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# Understanding the current evidence base for the commonly recommended management strategies for recurrent feline idiopathic cystitis: a systematic review

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## ABSTRACT

**Objectives:** This systematic review aims to describe and understand the evidence available for commonly recommended management strategies for feline idiopathic cystitis (FIC) to provide guidance for clinicians in their treatment of this condition. A subsequent objective was to identify gaps in the literature and areas where future research may be directed.

**Methods:** A computerised search of three electronic databases (Discover, Scopus and PubMed) was performed. Results were imported into a single EndNote library and duplicates were removed. Remaining records underwent a two-stage screening process with the aim to identify peer-reviewed primary literature on therapeutic strategies for FIC. Studies were categorised according to one of seven management strategies: environmental modification, dietary manipulation, anti-inflammatory drugs, amitriptyline, glycosaminoglycans, prazosin, and intravesical lidocaine.

**Results:** Twenty-two studies were included in the final review, with one study providing evidence in two categories. Two studies assessed environmental manipulation, with results showing encouraging evidence for multimodal environmental modification but little evidence to support the use of feline facial pheromone. Five papers examined dietary manipulation, with good evidence for the use of therapeutic urinary diets, and for increasing the moisture content of a cat's diet. Anti-inflammatory drugs were the focus of four studies, with none providing evidence to support their use. Four papers indicated that the evidence to support glycosaminoglycans is lacking. The antispasmodic drug prazosin was purported to be useful in one retrospective paper, while three papers comparing it to a placebo showed no evidence for its use. Three studies assessed amitriptyline, with two indicating that short-term use is not supported, and one long-term study suggesting it may be useful in some refractory cases. One study on intravesical instillation of lidocaine concluded that it was not a useful treatment strategy.

**Conclusions:** Multimodal environmental modification to reduce stress/conflict and therapeutic urinary foods (particularly if combined with an increase in moisture content of the diet) currently have the strongest evidence to support their use in managing FIC, and should, together, be considered the primary treatment approach. The evidence for other modalities, is currently insufficient to support their use. The overall lack of high quality studies emphasises the need for clinicians to be critical in their evaluation of the published literature on the management of this perplexing condition.

**Abbreviations:** FFP: Feline facial pheromone; FIC: Feline idiopathic cystitis; FLUTD: Feline lower urinary tract disease; MEMO: Multimodal environmental modification; NSAID: Non-steroidal anti-inflammatory drug

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FIC; FLUTD; MEMO; diet; therapy

## Introduction

Feline lower urinary tract disease (FLUTD) is a common presentation, accounting for 3–5% of feline cases in general practice, and up to 8% in referral or teaching hospitals (Forrester and Roudebush 2007; He *et al.* 2022). The term FLUTD is an over-arching label applied to cats displaying clinical signs relating to the lower urinary tract, including dysuria, stranguria, pollakiuria, haematuria and periuria, but does not

define the underlying problem (Dorsch *et al.* 2016; Westropp *et al.* 2019; He *et al.* 2022). When FLUTD has an identifiable cause such as bacterial infection, urolithiasis, urethral plug, structural abnormalities or neoplasia, targeted treatment can be given to resolve the problem. However, in 55–67% of cases, despite rigorous evaluation, no definitive cause can be found (Dorsch *et al.* 2016; Sparkes 2018; He *et al.* 2022). These cases are designated feline idiopathic cystitis

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(FIC) (Forrester and Towell 2015; Sparkes 2018). The clinical signs associated with FIC are distressing to both cats and owners and are often recurrent, with 40–65% of affected cats having one or more episodes a year (Chew *et al.* 1998; Kruger *et al.* 2015; Naarden and Corbee 2020).

Despite decades of investigation the aetiopathogenesis of FIC is still not fully elucidated (Forrester and Towell 2015; Sparkes 2018; Westropp *et al.* 2019). Current evidence suggests FIC is a syndrome resulting from a complex interaction between abnormalities of the bladder and the neuroendocrine system of affected cats, and perceived stressors in an individual's environment (Forrester and Towell 2015; He *et al.* 2022).

Several local bladder abnormalities have been identified in cats with FIC, such as decreased concentration of urinary glycosaminoglycans (Gunn-Moore and Shenoy 2004; Wallius and Tidholm 2009) and compromised bladder epithelium (Lavelle *et al.* 2000), as well as increased numbers of mast cells and mononuclear inflammatory cells, alongside submucosal oedema, haemorrhage and fibrosis (He *et al.* 2022).

