

## Standard Article

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## Subclinical Bacteriuria in Older Cats and its Association with Survival

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**Background:** Bacterial urinary tract infections are uncommon in cats in general but the prevalence increases to 29% in older cats with comorbidities (*Veterinary Clinical Pathology* 2008, 37, 317; *Journal of Feline Medicine & Surgery* 2007, 9, 124; *Veterinary Microbiology* 2009, 136, 130). Frequently, the infections are subclinical. The clinical relevance of subclinical bacteriuria (SB) is uncertain, and the optimal treatment requires clarification.

**Objective:** Prospective, observational study to: (i) identify the prevalence and incidence count of SB in older ( $\geq 7$  years), nonazotemic cats, (ii) evaluate specific risk factors for SB, and (iii) investigate the potential relationship between untreated SB and survival.

**Animals:** Sixty-seven, nonazotemic cats were tested on 5 occasions over 3 years.

**Methods:** Urine samples were obtained by cystocentesis for quantitative urine culture and blood samples for measurement of serum creatinine concentration. Episodes of SB were not treated. Serum creatinine concentration, body weight, urine specific gravity, sex, and age were evaluated as potential risk factors for a positive urine culture. The association between urine culture results and survival was evaluated with Cox's proportional hazard model.

**Results:** A total of 256 urine samples was obtained. The prevalence of SB varied between 10 and 13%, and incident infections were uncommon. Female cats were 21 times more likely to have a positive urine culture than were male cats (odds ratio [OR], 21.2; confidence interval [CI], 4.1–110;  $P = .00028$ ). Subclinical bacteriuria was not significantly associated with survival.

**Conclusion and clinical importance:** Subclinical bacteriuria is common in nonazotemic, older cats. Although antimicrobial treatment was withheld, the presence of SB was not adversely associated with survival.

**Key words:** Bacterial infections; Urinary tract.

Cats traditionally have been considered relatively resistant to bacterial urinary tract infections (UTIs),<sup>1–3</sup> but recent studies identified a relatively high prevalence of bacterial UTIs in older cats. Affected cats typically have concurrent disease, commonly chronic kidney disease (CKD), diabetes mellitus, or hyperthyroidism, and the infections frequently are not associated with clinical signs of lower urinary tract disease.<sup>4–7</sup>

Increasing age and female sex<sup>6</sup> are identified risk factors for UTIs, and it has been proposed that some aspects of concurrent diseases further increase an individual cat's susceptibility to UTI.<sup>8</sup> Clinically silent

## Abbreviations:

|      |                                      |
|------|--------------------------------------|
| SB   | subclinical bacteriuria              |
| OR   | odds ratio                           |
| CI   | confidence interval                  |
| UTI  | urinary tract infection              |
| CKD  | chronic kidney disease               |
| CFU  | colony forming units                 |
| ROC  | receiver operator curve              |
| sp   | species                              |
| IRIS | International Renal Interest Society |

UTI, or subclinical bacteriuria (SB), also has been identified in dogs with concurrent disease notably hyperadrenocorticism, diabetes mellitus, and long-term prednisolone treatment.<sup>9,10</sup>

Studies describing the optimal approach to SB in dogs and cats are lacking. However, studies of asymptomatic bacteriuria in healthy,<sup>11</sup> diabetic,<sup>12,13</sup> and elderly<sup>14</sup> women have shown that treatment does not decrease subsequent episodes of symptomatic UTI, pyelonephritis, development of renal impairment, or survival.

Although the existence and prevalence of SB in dogs and cats with concurrent disease have been documented, the prevalence of SB in older cats without overt disease and its association with survival are unknown. A prospective longitudinal study was designed to determine the prevalence and incidence count of, and to evaluate specific risk factors for SB in nonazotemic, older cats. Furthermore, the association between SB and survival was investigated. The null hypothesis was that SB would not be associated with all-cause mortality.

