Pre-mortem Risk Factors for Mortality in Kittens Under Eight Weeks Old at a Dedicated Kitten Nursery

Emily D. Dolan MS PhD [1*], Erin Doyle DVM DABVP (Shelter Medicine Practice) [2], Huyanh Ralph Tran DVM MS PhD [3] and Margaret R. Slater DVM PhD [4]

[1*] Corresponding author, Strategy and Research, American Society for the Prevention of Cruelty to Animals. New York, NY, USA. emily.dolan@aspca.org

[2] Shelter Medicine Services, American Society for the Prevention of Cruelty to Animals. New York, NY, USA.

[3] Adoptions, Helen Woodward Animal Center, San Diego, CA, USA.

[4] Strategy and Research, American Society for the Prevention of Cruelty to Animals. New York, NY, USA.

Key Words: kitten nursery; risk factors; mortality; shelter medicine; neonatal care

Abstract

Objectives: Kittens have unique requirements for care in a shelter setting given their higher susceptibility to infectious disease and socialization needs. Significant time and resources are necessary to care for this vulnerable population and dedicated kitten nurseries are one way to meet the requirements of kittens too young for neutering and placement. However, young kittens remain at a higher risk of dying relative to adult cats even in specialized settings. Efforts to investigate kitten mortality have focused on postmortem findings and little is known about pre-mortem clinical signs that may be associated with death. The purpose of this study was to elucidate predictors of mortality in underage kittens.

Methods: The medical records of kittens under eight weeks of age reared in a kitten nursery in New York City during 2017 were examined. The data collected included: signalment (estimated age and weight at intake, sex), physical findings (body condition score (BCS)), clinical signs (weight loss, anorexia, diarrhea, upper respiratory tract infection (URI)), diagnoses (panleukopenia, trauma), how early in the feline breeding season the kitten entered (April-November), and whether the kitten had died or was euthanized. These data were analyzed using Cox proportional hazard modeling with 1353 kittens to identify factors associated with any death or euthanasia.

Results: Elevated risk of dying was found for kittens in the lightest weight group (13 times greater), diagnosed with panleukopenia (13 times greater), exhibiting weight loss (over 9 times greater), diagnosed with URI (almost 4 times greater), exhibiting anorexia (3 times greater), identified with a low BCS at intake (2 times greater) and experiencing diarrhea (almost 2 times greater).

Conclusions and Relevance: These findings identify clinical signs and diagnoses that can serve as prognostic indicators for underage kitten survival in a shelter/rescue setting and can aid in enhancing protocols for monitoring, intervention and euthanasia decision making.

1.0 Introduction

Each year during the feline breeding season (April-November), most organizations caring for homeless felines experience a significant influx of kittens. This seasonal spike in feline admissions can stretch organizational capacity limits. Per national shelter statistics gathered by the organization Shelter Animals Count, kittens up to five months of age represented 42% of the 2017 feline intake for contributing organizations.[1] The high percentage of juvenile feline intake can pose a challenge for shelters.

Kittens have unique requirements for infection control and socialization that are most acute when kittens are below a safe age to be neutered and placed, typically at or around eight weeks of age. These underage kittens are highly vulnerable to infectious disease, have critical behavioral socialization needs and require care for an extended period prior to placement. Providing this care in the shelter increases the risk of disease exposure and taxes the shelter's overall capacity. In addition, many shelters are not staffed to provide for the intense around-the-clock husbandry and socialization needs of orphaned kittens.

Shelter programs caring for underage cats dedicate significant time and resources to each kitten. Yet underage kittens are at a higher risk of dying relative to adult cats, with Murray JK, et al. finding that, in a shelter setting, kittens less than seven weeks of age were four times more likely to die than cats one to three years of age.[2]

Existing literature describes kitten mortality rates ranging from 7.9% up to 29.1% for underage kittens in research or breeding colonies.[3–8] Risk factors for kitten mortality identified in these populations include increased litter size [8], low birth weight [9], and breed [5], while incompatible blood type between queen and tom was not identified as a risk factor. [10]