Interstitial cystitis/bladder pain syndrome in humans (see Panda and Pearce 2024 for a recent review of this condition) has similarities to FIC in cats (Gunn-Moore and Cameron 2004; Westropp *et al.* 2019). This is particularly the case for the neuroendocrine alterations, with chronic activation of the central threat response system leading to uncoupling of the hypothalamic–pituitary–adrenal axis, resulting in increased catecholamine release, alongside reduced cortisol response (Forrester and Towell 2015; Westropp *et al.* 2019). Other associated changes include increased corticotropin-releasing factor in the cerebrospinal fluid, and smaller adrenal gland volume and weight (Forrester and Towell 2015). The proximity of the pontine micturition centre to the fear pathway is thought to be the most likely reason that lower urinary tract signs are predominant during periods of stress (Forrester and Towell 2015). Co-morbidities are not uncommon, and cats with FIC may exhibit gastrointestinal, dermatological and behavioural signs (Westropp *et al.* 2019; He *et al.* 2022).

Given the nebulous pathogenesis and pathophysiology of FIC, it is not surprising that > 70 medications/interventional procedures have been suggested for the management of this disease over the last few decades (Kruger *et al.* 2003). The management of FIC is further complicated by the self-limiting nature of most clinical episodes (Markwell *et al.* 1999; Westropp *et al.* 2019). Due to this self-resolution, just about any or all treatments may appear efficacious when used to treat an individual cat, highlighting the need for an evidence-based approach to the management of FIC (Forrester and Towell 2015). This systematic review therefore aims to understand the current evidence base for common FIC management

strategies and provide guidance to veterinary practitioners in treating the condition.

## Materials and methods

### Search strategy

This systematic review was undertaken following the PRISMA guidelines (Page *et al.* 2021). A systematic literature search was performed across three databases (Discover (Massey University, Palmerston North, NZ), Scopus (Elsevier, Amsterdam, Netherlands) and PubMed (NIH, Bethesda, MD, USA)) with the aim of identifying peer-reviewed, primary literature regarding the management options for FIC. The population of interest was cats with idiopathic or interstitial cystitis, but not those with urinary tract infections, urolithiasis, or other identifiable underlying causes. Case series were allowed provided there were data from five or more cats.

The keywords and search terms used were as follows: {idiopathic cystitis OR interstitial cystitis OR FIC OR lower urinary tract disease OR FLUTD OR pandora syndrome OR urologic syndrome OR FUS} AND {feline OR cat OR cats} AND {management OR intervention OR treatment OR therapy}. No restrictions were applied regarding date or country of publication, other than the requirement that the language of publication was English. The last search was performed on 31 May 2023.

### Study selection

Search results from each database were imported into EndNote 20.5 reference manager (Clarivate Analytics, St Helier, Jersey). Prior to relevance screening, duplicates were removed using the “find duplicates” function. Relevance screening then involved a two-stage process as follows.

Stage 1: Screening of title and abstract to ensure papers were relevant to FIC management. Articles were excluded if they pertained to healthy animals, cystitis in species other than cats, or examined feline cystitis due to underlying processes (e.g. urolithiasis or other structural pathology). Articles relating to aspects of FIC other than management (e.g. risk factor studies or diagnostic procedures) were excluded along with unidentified duplicates and articles not in English. If the relevance of the article was unclear, it was retained for Stage 2 screening.

Stage 2: Full-text evaluation with the aim of identifying peer-reviewed, primary literature on the management or treatment of FIC. Articles were excluded if they were review articles or book chapters, the full text was not available, they were not published in English, their subject was not management/treatment of FIC, or if they were a case series of fewer than five cats. The reference lists of all papers included in this stage

**Table 1.** The level of evidence, treatment modality and study type of 22 studies included in a systematic review of commonly recommended management strategies for recurrent feline idiopathic cystitis.

Level of evidence <sup>a</sup>	Treatment	Study design
Level 2: Randomised trial or observational study with dramatic effect		
Osborne <i>et al.</i> 1996	Anti-inflammatory drug (prednisolone)	Randomised, double-blind, placebo-controlled
Kraijer <i>et al.</i> 2003	Amitriptyline	Randomised, double-blind, placebo-controlled
Kruger <i>et al.</i> 2003	Amitriptyline	Randomised, double-blind, placebo-controlled
Gunn-Moore and Cameron 2004	Environmental modification (FFP)	Randomised, double-blind, placebo-controlled, cross-over
Gunn-Moore and Shenoy 2004	Glycosaminoglycan	Randomised, double-blind, placebo-controlled
Buffington <i>et al.</i> 2006	Environmental modification (MEMO)	Observational, uncontrolled with apparent dramatic effect
Wallius and Tidholm 2009	Glycosaminoglycan	Randomised, double-blind, placebo-controlled
Zeza <i>et al.</i> 2012	Intravesical lidocaine	Randomised treatment-control
Bradley and Lappin 2014	Glycosaminoglycan	Randomised, double-blind, placebo-controlled
Delille <i>et al.</i> 2015	Glycosaminoglycan	Randomised, double-blind, placebo-controlled
Kruger <i>et al.</i> 2015	Dietary (food)	Randomised, double-blind, placebo-controlled
Dorsch <i>et al.</i> 2016	Anti-inflammatory drug (meloxicam)	Randomised, double-blind, placebo-controlled
Reineke <i>et al.</i> 2017	Prazosin	Randomised, double-blind, placebo-controlled
Nivy <i>et al.</i> 2019	Anti-inflammatory drug (meloxicam)	Randomised treatment-control
Hanson <i>et al.</i> 2021	Prazosin	Randomised, double-blind, placebo-controlled
Colombino <i>et al.</i> 2022	Dietary (supplement)	Randomised, treatment-control
Level 3: Non-randomised controlled cohort/follow-up study		
Naarden and Corbee 2020	Dietary (food)	Non-randomised, unblinded, treatment-control cohort
Level 4: Case-series, case-control studies, or historically controlled studies		
Chew <i>et al.</i> 1998	Amitriptyline	Observational, uncontrolled cohort
Markwell <i>et al.</i> 1999	Dietary (food)	Uncontrolled cohort
Hetrick and Davidow 2013	Anti-inflammatory drug (meloxicam), prazosin	Retrospective cohort
Meyer and Bečvářová 2016	Dietary (food)	Case series, masked, non-randomised, uncontrolled
Conway <i>et al.</i> 2022	Prazosin	Observational, uncontrolled cohort