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## Materials and Methods

### *Animal Selection*

The cats used in this study belonged to the Feline Nutrition Unit of Massey University, Palmerston North, New Zealand. The colony is a closed breeding unit of group-housed domestic short-haired cats, used to conduct nutritional research. All cats  $\geq 7$  years of age with serum creatinine concentrations lower than the upper end of the laboratory<sup>a</sup> reference range (80–178  $\mu\text{mol/L}$  [0.9–2.0 mg/dL]) were included. Intact female cats were not excluded from the study but were not tested if pregnant at the test time. Cats had ad libitum access to food and water. The staple diet was an Association of American Feed Control Officials growth and maintenance protocol tested commercial moist diet.<sup>b</sup> The cats were weighed weekly as part of the colony's standard management practices. Cats with persistent weight loss, defined as weight loss over 2 consecutive weeks resulting in a lower weight than the minimum weight recorded during the previous year, had a complete physical examination and any diagnostic tests (blood tests or imaging studies) performed as dictated by history and physical examination abnormalities. Hyperthyroidism was diagnosed by compatible physical examination findings and increased serum total thyroxine concentration. Other chronic diseases requiring invasive diagnostic tests to confirm or long-term medication were not treated, and cats with persistent weight loss were euthanized. Staff and veterinarians involved in the daily care and medical treatment of the cats were unaware of the urinalysis and culture results when making decisions regarding euthanasia. Information was retrieved regarding sex, age, and weight at the time of sampling. Any cat showing clinical signs of lower urinary tract disease (eg, stranguria, pollakiuria, dysuria) received veterinary evaluation and appropriate treatment. Cats with SB were not treated.

### *Ethics Approval*

This study was approved by the Massey University Animal Ethics committee.

### *Sample Collection*

Cats were sampled on 5 occasions between July 2010 and April 2013. The first 4 samples were obtained over approximately 1.5 years (baseline 5, 12, and 16 months) for determination of prevalence and incidence. The study was extended and a final sample obtained at 33 months to ensure adequate power for survival analysis. Survival was evaluated in December 2013, 3.5 years after the study began. Cats were not fasted before sampling. Urine and blood samples were obtained by manual restraint without sedation. Urine samples were obtained by antepubic cystocentesis for routine urinalysis and bacterial culture and antibiotic sensitivity, and blood samples were collected for determination of serum creatinine concentration. Cystocentesis was performed without sedation with cats in either lateral recumbency or standing with manual palpation of the bladder and alcohol skin preparation. Serum creatinine concentration was determined by an enzymatic method.<sup>c</sup>

### *Urinalysis and Bacterial Culture*

Urinalysis and bacterial culture were performed on-site at either the Institute of Veterinary, Animal and Biomedical Sciences microbiology laboratory or New Zealand Veterinary Pathology (NZVP),<sup>a</sup> an on-site university affiliated laboratory. In both cases, standardized techniques were used: Testing, including plating for culture, was performed the same day samples were collected. Urine samples were refrigerated pending analysis and plating. Urine

specific gravity was determined by refractometer. For urinalysis, 5 mL (or, if inadequate volume had been obtained, the urine remaining after dipstick analyses) was centrifuged at 500 G and sediment re-suspended and evaluated as a wet preparation. For bacterial culture, urine aliquots were plated onto 5% sheep blood agar and incubated at 37° C for 48 hours. The cutoff for a positive result for quantitative urine culture was 1000 colony forming units (cfu)/mL. Although pure growth from a cystocentesis sample of any number of bacteria could be considered clinically relevant,<sup>15</sup> because cats in this study had no clinical signs to support a diagnosis of cystitis, a higher colony count was chosen as the criterion for clinically relevant growth.<sup>16</sup> Positive cultures performed by NZVP were identified with standard biochemical tests, and antimicrobial sensitivity patterns were obtained.

Incidence count was defined as the number of cats with positive bacterial cultures for which the most recent previous culture was negative. Pyuria was defined as  $>5$  white blood cells/high-powered field.