Mortality information focused on shelter or rescue kittens, however, is limited. One study showed panleukopenia virus infection as an important cause of kitten death based on post-mortem evaluation of owned and rescue kittens, with a higher prevalence of infection demonstrated in the rescue kittens. [11] Both Ghosh et al. and Watson et al. identified altered intestinal microbiota in the intestines of terminally ill shelter kittens, including a higher prevalence of *E. faecalis* (20% in kittens who died versus 4% in healthy kittens) [12] and a higher prevalence of atypical enteropathogenic *E. coli* (18% in kittens who died versus 0% in healthy kittens). [13]

Most recently, Strong et al. investigated mortality risk factors in shelter kittens with diarrhea and found an 11% mortality rate in the study population with a reduction in risk of mortality related to administration of a vitamin and mineral supplement. [14]

There remains a need for published literature that provides a broad scope of risk factors for mortality in underage shelter kittens. Knowledge of pre-mortem risk factors is helpful to guide discussions about monitoring and prognosis with caretakers. The kitten nursery setting provides an opportunity to evaluate mortality risk factors given the targeted population served and the consistent, detailed monitoring and record keeping for each kitten in the nursery's care. Though the program has since switched to a foster care-based kitten rearing model, during the study year, kittens were cared for at a dedicated onsite kitten nursery program run by a private non-profit animal welfare organization. The following study evaluates retrospective data points that represent common signalment factors and clinical signs observed in neonatal kittens to determine which of these represent significant risk factors for mortality.

2.0 Materials and Methods

2.1 Subjects

A total of 1578 cats were admitted into a kitten nursery program operated by a private, non-profit animal welfare organization in New York City in 2017. The nursery limited intake to queens nursing kittens and underage kittens without a queen. Of these, 1162 were brought in as strays, 401 were transferred from the local open-admission municipal animal shelter, 11 were owner surrendered and four were taken into custody by law enforcement. Only 7 of the cats admitted in 2017 were identified as purebred (1 Ragdoll, 5 Siamese, and 1 Snowshoe). All other cats were identified as domestic short, medium or long-haired. Nursery intake statistics include queens, but data analysis for this study was limited to kittens under 8 weeks old, admitted during the 2017 season (April through November).

Only kittens who entered the nursery under eight weeks of age were eligible for the study. Kittens left the study as they transitioned out of the nursery for placement, typically at eight weeks of age. Some kittens remained in the nursery past eight weeks if they were not yet of weight for spay-neuter (2 pounds), required continued care for medical and/or behavioral concerns, or if there were placement capacity limitations.

Care was provided in a separate facility by staff dedicated to caring for this population according to written protocols. Data were routinely recorded during the intake examination and daily medical rounds. Intake examinations were utilized to determine sex and age. Age was estimated based on weight, dentition, other developmental characteristics, and comparison with littermates. For record keeping purposes and due to software requirements, a specific age in days was determined for each feline rather than an age range. Clinical signs were observed and noted by all nursery staff, including veterinarians, licensed veterinary technicians and kitten caregivers. Kitten caregivers weighed kittens daily and noted any clinical signs of concern for further evaluation by the medical staff.

Interventions were performed per written medical protocols with individual case management decisions determined by the licensed veterinary technician and/or veterinarian as needed. Infectious disease was managed at the nursery based on capacity considerations and prognosis. Isolation areas were designated for treatment of dermatophytosis, panleukopenia and upper respiratory infection. Biosecurity and sanitation protocols were in place to mitigate risks to population health. Kittens with non-contagious illness or injury were housed in the general

population while undergoing treatment. Ongoing care and treatment decisions for ill or injured kittens were guided by regular monitoring. Kittens with a poor or grave prognosis (per veterinarian determination) were euthanized.

All felines were housed in stainless steel single compartment housing in accordance with recommendations from the ASV Guidelines for Standards of Care in Animal Shelters [ASV Guidelines, 2011]. Kittens remained with littermates whenever possible to foster their behavioral well-being. Socialization with people was facilitated by staff members and trained volunteers in accordance with protocols designed by behavior staff. Socialization was provided to isolated kittens following biosecurity protocols and in consideration of the order of contagion. Kittens were not co-mingled between litters aside from thoughtful pairing of orphaned singletons per direction from behavior staff and the nursery veterinarians.