<sup>a</sup>Level of evidence based on the Oxford Centre for Evidence-Based Medicine Levels of Evidence (Howick *et al.* 2011). No studies included in this review met the criteria for Level 1.

FFP = feline facial pheromone; MEMO = multimodal environmental modification.

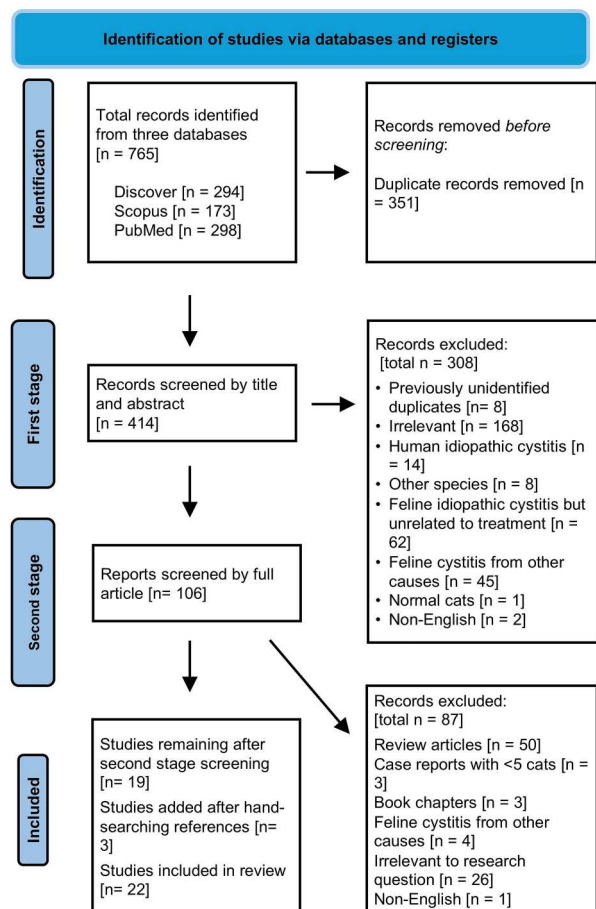
were searched to identify additional articles for inclusion that had not been identified previously.

### Collecting, categorising, and charting the data

Papers included in the review were categorised into groups based on the management strategy being assessed, and each paper was assigned a level of evidence based on the Oxford Centre for Evidence-Based Medicine Levels of Evidence (Howick *et al.* 2011) (Table 1). No further analysis, appraisal of methodological quality, or risk of bias was performed.

### Statistical analysis

Where suitable (e.g. where the effect of the management/treatment could be measured at the univariable level), and where such measures were not reported in the study, effect sizes were calculated. Mean differences and associated CI were calculated as per Gardner and Altman (1986) using the t-distribution and the assumption of different variances. Relative risks and associated CI were calculated as per Morris and Gardner (1988) to identify univariable associations between a test treatment and FIC-related outcomes. Where relevant, if the presentation of the data in the published paper allowed multivariable analyses to be undertaken, logistic regression was used to study the association. These analysis were undertaken using SPSS version 29 (IBM, Armonk, NY, USA); and Microsoft Excel (Microsoft, Seattle, WA, USA).



**Figure 1.** Flowchart showing the selection process used to identify studies in a systematic review of the commonly recommended management strategies for recurrent feline idiopathic cystitis.

## Results

The database search identified 765 results, with 414 remaining after removal of duplicates. Figure 1 summarises the search and screening outcomes. Stage 1 screening excluded 308 articles, leaving 106 for Stage 2 screening. Of these, 90 were excluded by the screening process (see Figure 1 for the rationale). By searching the reference lists of the papers remaining after Stage 2, a further three studies that satisfied the inclusion criteria were found (Hetrick and Davidow 2013; Hanson *et al.* 2021; Conway *et al.* 2022). Twenty-two papers were therefore included in the review.