### *Statistical Analysis*

Descriptive statistics for age, sex, urine specific gravity, and serum creatinine concentration were determined and stratified by test and urine culture results. For urine samples on which bacterial culture was performed but urine specific gravity or serum creatinine concentration was not performed, the missing data were replaced with the average of the previous and subsequent results. Multivariate regression analysis<sup>d</sup> by a generalized estimating equation (GEE) was conducted to evaluate specific risk factors for a positive urine culture. The explanatory variables evaluated were serum creatinine concentration, body weight, age, sex, and urine specific gravity. An exchangeable correlation structure was nominated for the GEE. The base model consisted of all potential explanatory variables. A stepwise backwards selection protocol was followed. The significance of each explanatory variable was tested by the Wald test. Explanatory variables that were not statistically significant were removed from the model 1 at a time, beginning with the least significant, until the estimated regression coefficients for all of the variables retained were significant ( $P \leq .05$ ). Biologically plausible, multiplicative 2-way interactions between the remaining variables were assessed for significance. The results of the final model are reported in terms of adjusted ORs for each explanatory variable. A receiver operator curve (ROC) was created to determine the predictive ability of the model to distinguish between cats with positive and negative urine cultures. The area under the curve provides a measure of the overall fit of the model. More specifically, it refers to the probability that a truly culture-positive cat would have a higher predicted probability of being culture-positive than a truly culture-negative cat.<sup>17</sup>

### *Survival*

Survival was calculated from the date of the first urine culture to the date of euthanasia. Cats were censored if azotemic or if still alive 8 months after the final urine collection. Azotemic cats were excluded because the prevalence of SB and UTIs in cats with CKD has previously been evaluated<sup>4,7</sup> and it was considered unethical to withhold antimicrobial treatment in azotemic cats without a practical method to definitively diagnose pyelonephritis. The cause of death was determined by a combination of physical examination, routine diagnostic blood tests, and necropsy. A multivariate regression model was used to evaluate the relationship between a positive urine culture and survival, accounting for the potential confounding variables of age, sex, and serum creatinine concentration. Cox's proportional hazard model with counting process was used to account for the time-dependent covariates. As for the logistic regression model, all potential explanatory

variables were entered into the base model followed by a backwards stepwise process. The assumption of proportional hazards was assessed by plotting the Schoenfeld residuals as a function of time. A generalized R-squared was calculated to estimate the goodness of fit of the final model. A posthoc power analysis was performed to estimate the difference in survival the study was capable of detecting considering the prevalence of SB and mortality in cats with a negative urine culture.

## Results

Sixty-seven nonazotemic cats (median age, 8.6 years) were tested on 5 occasions over 3 years with 256 urine cultures obtained. There were 28 female cats (20 intact and 8 neutered) and 39 male cats (1 intact and 38 neutered). Cats were censored if they developed azotemia (3 cats) or temporarily excluded if they were pregnant at the time of testing (1 cat). Samples were inconsistently obtained from 1 cat for behavioral reasons. Cats with persistent weight loss were euthanized, but their previous results were not excluded from analyses. No cat showed clinical signs of cystitis during the study.

Overall, 28 positive cultures were obtained from 11 cats. Nine of the 11 cats with positive urine cultures were female (7 intact female and 2 neutered female cats). Pyuria was present in 13 of the 28 urine samples with a positive culture. The bacterial species was identified in 20 of the 28 positive cultures; speciation was not attempted for the remaining 8 samples. Of the unidentified infections, 7 were gram-negative rods. *Escherichia* was identified in 16 and coagulase-negative *Staphylococcus* spp in 4 cultures. Quantitative cultures identified 1100 cfu/mL for 1 sample, 10,000 cfu/mL in 1 sample, and >100,000 cfu/mL or too numerous to count in the remaining positive samples. Five samples with 800, 600,

400, 220, 200, and 160 cfu/mL, although suspicious for SB, were considered negative. Samples with <100 cfu were considered likely to represent contamination.

### Prevalence and Incidence Count

The prevalence of SB at each test was between 10 and 13% (Table 1). Incident infections were uncommon, with between 0 and 2 incident infections at each test. Infections tended to persist. In 6 female cats, urine cultures were repeatedly positive. Two female cats with positive urine cultures on the first test were euthanized before subsequent tests, whereas 1 female cat had 3 positive urine cultures with 1 intervening culture that was negative. In the only 2 male cats with positive urine cultures, positive urine cultures were followed by at least 2 negative urine cultures.