Examinations, monitoring, and diagnostics were recorded on medical charts. All charts were examined from the 2017 season. Paper charts were retrieved from storage and the key information from the records was entered in Microsoft Excel (Microsoft Office 365 ProPlus) by a team of medical data transcriptionists. Almost 70% of data records entered were checked for accuracy against the original paper

record by a second transcriptionist. Five percent of the records were spot checked for accuracy against the original paper record by a veterinarian. Transcriptionists were supervised by the study lead and received training and support from a staff veterinarian who responded to questions and interpreted ambiguous or unclear medical notes.

Data transcribed from the medical charts contained intake characteristics including:

- sex, estimated age at intake (in days)
- weight at intake (in grams)
- date of intake and body condition score (BCS; from 1-9 as based on the Purina Body Condition System). [15] If the body condition score was written in the record as a range, it was recorded in our data as the corresponding half point. For example, if the body condition score was written as 3-4 it was recorded as 3.5.

Data also included the following clinical signs or diagnoses and the dates of onset and resolution:

- panleukopenia (presumptive diagnosis by the nursery veterinarian based on appropriate clinical signs, fecal parvovirus Ag ELISA results, and/or additional diagnostics as clinically indicated; yes/no)
- weight loss (greater than one gram across any time period; yes/no)
- upper respiratory tract disease (URI; upper respiratory signs severe enough to warrant treatment; yes/no)
- anorexia (any instance of appetite score of 0 /1 [see Appendix 1] or 0-2 mL of formula)
- diarrhea (D+ or FS 6/7 based on the Purina Fecal Scoring Chart) [16]
- the presence of trauma (any trauma, injury or abscess recorded).

2.2 Statistical Analysis

All analyses were performed using Stata/IC 15.1 (StataCorp LP, College Station, TX, USA). Reported clinical signs and key diagnoses of interest (panleukopenia, weight loss, URI, anorexia, BCS less than 3.5 at intake, diarrhea, and trauma) as well as the kittens' sex were described using frequencies and percentages. Several categorical covariates of three equal groups were created and described using frequencies for intake date (early in the season: 10 April 2017 – 12 June 2017;

middle of the season: 13 June 2017- 22 August 2017; late in the season: 23 August 2017 – 12 November 2017) and estimated age in days (youngest: 0-20; middle: 21-34; and oldest: 35-56). Four groups were also created for weight in grams (g) by percentiles: 65-258 g; 259-393 g; 394-575 g; 576-1202 g and whether the BCS at intake was under 3.5 (thin or emaciated at intake) or not. All above variables were included as main effects in the model. Outcome was the time to death, measured as euthanized or died.

In order to account for the diagnosis/signs of panleukopenia, weight loss, URI, anorexia, diarrhea and trauma as potentially time-varying covariates, the data were subjected to episode splitting, where separate episode records were created for each kitten to reflect the beginning and end of an episode of a specific clinical sign. The variables for panleukopenia, weight loss, URI, anorexia, diarrhea and trauma took the value zero up until the time the kittens experienced signs as marked in their medical chart. At that point, a new episode record was created where that sign variable took the value “one”. If the sign resolved, the variable returned to the value “zero”. Time varying covariates were assumed to be constant within an episode (record).

A Cox proportional hazard model with robust standard errors was fit to identify hazard ratios and predict risk of overall death as the main model. The model presented here considered the changing rate of events over time as well as the changing number of kittens at risk. Kittens still alive at the end of the study were considered censored. A base model was tested with all covariates as main effects only. Interactions with time were explored and all possible interactions were tested individually for significance. P<0.05 was considered significant. A likelihood ratio test ($p < 0.05$) was used to compare the model without interactions against a model containing interactions. If the likelihood ratio test was found to be significant, this suggested the model with interactions was a better fitting model and the interaction term was included. The link test was used to determine that the model was well specified, i.e., all the relevant variables had been included and no additional variables would be statistically significant beyond chance. The proportional hazards assumption was checked using *stphtest* and was considered met if the global test was not significant. Robust standard errors were calculated to account for kittens having multiple records in the hazard analysis.

