at intake and subsequent doses may not be necessary. This idea merits additional study to determine an ideal dosing schedule, perhaps with larger numbers in each group (the smallest number in the trazodone comparison groups was 16, the largest 158) for a more robust comparison. Should a single dose prove to be effective, it will make trazodone an even easier and more cost-effective intervention. Should further study confirm these findings, trazodone becomes a truly viable option for many animal shelters to address the ongoing concern of transitional stress. At a cost of approximately nine cents per 100mg pill, it falls within a range of budgets, and as it is administered orally it requires relatively few resources. Even the most purpose-built, well-designed and well-staffed animal shelters

present a range of uncontrollable stressors to dogs, so the scope of benefit for this intervention is wide-ranging.

ACC's policies, procedures, and facilities are continually changing in line with emerging best practices and new reports from the welfare industry. While this study was controlled to the extent possible, a number of changes have occurred that may influence lengths of stay, adoption rates, and illness rates over the three years surveyed. These include changes in adoption policy (from closed holding rooms in 2016 to an open building and a pre-adoption policy in 2017), changes made to kennels (some kennels were replaced and/or altered in early 2017, including a shift from single kennels to open transfer doors and double kennels for dogs whenever population allows), changes to feeding times and introduction of an overnight lights-out period of rest for the dogs in early 2017, removal of breed labels, staffing changes, soft music playing in the rooms in 2016 and 2018 but not 2017, changes to the enrichment program (more varied and more frequent in-kennel enrichment as the years progress), and a shift of databases in 2017 from Chameleon to Shelter Buddy for record-keeping. All diagnoses were made by licensed and practicing veterinarians, but the medical staff experienced numerous changes from the start to the end of the study, and diagnoses were made by different veterinarians both within and between the months evaluated.

This study finds a correlation between the administration of trazodone and decreased illness rates, decreased LOS, and increased adoption rates, but is unable to suggest causation. Pains were taken to control what was able to be controlled in such a setting and to create meaningful comparisons between groups. The data analysis took these limitations into consideration as well by comparing individual years against one another to further isolate the

effect of the trazodone. While 2016 and 2017 were ultimately combined to form the baseline data, all three years were looked at separately in the course of the analysis. Trazodone as the sole cause for the significantly lower rate of illness in 2018 cannot be claimed from this study; however, the fact that no difference was found between 2016 and 2017, during which a number of in-shelter changes to the facility and the practices took place, but a significant difference was found between 2018 and combined 2016/2017, does make for a stronger argument.

Rather than looking at physiological, chemical, or behavior measures (alone or in combination), this study evaluated outcome. It therefore presents a means of measure that has not been explored in depth in previous studies. With the remarkable challenge that measuring animal welfare entails, and the problems with the different parameters that have been investigated (Beerda et al., 1998; Hilby et al., 2006; Hekman et al, 2014), additional methods to try and measure this elusive notion will create new study opportunities.

The decrease in length of stay and increase in adoption rates in 2018 cannot be fully explained by the results of this study and is likely the outcome of a number of influences. However, extrapolating from trazodone's mechanism of action and the results seen during this study, it is possible that a decrease in stress levels has resulted in improved behavior in the shelter, better kennel presence and more engaged adoption interactions. This could have an overall effect of more frequent and faster adoptions and placements, resulting in shorter lengths of stay. While overall numbers used in this study were large, when broken down by outcome type some of the groups became significantly smaller (as few as 2), making analysis somewhat less robust. Overall, though, with a trend toward decreased illness, decreased length of stay, and

increased adoption in months of trazodone administration, this pilot produced exciting and promising preliminary results for single agent therapy with trazodone hydrochloride.

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