### Descriptive Statistics

In 4 of 256 tests, either urine specific gravity or serum creatinine was not measured. Descriptive statistics, stratified by test and culture results (Tables 1 and 2), identified a low, relatively stable prevalence of SB predominantly among female cats that were older, of lower body weight and with a lower serum creatinine concentration than cats with a negative urine culture results. There was no difference in median urine specific gravity between urine culture-positive and culture-negative cats.

### Generalized Estimating Equation

In the multivariate analysis, only female cats remained at increased risk of SB. Female cats were 21

**Table 1.** Descriptive statistics of urine cultures from 67 cats stratified by test.

|  | Test 1              | 2                   | 3                   | 4                   | 5                   |
|--|---------------------|---------------------|---------------------|---------------------|---------------------|
| Prevalence:  |                     |                     |                     |                     |                     |
| Culture positive/total tested (number of cats) (%) | 8/63 (12.7)         | 6/57 (10.5)         | 5/50 (10)           | 5/51 (9.8)          | 4/35 (11.4)         |
| Age (years) median (Q1–Q3)                         | 8.6 (7.7–10.3)      | 9 (8.2–10.2)        | 8.9 (8.9–10.4)      | 9.3 (9.3–11.1)      | 10.6 (9.8–11.6)     |
| Creatinine median                                  |                     |                     |                     |                     |                     |
| (mg/dL) (Q1–Q3)                                    | 0.97 (0.84–1.13)    | 1.1 (0.94–1.2)      | 0.89 (0.87–1.0)     | 1.0 (0.88–1.2)      | 1.0 (0.9–1.2)       |
| ( $\mu$ mol/L) (Q1–Q3)                             | 86 (74.5–100)       | 97 (83–110)         | 79 (77.3–92)        | 89 (78–103)         | 89 (79.5–105.5)     |
| Urine specific gravity median (Q1–Q3)              | 1.030 (1.026–1.035) | 1.025 (1.018–1.030) | 1.024 (1.021–1.028) | 1.025 (1.023–1.028) | 1.024 (1.022–1.026) |
| Weight (grams) mean (SD)                           | 4427 (995.1)        | 4478 (889.5)        | 4448 (955.5)        | 4429 (858.1)        | 4148 (775.2)        |
| Sex (number of cats male:female)                   | 36 : 27             | 36 : 21             | 32 : 18             | 32 : 19             | 21 : 14             |
| Incident infections                                | Na                  | 1                   | 1                   | 2*                  | 0                   |

\*Of 2 incident infections, 1 had a positive urine culture earlier in the study.

Sixty-three cats were originally tested, 4 cats were added to the study at 5 months (Test 2) for a total of 67 cats tested.

**Table 2.** Descriptive statistics of 256 urine cultures from 67 cats stratified by culture result.\*

|                                       | Urine Culture Positive | Urine Culture Negative |
|---------------------------------------|------------------------|------------------------|
| Number                                | 28                     | 228                    |
| Age (years) median (Q1-Q3)            | 9.8 (8.8–11.3)         | 9.3 (8.2–10.6)         |
| Creatinine median (mg/dL) (Q1-Q3)     | 0.93 (0.86–1.2)        | 1.0 (0.87–1.17)        |
| ( $\mu\text{mol/L}$ ) (Q1-Q3)         | 82.5 (76.5–104.5)      | 90.4 (77–103)          |
| Urine specific gravity median (Q1-Q3) | 1.022 (1.017–1.027)    | 1.022 (1.017–1.027)    |
| Weight (grams) mean (SD)              | 4094 (713)             | 4443 (923)             |
| Sex (number of cats male:female)      | 3 : 25                 | 154 : 74               |

\*In the multivariate analysis that accounted for repeated urine cultures per cat, only sex remained significant, with female cats 17 times more likely than male cats to have subclinical bacteriuria ( $P = .00028$ ).

times more likely to have a positive urine culture than were male cats (OR, 21.2; CI, 4.1–110;  $P = .00028$ ). The area under the ROC curve was 78.4%.