The level of evidence for each of the 22 papers was identified (summarised in Table 1) and the studies detailed in the papers were grouped by management/treatment strategy: (i) environmental modification; (ii) dietary manipulation; (iii) anti-inflammatory drugs; (iv) amitriptyline; (v) glycosaminoglycans; (vi) prazosin; and (vii) intravesical lidocaine (also known as lignocaine). One study (Hetrick and Davidow 2013) was included in both groups iii and vi.

### Environmental modification

Two studies evaluated the effect on FIC of modifying a cat's environment. One of these studies, conducted by Gunn-Moore and Cameron (2004), was a randomised placebo-controlled cross-over study that assessed the use of feline facial pheromone (FFP). This was a small-scale study with 12 cats (of which only nine completed the study). Due to the limited sample size, the study lacked the power to detect clinically meaningful differences in any of the FIC-related outcomes. Although Gunn-Moore and Cameron (2004) stated that their raw data indicated that cats exposed to FFP had shorter, less severe episodes of cystitis than cats exposed to a placebo (e.g. they reported that treated cats had 4.3 (SD 6.7) days on average of cystitis vs. 9.9 (SD 19.1) days for placebo-treated cats), the study's lack of power means these data could also be consistent with large increases in duration and severity of cystitis in cats exposed to FFP.

The other study of environmental modification used multimodal environmental modification (MEMO). This was a prospective observational study of 46 cats (including cats from single- and multiple-cat households) (Buffington *et al.* 2006). Individualised MEMO plans were created in collaboration with the client based on environmental factors identified during a standardised interview. Of the 46 cats, only 13 (28%) showed a recurrence of clinical signs of FIC after the MEMO plans were put in place (mean follow-up period ~300 days), and the median frequency of clinical signs reduced from weekly to never. Buffington

*et al.* (2006) concluded that although their results were promising, their study was only "a preliminary trial of the approach" and further prospective controlled trials were indicated.

### Dietary manipulation

Dietary manipulation was the subject of five papers (Markwell *et al.* 1999; Kruger *et al.* 2015; Meyer and Bečvářová 2016; Naarden and Corbee 2020; Colombino *et al.* 2022). Markwell *et al.* (1999) evaluated the recurrence of FIC in 54 cats fed either the dry or canned formulation of a urinary acidification diet. Cats were not randomly assigned to treatment (owners were allowed to choose their cat's diet). Cats were followed until recurrence or 12 months, whichever was longer. Data were analysed from 46 cats (28 on the dry diet, 18 on the canned diet) as eight cats were withdrawn from the study for non-compliance (two dry diet, six canned diet). Over the 12-month study, 11/28 cats on the dry diet had recurrence of lower urinary tract signs (of which three were in the first 8 weeks) while only 2/18 cats on the canned diet had recurrent signs (both in the first 8 weeks of the study). Markwell *et al.* (1999), using a  $\chi^2$  test, found that this was "a statistically significant difference" ( $p = 0.04$ ). However, no effect size was presented, and the small numbers in the study meant that the effect of diet was not well characterised, i.e. when we calculated the relative risk of recurrent disease in cats fed dry vs canned diets it was 3.5 with wide 95% CI (0.9–14.1).

Kruger *et al.* (2015) randomly assigned 31 cats with non-obstructive FIC to receive either a multipurpose cystitis prevention food (c/d Multicare; Hill's Pet Nutrition) or a control food for 12 months. Both clinicians and clients were blinded as to which food each cat was provided, however clients were able to choose either a dry or wet formulation based on their own preference. The analysis of efficacy was based on client's daily records of lower urinary tract signs. Due to exclusions, data were analysed from only 25 cats (11 prevention and 14 control). Their main focus was the number of episodes when cats exhibited  $\geq 2$  clinical signs of FLUTD at least 2 days after the last time they had had multiple signs. After accounting for time on the study, there was a clear and very strong effect in favour of the prevention diet on the incidence of recurrent urinary tract disease with multiple signs, with the authors reporting that relative risk of recurrent disease for control cats compared to those on the prevention diet was 7.89 (95% CI = 3.58–17.36). Kruger *et al.* (2015) could not confirm that FIC was responsible for the clinical signs as only 13/25 cats with recurrent disease returned for re-evaluation, although they hypothesised that the limited nature of most recurrences indicated that FIC was the most likely cause.