3.0 Results

One thousand five hundred seventy-eight cats were admitted into the nursery in 2017. After excluding queens and kittens eight weeks of age or older at admission (98 records) as well as those cats who did not have medical records available (117 records, 16 of which had died) for analysis, the resulting data set contained 1363 kittens. Ten kittens were dropped for extreme values of length of stay that lay outside 1.5 times the interquartile range. Thus, a total of 1353 kitten records were included in the analysis. The frequencies of reported clinical signs and intake characteristics in all study kittens are described in Table 1.

The median estimated age was 29 days (range: 0-56 days) and the median weight was 395.5 g (range: 65-1202 g) at the time of intake. Kittens had a median length of stay (LOS) in the nursery of 43 days (range: 0-110).

Table 1: Frequencies of reported clinical signs, diagnoses, and intake characteristics for 1353 kittens from a NYC kitten nursery in 2017.

	Did not die (n=1183) Frequency (percentage)	**Died (n=170) Frequency (percentage)**	**Total (n=1353) Frequency (percentage)**

Clinical signs/diagnoses			
Panleukopenia			
No	1174(99)	166(98)	1340 (99)
Yes	9(1)	4(2)	13 (1)
Weight Loss			
No	225 (19)	61 (36)	286 (21)
Yes	958 (81)	109 (64)	1067 (79)
URI			
No	696(59)	139(82)	835 (62)
Yes	487(41)	31(18)	518 (38)
Anorexia			
No	545(46)	102(60)	647 (48)
Yes	638(54)	68(40)	706 (52)
BCS less than 3.5 upon intake			
No	896(76)	89(52)	985 (73)
Yes	191(16)	52(31)	243 (18)
Missing	96(8)	29(17)	125(9)

Diarrhea			
No	291 (25)	87 (51)	378 (28)
Yes	892 (75)	83 (49)	975 (72)
Trauma			
No	1030(87)	155(91)	1185 (88)
Yes	153(13)	15(9)	168 (12)
Intake Characteristics			
Weight at intake, categorized			
65-258 g	215(18)	119(70)	334(25)
259-393 g	308(26)	27(16)	335(25)
394-575 g	332(28)	9(5)	341(25)
576-1202 g	326(28)	12(7)	338(25)
Missing	2(0.2)	3(2)	5(0.4)
Time in feline breeding season intake occurred			

early (4/10/17-6/12/17)	378(32)	67(39)	445(33)
middle (6/13/17-8/22/17)	390(33)	61(36)	451(33)
late (8/23/17-11/12/17)	415(35)	42(25)	457(33)
Sex			
Female	572(48)	72(42)	644 (48)
Male	611(52)	97(57)	708 (52)
Missing	0(0.0)	1(0.6)	1(0.1)
Age, categorized			
Youngest	258(22)	118(69)	376(28)
Middle	394(33)	29(17)	423(31)
Oldest	531(45)	23(14)	554(41)

243

Results from the multivariable model are shown in Table 2. The global test revealed the proportional hazards assumption was met. There were two interactions that improved the model fit: weight loss by intake weight and URI by time in the kitten season. An example of the interpretation of the adjusted hazard ratio is as follows: after adjusting for all other variables, the risk of dying with panleukopenia was very high, 13 times greater than a kitten without panleukopenia. When a kitten had experienced a trauma, however, the risk of dying decreased by approximately 60% (1-0.4) after accounting for all other variables.

Table 2: Multiple Cox Proportional hazard model of kittens' risk for dying for 1353 kittens from a NYC kitten nursery in 2017. The referent category for each variable was no unless otherwise indicated.

Variable	**Adjusted Hazard Ratio (CI)**	**p-value**
Clinical Signs/Diagnoses		
Panleukopenia	13(1.2-133)	.03
Weight loss	9.3(2.7-32)	<.001