### Survival

Thirty-five cats (median age, 11.4 years), 5 of 11 cats with a positive urine culture and 30 of 56 cats with negative urine culture, were euthanized for persistent weight loss during the study. Necropsies were performed in 27 cats; all culture-positive cats were necropsied.

Azotemia was detected in 3 cats during the study, 1 with concurrent hyperthyroidism. An additional 6 cats had renal pathology at necropsy. Specifically, pyelonephritis, chronic kidney disease, and glomerulonephropathy were identified as comorbidities in cats with hyperthyroidism (4 cats), neoplasia (squamous cell carcinoma in 1 cat), and enteritis (2 cats, 1 with concurrent hyperthyroidism). In 9 cats with renal disease identified pre- or postmortem, all urine cultures (29) were negative.

Hyperthyroidism was detected in 14 cats either based on increased serum thyroxine concentration and consistent clinical signs (12 cats) or at necropsy (2 cats with concurrent disease).

Nine cats with hyperthyroidism were treated medically with carbimazole or topical methimazole,<sup>c</sup> 2 of these cats remained alive at the end of the study. Of 12 cats euthanized because of clinical signs of hyperthyroidism, hyperthyroidism was considered to be the primary disease process in 5, and a comorbidity in 7.

Cats with positive urine cultures were euthanized because of cardiac disease (1 cat), hyperthyroidism (2

cats), and neoplasia (2 cats). Cats with negative urine cultures were euthanized because of neoplasia (9 cats, including 2 with nasal planum squamous cell carcinoma), cardiac disease (2 cats), hyperthyroidism (3 cats predominant disease, 7 cats with co-morbidities), a palpable abdominal mass (3 cats), renal disease (9 cats), gastrointestinal disease including diffuse lymphoma and fibroplasia sclerosing enteritis (3 cats), and individual cats with feline infectious peritonitis, nasopharyngeal mass, fractured femur, and acute pulmonary edema. Ten cats had concurrent disease.

In the Cox's proportional hazard model, SB was not significantly associated with survival. Age was significantly associated with survival; each increase in year of age was associated with a 1.7-fold increase in the hazard of dying (95% CI, 1.41–2.07;  $P < .0001$ ). The generalized  $R$ -squared ( $R^2$ ) of 0.1 indicated that the cause of death or euthanasia was largely unexplained by this model.

Considering the observed mortality rate of 54% over 3.5 years in the cats with negative urine culture results and 11 of 67 cats having at least 1 positive urine culture, the study had adequate power (80%) to detect a 1.5-fold difference in mortality between culture-positive and culture-negative cats.

### Discussion

Subclinical bacteriuria was present in between 10 and 13% of nonazotemic, predominantly female cats over 7 years of age, and no association was detected between SB and body weight, serum creatinine concentration, or survival. Although only a small number of cats in this study developed clinicopathologic or histologic evidence of kidney disease, all affected cats were repeatedly culture negative suggesting that SB did not contribute to the development of clinically relevant renal disease in these cats.

Although direct comparisons to previous studies are hampered by differences in study design and the populations studied, the prevalence of SB in older cats in our study was not notably different than the prevalence of UTIs, both symptomatic and SB, in cats with diabetes mellitus<sup>4,5</sup> and hyperthyroidism<sup>4</sup> but was lower than the prevalence of SB in cats with a variety of medical conditions<sup>6</sup> and CKD.<sup>7</sup> Symptomatic UTIs and SB should be defined separately in future studies to facilitate such comparisons.