In a case series, Meyer and Bečvářová (2016) evaluated the benefits of feeding cats with FIC a urinary cystitis prevention diet which also contained feed ingredients that reduced anxiety (L-tryptophan and  $\alpha$ -casozepine) (c/d Multicare Stress; Hill's Pet Nutrition). The formulation fed to each cat (wet, dry or combination) was chosen by the owner and fed for 8 weeks. Data were recorded by the owners on cat behaviour and individual clinical signs of FLUTD. The clinical outcome on the study diet was then related to that prior to starting the diet. Eighteen cats started the diet, but data were available from only 10 as eight cats were lost to follow-up (two because of issues with the prevention diet). For clinical signs of FLUTD, the median clinical score for the 10 cats was 0 for dysuria, stranguria, haematuria and periuria throughout the study period from the first owner report at 2 weeks. At 8 weeks, dysuria, stranguria and haematuria were absent in all cats. The data thus support the claim that the prevention diet can decrease FIC, but the small numbers (and resultant limited statistical analysis), combined with the absence of a control group, means that detail of the size of the benefit is lacking. In addition, the absence of a control group means that, although anxiety improved, this case series does not demonstrate that any benefits of the prevention diet on clinical signs of FLUTD were due to the anxiolytic supplements.

Naarden and Corbee (2020) evaluated c/d Multicare Stress diet (Hill's Pet Nutrition) in a larger but still non-randomised study. The study included 17 cats fed the prevention diet and a control group of 14 cats fed a variety of commercial adult foods. All cats were Domestic Shorthairs. The choice of therapeutic or control food and the formulation fed to each cat was based on owner preference. The main research outcome was recurrence of FLUTD (one day with at least two clinical signs) over a period of 5 weeks. In cats fed the control diet, 11/14 (79%) showed recurrence of FIC during the study period, compared to 5/17 (29%) fed the prevention diet. As with the study by Meyer and Bečvářová (2016), this is consistent with the claim that the prevention diet can decrease FIC. However, the small numbers in the study meant that the benefit of the diet was not well characterised (relative risk calculated for this review = 2.7 (95% CI = 1.2–5.9)). Thus, based on the data from Naarden and Corbee (2020), the true effect of not feeding the prevention diet could be anywhere from increasing the risk of FLUTD recurrence by 1.2 times to increasing it by 5.9 times.

One paper, Colombino *et al.* (2022), assessed the efficacy of a dietary supplement containing 4% cranberry pulp in controlling FIC. Twenty-one cats were randomly assigned to either one supplement tablet (containing 60 mg pulp) per day for 60 days ( $n = 10$ )

or no treatment ( $n = 11$ ). Three control cats were subsequently excluded from analysis as they developed bacteriuria. Colombino *et al.* (2022) reported that on days 30 and 60, no cats in the treatment group showed signs of dysuria or periuria, while these signs were still present in some control cats ( $p < 0.01$ ).

### Anti-inflammatory drugs

Four studies explored the use of anti-inflammatory drugs (Osborne *et al.* 1996; Hetrick and Davidow 2013; Dorsch *et al.* 2016; Nivy *et al.* 2019). Osborne *et al.* (1996) compared prednisolone administration to a placebo in reducing the severity of dysuria and haematuria. Twelve cats with non-obstructive FIC were hospitalised for 10 days. Six were administered 1 mg/kg prednisolone orally twice daily, while the other six were given a placebo. The key outcomes of this study were time to remission of clinical signs and time to remission of microscopic haematuria. Osborne *et al.* (1996) stated that they found no evidence of a benefit of prednisolone, but their study lacked the power to detect clinically meaningful differences between treatments, so a claim of "no effect" is of limited value.

The remaining three studies focused on the use of meloxicam, a non-steroidal anti-inflammatory drug, in cases of obstructive idiopathic cystitis. Hetrick and Davidow (2013) conducted a retrospective cohort study using the medical records of 192 male cats with urethral obstruction due to FIC. Details of meloxicam treatment were not reported but the initial dose was  $\sim 0.1$  mg/kg with treated cats being given, on average,  $\sim 3.6$  days of medication. In the dataset, the proportion of meloxicam-treated cats with urethral obstruction within 24 hours of catheter removal was 5/46 and within 30 hours it was 10/39. The equivalent figures for cats that were not treated with meloxicam were 10/146 and 27/118, respectively. Hetrick and Davidow (2013) stated that the use of meloxicam did not change the risk of urethral obstruction. This is consistent with their data, but again small sample size means their effect estimates have wide CI and their data are compatible with both large negative and large positive effects: unadjusted relative risk, calculated for this review, for obstruction within 24 hours for meloxicam-treated vs. no meloxicam cats was 0.99 (95%CI = 0.38–2.56), while for within 30 days, the relative risk was 1.12 (95% CI = 0.6–2.1).

Dorsch *et al.* (2016) undertook a placebo-controlled trial of the impact of meloxicam on the incidence of recurrent urethral obstruction within the first 7 days after catheter removal. The 18 cats randomly assigned to meloxicam were administered 0.1 mg/kg meloxicam on day 1, then 0.05 mg/kg on days 2–5. The remaining 17 cats received placebo medication. Of the meloxicam-treated cats, 4/18 (22%) experienced

recurrent urethral obstruction, compared to 5/19 (26%) of the placebo-treated cats. This is again consistent with the conclusion that meloxicam has no benefit in preventing obstruction but, again, small study size precludes a definitive conclusion: relative risk, calculated for this review, for recurrence in meloxicam vs placebo-treated cats was 0.84 (95%CI 0.27–2.66).