URI	3.8(1.3-11)	.01
Anorexia	3.3(2.0-5.4)	<.001
BCS less than 3.5 at intake	1.9(1.2-2.9)	<.01
Diarrhea	1.5(1.0-2.1)	.05
Trauma	0.4(.2-.7)	<.01
Intake Characteristics		
Weight at intake, categorized		
65-258 g	13(3.1-58)	.001
259-393 g	3.0(.7-13)	.1
394-575 g	1.4(.4-5.7)	.6
576-1202 g	Ref.	
Time in season intake occurred		
early (4/10/17-6/12/17)	.1(.01-.2)	<.001

middle (6/13/17-8/22/17)	.3(.1-.8)	.02
late (8/23/17-11/12/17)	Ref.	
Female	.9(.6-1.3)	.6
Age, categorized		
Youngest	Ref.	
Middle	.6(.3-1.1)	.1
Oldest	.7(.3-2.0)	.5
Interactions		
Weight loss by intake weight interaction		.02
weight loss in 65-258 g group	34(-20-88)	.2

no weight loss in 65-258 g group	13(-6.2-33)	.2
weight loss in 259-393 g group	4.8(-3.4-13)	.3
no weight loss in 259-393 g group	3.0(-1.3-7.3)	.2
weight loss in 394-575 g group	4.7(-2.9-12)	.2
no weight loss in 394-575 g group	1.4(-.6-2.4)	.2
weight loss in 576-1202 g group	9.3(-2.1-21)	.1
no weight loss in 576-1202 g group	Ref.	
URI by time in season intake occurred interaction		.02

URI * intake early in season (4/10/17-6/12/17)	.03 (-.02-.1)	.3
No URI * intake early in season (4/10/17-6/12/17)	.1(-.01-.1)	.1
URI * intake in middle of season (6/13/17-8/22/17)	.7 (-.1-1.5)	.1
No URI * intake in middle of season (6/13/17-8/22/17)	.3 (.03-.6)	.03
URI * intake late in season (8/23/17-11/12/17)	3.8 (-.3-7.9)	.1
No URI * intake late in season (8/23/17-11/12/17)	Ref.	

The adjusted hazard rates in Table 2 show that kittens with weight loss had higher risk of dying compared to kittens without weight loss. Similarly, kittens who entered the nursery in the lower and mid weight ranges had a greater risk of death

compared to kittens in the higher weight range. Coupling these factors, while not significant, it is noteworthy that kittens who were in the lowest weight range at intake and also lost weight while in the nursery were at substantially higher risk of dying (34 times) compared to not losing weight and being in the heavier weight ranges.

The adjusted hazard rates in Table 2 for the interaction of URI with the time in the season that a kitten entered the nursery show that kittens who came in earlier in the season and also showed clinical signs of URI had a lower risk of death compared to kittens who came in later in the season and showed signs of URI.

4.0 Discussion

The results of this study reveal that there are intake characteristics, clinical signs and diagnoses that can be utilized to identify the most vulnerable underage kittens in a nursery or shelter setting. Low weight at intake, panleukopenia infection, weight loss, upper respiratory signs, anorexia, low BCS at intake, and diarrhea were all identified as significant risk factors for mortality in this study. The identification of these risk factors can help clinicians to assess relative risk of mortality for underage kittens, which in turn can guide intervention decisions.

The highest mortality risk factor identified in this population was weight at intake, with the lightest kittens having a risk of death 13 times greater than those kittens in the heaviest weight group. As would be expected given the relationship between age and weight [17], most kittens in the 65-258 g (lightest) group were indeed also in the youngest age group. A portion of the kittens in the 65-258 g (lightest) group, however, was in an older age percentile, indicating that they were underweight for their age, though this could be normal variation. Breed could be a potential cause of normal size variation. The low prevalence of purebred cats in this population, however, made breed unlikely to be a major factor in these findings. Interestingly, the majority of underweight kittens did not have a BCS below 3.5 supporting potential for normal variation in this population. However, a low birth weight, poor weight gain and/or weight loss may all result in a kitten being underweight and might all correlate with malnutrition or disease.[7] We did not capture data on colostrum ingestion in study kittens, though lack of adequate colostrum ingestion may also have contributed to the higher mortality risk in these young and underweight kittens. [18]

As expected, weight loss was also a significant risk factor for mortality, with kittens displaying weight loss being about nine times more likely to die than those kittens without weight loss. Not surprisingly, kittens who were smaller at intake and also displayed weight loss were more likely to die than either kittens with weight loss who were larger at intake or smaller kittens who did not experience weight loss. This finding is clinically intuitive as weight loss is a common indicator of illness or malnutrition and the smallest kittens would be expected to be the most susceptible to these concerns. This also highlights the critical need to closely monitor weight of kittens especially those who are in the lightest weigh group, even when their BCS is adequate.