Among the limited number of risk factors evaluated for the development of SB in our study, only female cats were at increased risk, an association that has been a consistent finding in previous studies.<sup>1,4,6,18</sup> Increasing age previously has been proposed as a risk factor for UTIs.<sup>1,6</sup> Because our study consisted only of cats >7 years of age, age could have been significant if cats with a wider age range were assessed. Decreased urine concentrating ability is another proposed risk factor for UTIs and SBs because of loss of the bacteriostatic nature of hypertonic urine and dilution of innate urinary antimicrobial factors.<sup>6</sup> Urine concentration was not associated with an increased risk of SB in our study,



and it has not been consistently associated with UTI in cats,<sup>4,6</sup> especially when the confounding effects of concurrent disease were considered.<sup>18</sup> The cats in the colony used in our study consistently produced urine of lower specific gravity than that of cats fed predominantly dry food. It may be that an association between urine concentration and SB can be detected only when cats with consistently higher urine concentration are included in the study population.

Results of our study suggest that SB in nonazotemic older cats may not warrant treatment, but larger or longer studies could identify differences in survival associated with the presence of untreated SB. In people, SB is not associated with morbidity or mortality and, other than in pregnant women or before invasive genitourinary procedures, neither screening for or treatment of SB is recommended.<sup>19,20</sup>

Treatment of SB in dogs and cats is not without potential complications. Cost, difficulties in administering medication, and resulting poor compliance are all recognized issues in the use of antibiotics in small animal medicine. More importantly, antimicrobial treatment can result in the acquisition of antibiotic resistance,<sup>21,22</sup> and uropathogenic *E. coli* can be transmitted between people and animals living in the same household.<sup>23</sup>

Pyuria was present in the many cats with SB suggesting that an inflammatory response was present, despite the lack of clinical signs of cystitis. Pyuria is a common occurrence in humans with SB and has been identified in 90% of elderly people with SB, compared with only 30% of healthy adult women with SB.<sup>24,25</sup> The presence or magnitude of pyuria in humans with asymptomatic bacteriuria is of no prognostic importance, has not been shown to have clinical relevance, and is not recommended as a basis for prescribing antimicrobial treatment.<sup>20</sup> The findings of our study are supportive of the same approach to interpreting the clinical relevance of pyuria in older cats with SB.

Either host or pathogen factors or a combination could be involved in the lack of apparent clinical signs. The species of bacteria isolated from cats with SB were similar to those found in dogs and cats with clinical UTIs<sup>26</sup> (ie, *E. coli* and coagulase-negative *Staphylococcus* sp.) although no *Enterococcus* sp. or *Streptococcus* sp. were cultured. There may be differences in urovirulence factors between strains involved in clinical UTIs and SBs, although many of the bacteria isolated from dogs with clinical UTIs lack known urovirulence factors,<sup>21</sup> highlighting the importance of altered host defenses. Future studies should consider if bacterial species or bacterial virulence factors are associated with clinical signs of cystitis or the ability to ascend and cause pyelonephritis.

The cats in our study were exclusively fed a moist diet which is the most probable explanation for the low urine specific gravities that were a consistent observation across all age groups in the nutrition colony. Although cats with International Renal Interest Society (IRIS) stage 1 CKD have creatinine concentrations within the current reference range, concurrent abnormalities such as renal proteinuria are required to

confirm the diagnosis. In our colony of cats, minimally concentrated urine was not an abnormal finding. In the absence of glomerular filtration rate determination or renal biopsy, it is difficult to rule out IRIS stage 1 CKD in the cats in our study. Cats were monitored daily and weighed weekly by trained staff. When persistent weight loss was observed, full physical examination and routine diagnostic tests were performed. Cats were assumed to be healthy if they were nonazotemic and had stable body weight. Necropsies were performed on most cats that were euthanized but it is possible that study cats had subclinical disease that predisposed them to SB.