Nivy *et al.* (2019) also studied cats with urethral obstruction due to FIC. However, their intervention was focused on treatment after discharge. Cats were randomly assigned to receive either 14 days phenoxybenzamine (2 mg/cat twice daily) and alprazolam (0.125 mg/cat twice daily) (control group  $n=27$ ) or the same protocol with the addition of 0.025 mg/kg meloxicam daily ( $n=24$ ). Across the 6 months of the study, the signs of FIC recurred in 6/24 cats in the meloxicam group and 6/27 of the control group, with urethral obstruction observed in 3/24 meloxicam-treated cats and 5/27 control group cats. As with the previous studies of meloxicam and urethral obstruction due to FIC, this study lacked the power to determine whether there was a useful benefit of meloxicam in such circumstances, i.e. the authors calculated that the OR for cumulative recurrence of obstruction within 6 months was 0.63 (95% CI = 0.13–2.97).

### Amitriptyline

The use of the tricyclic antidepressant drug amitriptyline, which has been used extensively in humans for the treatment of interstitial cystitis, was the focus of three studies (Chew *et al.* 1998; Kraijer *et al.* 2003; Kruger *et al.* 2003). Chew *et al.* (1998) studied the response to 10 mg amitriptyline daily for 12 months in 15 cats with persistent, recurrent FIC. The dose was well tolerated by most of the cats, but in two cats, the dose was reduced to 5 mg because of somnolence. Chew *et al.* (1998) reported that 11/15 cats showed no recurrence of FIC in the first 6 months, and 9/15 cats had no recurrence over the 12 months of the study. In the 9 cats with no recurrence, Chew *et al.* (1998) reported that microscopic haematuria and proteinuria were significantly reduced over the study, whereas in cats where FIC recurred, no such change was observed. However, no data were shown, so it is unclear how large this effect was.

The remaining two studies assessed the impact of short-term amitriptyline use in FIC. Kruger *et al.* (2003) assessed the effect of 5 mg amitriptyline on the likelihood and rate of recovery from acute, non-obstructive FIC of < 14 days duration. Cats were randomly assigned to receive 5 mg/cat amitriptyline daily for 8 days ( $n=16$ ) or a placebo ( $n=15$ ). The main outcomes were time to recovery from pollakiuria and haematuria, and time to recurrence of clinical signs. Two cats on amitriptyline developed urinary

tract infection and were excluded from the analysis. The authors stated that there were no significant differences between treatment groups in rate of recovery. However, low study numbers meant that their results were consistent with both a significant benefit of amitriptyline and a significant negative effect. For example, for recovery from pollakiuria, the authors calculated that the hazard of recovery in amitriptyline-treated cats was 0.7 times that of placebo-treated cats, but the 95% CI of this estimate was 0.3–1.8. That is, the true hazard of recovery in amitriptyline-treated cats could have been anywhere from ~one-third to twice that of placebo-treated cats. For the time to recurrence of clinical signs, the authors' results were also inconclusive. Considering all recurrence of clinical signs, the hazard of recurrence in placebo-treated cats was lower than in amitriptyline-treated cats (hazard ratio = 0.3 (95% CI = 0.07–0.99)), but excluding recurrences within 7 days (which may have been associated with incomplete resolution of signs) resulted in a similar hazard ratio of recurrence (0.4) but with wider CI that included both a large decrease in hazard of recurrence with placebo and a moderate increase (95% CI = 0.1–1.8).

Kraijer *et al.* (2003) evaluated the benefit of treatment with 10 mg/cat amitriptyline for 7 days in 24 cats randomly assigned to receive a placebo ( $n=13$ ) or amitriptyline ( $n=11$ ). They reported no significant difference in the severity of clinical signs at 7 or 14 days post-treatment. However, no effect sizes were reported, so the strength of this claim cannot be judged. They also claimed that there was no difference between the two groups in the "cure rate" on day 14; however, they lacked the data to make this conclusion. For example, based on investigator assessment, 7/13 placebo-treated cats were "cured" compared to 4/11 amitriptyline-treated cats (relative risk, calculated for this review, of cure for placebo vs amitriptyline = 1.48 (95% CI = 0.58–3.75)).