URI was also significantly associated with mortality, with kittens nearly four times more likely to die when they were clinically affected with URI. While URI is not considered generally fatal, underage kittens are at greater risk for more significant sequelae to infection. [19,20] In our population, there was a small significant interaction between the URI mortality risk and the time of year of admission into the nursery ($p=.02$), with kittens admitted in the middle of the season who developed URI less likely to die than kittens with URI admitted late in the season. The nursery is an inherently limited admission program with capacity limitations

316 dictated by housing and staffing, but in the first few weeks of the season it often
317 operates well below capacity potentially allowing for enhanced monitoring and
318 intervention capabilities. Later in the season, as the nursery population reaches
319 capacity, there may also be the potential for pathogen transmission despite
320 protocols and procedures to mitigate this risk. Seasonal variations in the
321 prevalence of different URI pathogens would also have the potential to impact URI
322 associated mortality. The seasonal variation in this study could also be unique to
323 the 2017 season or the New York City location. Further research to explore URI
324 mortality risk factors in a foster-care-based kitten rearing model as well as seasonal
325 URI pathogen variation could provide additional valuable information regarding
326 URI and kitten mortality risk.
327
328 Kittens with anorexia or a low BCS at intake were approximately two to three times
329 more likely to die compared to kittens with normal appetites or adequate body
330 conditions, respectively. Both findings are clinically intuitive given the association
331 between anorexia and poor body condition with illness. Whether one leads to the
332 other or whether there is an underlying disease or nutritional component could not
333 be determined from this study. Our findings indicate, however, that both are risk
334 factors that signal a need for prompt intervention when identified in kittens.

Kittens with diarrhea had a risk of dying that was 45% higher than kittens without diarrhea. Seventy two percent of the kittens in this study were diagnosed with diarrhea at some point during their nursery stay, making it the second most commonly noted clinical sign after weight loss. This incidence is higher than that noted elsewhere in the literature [14] which may be reflective of the close monitoring of kittens in the nursery. Diarrhea may also be more common in a nursery setting as compared to other environments such as foster care due to the interplay between crowding, disease exposure, stress and nutrition in underage kittens. While diarrhea alone resulted in a modest increase in mortality risk, panleukopenia infection as diagnosed by the veterinarian was associated with nearly 13 times the risk of dying. This is expected given the serious nature of panleukopenia infection and is consistent with other findings demonstrating panleukopenia as a common cause of death in kittens [11], though it is worth noting that the majority of kittens diagnosed with panleukopenia infection did not die.

The precise timing of the clinical signs was estimated as closely as possible based on daily records; however, if clinical signs occurred within a close time frame to each other (within about 24 hours) the data did not indicate which sign or

diagnosis came first. The current results show that diarrhea and anorexia as well as weight loss and panleukopenia were all independent predictors of mortality; this implies that these clinical signs and diagnoses are important separately and the results are likely not due to a cascade of signs being caused by each other (ex. anorexia or diarrhea leading to weight loss).

The episode splitting technique utilized for data analysis in this population provided the ability to assess mortality risk at the time of death for the clinical sign of concern. This technique allowed for the deemphasis of the clinical signs that did not coincide with the time of mortality for specific kittens. More closely evaluating the timing of signs relative to the time of the outcome maximizes the clinical applicability of these risk factors of mortality.

Not all variables analyzed resulted in an increased risk of mortality. Sex had no significant impact on mortality risk. Trauma also did not increase the risk of mortality in our population and in fact had a protective effect. Trauma is a broad category that reflects both very minor concerns such as a collar caught in the mouth ranging to more serious concerns such as an abscess or musculoskeletal trauma. As such, it is difficult to draw definitive conclusions regarding the reason behind

the protective effect noted in this population. It is possible that these kittens received intervention and close monitoring that prevented other more significant disease and/or that minor trauma may have been overlooked by the clinician if more serious disease concerns were present. While the protective impact of trauma cannot be fully elucidated, these findings at least suggest that kittens diagnosed with mild to moderate trauma generally do not need to be considered at higher risk of mortality.