The main limitation of our study is its external validity. Cats from the nutrition colony are genetically related, with identical husbandry and similar standards of veterinary care. Importantly, at the beginning of the study, cats had consistent body weight and serum creatinine concentration within the reference range. Chronic conditions, other than hyperthyroidism, often were not treated. For example, inflammatory bowel disease and congestive heart failure, diseases commonly treated in client-owned cats, typically resulted in euthanasia once substantial weight loss was documented. Consequently, the median age of euthanasia was 11.4 years which is younger than the median survival for cats in Sweden<sup>27</sup> or the United Kingdom.<sup>28</sup> Therefore, the results of our study cannot be easily extrapolated to older cats with clinically relevant concurrent disease. Whether cats with CKD should be routinely screened for SB remains to be determined. No association was identified between SB and azotemia or renal pathology at necropsy, but cats with pre-existing CKD are at risk of clinical deterioration if pyelonephritis develops. Whether or not the bacterial isolates that cause pyelonephritis are the same as those associated with SB in cats is unknown. Similarly, cats receiving immunosuppressive treatments and chemotherapy may be at increased risk of urosepsis, and it is unknown whether SB should be treated in these specific subgroups of animals.

A final limitation of our study is the inability to detect small differences in survival associated with SB. There was insufficient power to detect a <1.5-fold difference in survival between cats with and without SB, and future prospective studies with larger numbers of healthy cats and studies of cats with specific risk factors for pyelonephritis or urosepsis will be required before definitive recommendations for the treatment of SB can be made.

In conclusion, SB is common in older, nonazotemic cats at a similar prevalence to previous studies of cats with hyperthyroidism and diabetes mellitus. Cats in our study were nonazotemic, and some cats were euthanized for progressive weight loss associated with chronic conditions often treated in private practice. Among this cohort of cats, SB was not associated with body weight, azotemia, the development of CKD at necropsy, or overall survival. These findings are consistent with large studies in people and suggest that treatment of SB in the absence of risk factors for urosepsis or urogenital disease may be unnecessary.

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## Footnotes

- <sup>a</sup> New Zealand Veterinary Pathology, Massey University, an IANZ (International Accredited New Zealand) veterinary laboratory
- <sup>b</sup> Chef; Heinz Wattie's Ltd, Hastings, New Zealand
- <sup>c</sup> Roche/Hitachi analysers, Cobas
- <sup>d</sup> epiR: An R package for the analysis of epidemiological data. R package version 0.9-54. <http://CRAN.R-project.org/package=e-piR>
- <sup>e</sup> Neo-Mercazole<sup>®</sup> Vildalta<sup>®</sup> MSD Animal Health HyperT Ear-Spot<sup>®</sup>, Bayer
- 

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*Conflict of Interest Declaration:* Authors declare no conflict of interest.

*Off-label Antimicrobial Declaration:* Authors declare no off-label use of antimicrobials.