### Glycosaminoglycans

Glycosaminoglycans, delivered orally, subcutaneously or by infusion into the bladder were studied in four papers (Gunn-Moore and Shenoy 2004; Wallius and Tidholm 2009; Bradley and Lappin 2014; Delille *et al.* 2015). For non-obstructive FIC, Gunn-Moore and Shenoy (2004) compared 20 cats randomly assigned to 125 mg N-acetyl-glucosamine administered orally daily for 6 months with 20 cats provided a placebo capsule for 6 months. The two key outcomes were average monthly clinical cystitis score (recorded by owners) and the average number of days with clinical signs. Gunn-Moore and Shenoy (2004) reported that neither outcome was significantly affected by treatment with glucosamine, with the mean monthly clinical cystitis score and the number of days with cystitis

being higher in the glucosamine than the placebo group (4,113 vs. 1,872 and 15 vs. 7.2 days, respectively). The study lacked the power to detect biologically meaningful differences. For example, for number of days with cystitis, the mean difference calculated for this review between the glucosamine and placebo groups was 7.8 days (95% CI = -6.5 to 22.1 days), i.e. the data were consistent with a very large increase in cystitis (~22 days) in the glucosamine-treated cats and a moderate decrease (~6 days). Over the study period, owners in both groups reported that their cat's mean health score markedly improved (from 0.5 to ~4 on a 1 to 5 scale). Gunn-Moore and Shenoy (2004) suggested that this was probably due to 36/40 owners markedly reducing the proportion of their cat's diets that was dry food, perhaps in response to being provided with detailed information regarding the current understanding of the pathogenesis of FIC.

Wallius and Tidholm (2009) randomly assigned 18 cats with non-obstructive FIC to SC pentosan polysulfate on treatment days 1, 2, 5 and 10 (n=9) or a saline placebo (n=9). Owners assessed recurrence of clinical signs at 2 weeks and 2, 6 and 12 months after treatment. Only 5/18 cats showed recurrence of clinical signs during the entire study period, and Wallius and Tidholm (2009) stated there were "no statistically significant differences between groups." However, they reported no results beyond recurrence, so the strength of this claim cannot be evaluated (although with only nine cats per group it is highly likely that this lack of statistical difference masks a wide range of potential beneficial and negative effects).

The remaining two studies (Bradley and Lappin 2014; Delille *et al.* 2015) examined the effects of intravesical glycosaminoglycans in cats suffering from obstructive FIC. Bradley and Lappin (2014) randomised 14 cats to either intravesical glycosaminoglycans (commercial mix of hyaluronic acid, sodium chondroitin and N-acetyl-glucosamine) or a saline placebo at the time of catheter placement, and again 12 and 24 hours later. Of the initial seven cats treated with a placebo, three became obstructed within 7 days of treatment, compared to none of the seven cats treated with glycosaminoglycans. Two of the placebo cats that became obstructed were re-treated using intravesical glycosaminoglycans, and neither of these cats obstructed within the following 7 days. Bradley and Lappin (2014) suggested that intravesical glycosaminoglycans should be tested in a larger study.

Delille *et al.* (2015) evaluated intravesical pentosan polysulfate as a means of reducing recurrent urethral obstruction. All cats in the study received IV fluid therapy, an indwelling urinary catheter for 48 hours and a standardised medication protocol with buprenorphine, phenoxybenzamine and acepromazine. The treatment group (n=22) had 30 mg of pentosan

polysulfate in 10 mL of saline infused into the bladder at the time of catheter placement and held in place for 30 minutes. This was repeated at 24 and 48 hours. The placebo group (n=22) had the same protocol with 10 mL saline only. Treatment was effective, with the authors' clinical score decreasing markedly (and similarly) in both groups. The main outcome was recurrence of urethral obstruction, which recurred within 5 days for 3/18 of pentosan-treated cats and 3/17 of placebo-treated cats. This was not statistically significantly different, but small study size meant that neither a large benefit nor a large negative effect of pentosan could be ruled out. Relative risk, calculated for this review, of recurrence for pentosan vs. placebo = 0.94 (95% CI = 0.22-4.05).

### Prazosin

Prazosin, an alpha-adrenergic blocking agent, was evaluated in four studies as a method of reducing the risk of recurrence of urinary obstruction secondary to idiopathic cystitis (Hetrick and Davidow 2013; Reineke *et al.* 2017; Hanson *et al.* 2021; Conway *et al.* 2022). Alongside their retrospective analysis of the benefit of using meloxicam in 192 such cats, Hetrick and Davidow (2013) also compared prazosin (at a dose rate for most cats of 0.5 mg every 12 hours for 7 days) to phenoxybenzamine (2.5 mg every 12 hours for 7 days). Recurrence of urethral obstruction within 24 hours was seen in 10/140 cats given prazosin and 10/46 cats given phenoxybenzamine (relative risk for recurrence after prazosin compared to phenoxybenzamine = 0.33 (95% CI = 0.15-0.74)), and within 30 days in 20/110 cats given prazosin, and 16/41 given phenoxybenzamine (unadjusted relative risk for recurrence after prazosin compared to phenoxybenzamine = 0.47 (95% CI = 0.27-0.81)). However, the change during their study period in their primary antispasmodic from phenoxybenzamine to prazosin was confounded by other changes in the protocol at the same time (e.g. increased use of small catheters and buprenorphine for pain relief). As such, the significant decrease in the recurrence of urethral obstruction associated with prazosin (at the univariable level), may be, at least in part, due to those changes.