Limited information exists with which to compare this study population. The overall mortality rate in this study (13%) is comparable with published mortality rates of underage kittens. No apparent intake demographics in this study population differ importantly from the demographics of other underage shelter kitten populations, though potential geographic variation in infectious disease prevalence is important to consider. The transfer of many kittens from a local partner organization would exclude from our study population severely ill or injured kittens who were euthanized or died prior to transfer; however, in the study year few kittens were excluded from transfer. It is uncertain how mortality risk factors for the nursery model compare with foster-based programs or other shelter kitten management models; however, some degree of commonality can be

anticipated given the similar conditions kittens were exposed to prior to shelter intake.

While these results provide robust information to evaluate kitten mortality risk factors for shelter kittens, several limitations of the study are important to consider. The identified risk factors describe associations but do not necessarily identify the cause of death for at-risk kittens. Many variables overlap with one another in typical clinical presentations. Although the model did not show a significant interaction between many putatively related issues, it is still possible that kittens with multiple issues are at higher risk of death.

Another limitation is that data transcription from paper records was utilized to capture the information analyzed in this study. While a vigorous quality assurance process that included multiple quality checks was instituted, there is still the possibility that the data may contain recoding mistakes. Further, because of the paper record procedures at the nursery and the retrospective nature of this study (clinicians were unaware at the time of recording that their notes would be used for data and were not following a formal study protocol) clinicians may not have recorded events as completely or reliably on each and every record. In addition,

411 while there was some information on whether kittens had littermates and/or
412 queens, it was not possible to reliably match the litters/queens or to determine if
413 littermates had signs or had died.
414
415 Finally, this study is focused on the kittens cared for by one program during a
416 single season in a large metropolitan area and caution should be exercised in
417 extrapolating these results to all programs, populations, or areas where kittens are
418 cared for. It is difficult to determine how relevant these findings may be for kittens
419 primarily reared in a foster home compared to a nursery setting, for example, as
420 foster care would be expected to mitigate certain concerns such as disease
421 transmission, socialization, and caregiver capacity limitations. More research on
422 clinical signs and timing are needed to help support and guide foster-based
423 programs about risk of kitten mortality. However, because this study population
424 represents a typical underage kitten population entering an animal welfare
425 organization there is reason to support generalizability of these findings to provide
426 important information about risk of factors for mortality in shelter kittens.

427 **5.0 Conclusions**

While these results alone cannot dictate clinical decision making, they provide another tool for the clinician to determine prognosis and guide care decisions for underage kittens in the shelter setting. Kittens in the lowest weight category at intake were at highest risk of mortality, followed by kittens diagnosed with panleukopenia virus and then those displaying weight loss. Upper respiratory infection, anorexia or a thin body condition resulted in moderate increases in the mortality risk while diarrhea brought about a smaller increase in the risk of dying. This information provides a window into which kittens are at greatest risk of mortality in a nursery population. Mortality risk factors can be used to aid kitten nursery programs in fine-tuning protocols to quickly identify and more closely intervene for kittens who may die and to help guide euthanasia decisions.

Acknowledgements

The authors wish to thank the team of medical data transcriptionists for collecting the data for this study. We wish to thank Sharon Pailler, Vic Spain and H. Morgan Scott for technical assistance and advice on the statistical methods. We wish like to thank Holly Memoli and Stephanie Janeczko for thoughts on the design and execution of the study. We wish to thank Hugh Mulligan for data assistance.

Author note

Early findings were presented at the American Board of Veterinary Practitioners Symposium, 2019.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Ethical Approval

This work involved the use of non-experimental animals only. Established internationally recognized high standards ('best practice') of individual veterinary clinical patient care were followed. Ethical approval from a committee was therefore not necessarily required.

Informed Consent

Informed consent (either verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (either experimental or non-experimental animals) for the procedure(s) undertaken (either prospective or retrospective studies).

Informed Consent for publication

No animals or humans are identifiable within this publication, and therefore additional informed consent for publication was not required.