## References

- Lekcharoensuk C, Osborne CA, Lulich JP. Epidemiologic study of risk factors for lower urinary tract diseases in cats. *J Am Vet Med Assoc* 2001;218:1429–1435.
- Kruger JM, Osborne CA, Goyal SM, et al. Clinical evaluation of cats with lower urinary tract disease. *J Am Vet Med Assoc* 1991;199:211–216.
- Buffington CA, Chew DJ, Kendall MS, et al. Clinical evaluation of cats with nonobstructive urinary tract diseases. *J Am Vet Med Assoc* 1997;210:46–50.
- Mayer-Roenne B, Goldstein RE, Erb HN. Urinary tract infections in cats with hyperthyroidism, diabetes mellitus and chronic kidney disease. *J Feline Med Surg* 2007;9:124–132.
- Bailiff NL, Nelson RW, Feldman EC, et al. Frequency and risk factors for urinary tract infection in cats with diabetes mellitus. *J Vet Intern Med* 2006;20:850–855.
- Litster A, Moss S, Platell J, et al. Occult bacterial lower urinary tract infections in cats—Urinalysis and culture findings. *Vet Microbiol* 2009;136:130–134.
- White JD, Stevenson M, Malik R, et al. Urinary tract infections in cats with chronic kidney disease. *J Feline Med Surg* 2013;15:459–465.
- Bartges JW, Barsanti JA. Bacterial urinary tract infection in cats. In: Bonagura JD, ed. *Kirk's Current Veterinary Therapy XIII: Small Animal Practice*. Philadelphia: Elsevier Saunders; 2000:880–886.
- Forrester SD, Troy GC, Dalton MN, et al. Retrospective evaluation of urinary tract infection in 42 dogs with hyperadrenocorticism or diabetes mellitus or both. *J Vet Intern Med* 1999;13:557–560.
- Torres SME, Diaz SE, Nogueira SA, et al. Frequency of urinary tract infection among dogs with pruritic disorders receiving long-term glucocorticoid treatment. *J Am Vet Med Assoc* 2005;227:239–243.
- Asscher AW, Sussman M, Waters WE, et al. Asymptomatic significant bacteriuria in non-pregnant woman. 2. Response to treatment and follow-up. *Br Med J* 1969;1:804–806.
- Harding GKM, Zhanell GG, Nicolle LE, et al. Antimicrobial treatment in diabetic women with asymptomatic bacteriuria. *N Engl J Med* 2002;347:1576–1583.
- Meiland R, Geerlings SE, Stolk RP, et al. Asymptomatic bacteriuria in women with diabetes mellitus – Effect on renal function after 6 years of follow-up. *Arch Intern Med* 2006;166:2222–2227.
- Abrutyn E, Mossey J, Berlin JA, et al. Does asymptomatic bacteriuria predict mortality and does antimicrobial treatment reduce mortality in elderly ambulatory women. *Ann Intern Med* 1994;120:827–833.
- Sykes JE, Rankin SC. Isolation and identification of aerobic and anaerobic bacteria. In: Sykes JE, ed. *Canine and Feline Infectious Diseases*. Missouri: Saunders Elsevier; 2014.
- Pressler B, Bartges JW. Urinary tract infections. In: Ettinger SJ, Feldman EC, eds. *Textbook of Veterinary Internal Medicine*, 7th ed. Missouri: Elsevier Saunders; 2010.
- Bewick V, Cheek L, Ball J. Statistics review 14: Logistic regression. *Crit Care* 2005;9:112–118.
- Bailiff NL, Westropp JL, Nelson RW, et al. Evaluation of urine specific gravity and urine sediment as risk factors for urinary tract infections in cats. *Vet Clin Pathol* 2008;37:317–322.
- Calonge N, Petitti DB, DeWitt TG, et al. Screening for asymptomatic bacteriuria in adults: US preventive services task force reaffirmation recommendation statement. *Ann Intern Med* 2008;149:43–47.
- Nicolle LE. Asymptomatic bacteriuria: Review and discussion of the IDSA guidelines. *Int J Antimicrob Agents* 2006;28:S42–S48.
- Drazenovich N, Ling GV, Foley J. Molecular investigation of *Escherichia coli* strains associated with apparently persistent urinary tract infection in dogs. *J Vet Intern Med* 2004;18:301–306.
- Freitag T, Squires RA, Schmid J, et al. Antibiotic sensitivity profiles do not reliably distinguish relapsing or persisting infections from reinfections in cats with chronic renal failure and multiple diagnoses of *Escherichia coli* urinary tract infection. *J Vet Intern Med* 2006;20:245–249.
- Johnson JR, Owens K, Gajewski A, et al. *Escherichia coli* colonization patterns among human household members and pets, with attention to acute urinary tract infection. *J Infect Dis* 2008;197:218–224.
- Nicolle LE. Urinary tract infections in the elderly. *Clin Geriatr Med* 2009;25:423–436.
- Hooton TM, Scholes D, Stapleton AE, et al. A prospective study of asymptomatic bacteriuria in sexually active young women. *N Engl J Med* 2000;343:992–997.
- Barsanti JA. Genitourinary infections. In: Greene CE, ed. *Infectious Diseases of the Dog and Cat*, 4th ed. Georgia: Elsevier; 2012:1013–1044.
- Egenvall A, Nodtvedt A, Haggstrom J, et al. Mortality of life-insured Swedish cats during 1999–2006: Age, breed, sex, and diagnosis. *J Vet Intern Med* 2009;23:1175–1183.
- O'Neill DG, Church DB, McGreevy PD, et al. Longevity and mortality of cats attending primary care veterinary practices in England. *J Feline Med Surg* 2015;17:125–133.