6.0 References

1. Shelter Animals Count. *Nartional Database*, https://shelteranimalscount.org/ (2017).
2. Murray JK, Skillings E, Gruffydd-Jones TJ. A study of risk factors for cat mortality in adoption centres of a UK cat charity. *J Feline Med Surg* 2008; 10: 338–345.

3. Sparkes AH, Rogers K, Henley WE, et al. A questionnaire-based study of gestation, parturition and neonatal mortality in pedigree breeding cats in the UK. *J Feline Med Surg* 2006; 8: 145–157.
4. Young C. Preweaning mortality in specific pathogen free kittens. *J Small Anim Pract* 1973; 14: 391–398.
5. Ström Holst B, Frössling J. The Swedish breeding cat: population description, infectious diseases and reproductive performance evaluated by a questionnaire. *J Feline Med Surg* 2009; 11: 793–802.
6. Fournier A, Masson M, Corbière F, et al. Epidemiological analysis of reproductive performances and kitten mortality rates in 5,303 purebred queens of 45 different breeds and 28,065 kittens in France. *Reprod Domest Anim* 2017; 52: 153–157.
7. Root Kustritz M V. *History and physical Examination of the Neonate*. Elsevier Inc., 2011. Epub ahead of print 2011. DOI: 10.1016/B978-1-4160-4889-3.00003-6.
8. Romagnoli S, Bensaia C, Ferre-Dolcet L. Fertility parameters and reproductive management of Norwegian Forest Cats, Maine Coon, Persian and Bengal cats raised in Italy: a questionnaire-based study. *J Feline Med Surg*; 21, https://journals.sagepub.com/doi/abs/10.1177/1098612X18824181

(2019).

9. Lawler DF, Monti KL. Morbidity and Mortalitiy in Neonatal Kittens. *Am J Vet Res* 1984; 45: 1455–1459.

10. Axnér E. A questionnaire on survival of kittens depending on the blood groups of the parents. *J Feline Med Surg* 2014; 16: 781–787.

11. Cave TA, Thompson H, Reid SWJ, et al. Kitten mortality in the United Kingdom: A retrospective analysis of 274 histopathological examinations (1986 to 2000). *Vet Rec* 2002; 151: 497–501.

12. Ghosh A, Borst L, Stauffer SH, et al. Mortality in kittens is associated with a shift in ileum mucosa-associated enterococci from enterococcus hirae to biofilm-forming enterococcus faecalis and adherent escherichia coli. *J Clin Microbiol* 2013; 51: 3567–3578.

13. Watson VE, Jacob ME, Flowers JR, et al. Association of atypical enteropathogenic Escherichia coli with diarrhea and related mortality in kittens. *J Clin Microbiol* 2017; 55: 2719–2735.

14. Strong SJ, Gookin JL, Correa MT, et al. Interventions and observations associated with survival of orphaned shelter kittens undergoing treatment for diarrhea. *J Feline Med Surg*. Epub ahead of print 2019. DOI: 10.1177/1098612X19840459.

15. Nestle Purina Pet Care Center. Nestle Purina Body Condition System, https://www.aspcapro.org/sites/default/files/nestle_body_condition_scale.pdf (accessed 22 November 2019).
16. Purina. Fecal Scoring Chart, https://www.proplanveterinarydiets.ca/wp-content/uploads/2016/04/PPPVD-Fecal-Scoring-Chart-EN-FINAL.pdf.
17. DiGangi BA, Graves J, Budke CM, et al. Assessment of body weight for age determination in kittens. *J Feline Med Surg*. Epub ahead of print 2019. DOI: 10.1177/1098612X19844846.
18. Chastant-Maillard S, Aggouni C, Albaret A, et al. Canine and feline colostrum. *Reprod Domest Anim* 2017; 52: 148–152.
19. Sykes JE. Pediatric feline upper respiratory disease. *Veterinary Clinics of North America - Small Animal Practice* 2014; 44: 331–342.
20. Ruaux C. The Respiratory System. In: *Small Animal Pediatrics*. Elsevier, pp. 328–339.

Appendix 1: Kitten nursery appetite score

	**0 = no appetite**
	**1 = a few bites to ¼ meal**
	**2 = ½ meal**

		**3 = full meal**

534