It is possible to account for some of this confounding by a bivariable analysis, because all cats treated with phenoxybenzamine were treated prior to June 2006 and all cats treated with prazosin in June 2006 or later. For example, we can re-analyse the data reported by Hetrick and Davidow (2013) to include both catheter size and anti-spasmodic. If we assume that all cats with a recorded catheter size were also treated with an anti-spasmodic, the effect of catheter size on the recurrence of obstruction was clear: odds of recurrence after use of 3.5 F catheter were 0.31

(95% CI = 0.1–0.93) times those of cats in which a 5 F catheter was used, but for prazosin compared to phenoxybenzamine the OR of recurrence was 0.45 (95%CI = 0.15–1.34). Thus, the data were compatible with no effect of prazosin on recurrence of obstruction (as well as a large positive effect and a small negative one). This analysis is, of course, incomplete but it does illustrate that confounding could explain the finding that prazosin reduced recurrence of urethral obstruction.

Reineke *et al.* (2017) compared prazosin (0.25 mg/kg every 12 hours for 30 days) to a placebo in male cats hospitalised and treated for urethral obstruction. The study was designed to detect an absolute difference of 37.5% in recurrence rate between placebo and prazosin-treated cats based on 28 cats being allocated to each group, but only 20 were allocated to the placebo group and 27 to the prazosin group. Following allocation to treatment group, two cats were withdrawn from the study, one from each group, and a further cat in the placebo group was lost to follow-up following the 1-week phone call. The 1-month recurrence rate of cats in the prazosin group was 4/26, while that of the cats in the placebo group was 3/18 (relative risk, calculated for this review, of recurrence for prazosin vs. placebo was 0.92 (95% CI = 0.23–3.64)). The equivalent figures for 6-month recurrence rate were 7/19 and 4/13 (relative risk, calculated for this review, of recurrence for prazosin vs placebo was 1.2 (95%CI = 0.44–3.27)). These inconclusive results reflect a smaller-than-designed study and a lower recurrence rate in the placebo group than the anticipated 50%.

Hanson *et al.* (2021) also compared the impact of prazosin to a placebo on the likelihood of recurrent urethral obstruction. Cats were randomly allocated to receive either 0.5 mg/kg prazosin orally every 12 hours for 7 days or a placebo after standardised hospital treatment for urinary obstruction. Based on an allocation of 40 cats per group, the study was powered to detect a difference between a 36% recurrence rate in the placebo group over the first 30 days and 4% in the treated group (80% power; 5% confidence). However, data were analysed from 37 prazosin-treated cats and 28 placebo-treated cats. Recurrence was observed in 11/37 cats in the prazosin group and 5/28 placebo cats. The authors' Cox-proportional hazard model produced an inconclusive result with the hazard ratio of recurrence for prazosin-treated vs placebo cats being 1.87 (95% CI = 0.65–5.39); i.e. over the 30 days of the study the hazard of recurrence in prazosin-treated cats was almost twice that of placebo-treated cats, but the data were compatible with a range of effects from a moderate reduction in hazard due to prazosin (0.65) to a large increase (5.39).

Conway *et al.* (2022) used a multi-centre, observational, retrospective cohort study to evaluate whether prazosin use decreased the recurrence of urethral obstruction from the start of treatment to 14 days after discharge. Data were collected electronically from clinicians who either always or never prescribed prazosin to cats. The study identified data from 388 eligible male cats, of which 302 cats received prazosin and 86 cats did not. In treated cats, recurrence of obstruction prior to discharge was 34/302 (11%) and for untreated cats, it was 5/86 (6%) (relative risk, calculated for this review, of prazosin vs no prazosin was 1.94 (95% CI = 0.78–4.8)). The equivalent figures for the re-obstruction rate within 14 days of discharge were 72/302 (24%) and 11/86 (13%), respectively (relative risk, calculated for this review, of prazosin vs. no prazosin = 1.86 (95% CI = 1.04–3.35)). Conway *et al.* (2022) concluded that their data showed that prazosin increased the risk of recurrence and supported this by combining their recurrence data within 14 days with the recurrence rate reported by Reineke *et al.* (2017) and Hanson *et al.* (2021) in the first 30 days. Conway *et al.* (2022) stated that this latter analysis “provided even more robust evidence of the lack of efficacy of prazosin in preventing recurrence of urethral obstruction.”

### **Intravesical lidocaine**

Zeza *et al.* (2012) evaluated whether the instillation of alkalised lidocaine into the bladder during treatment for obstructive FIC decreased the recurrence of obstruction and/or the severity of clinical signs. Data from 26 cats were included in the analysis, with data available from four cats treated during the initial phase of the study with 0.1 mL/kg 2% lidocaine and 0.06 mL/kg 8.4% sodium bicarbonate, 16 cats randomly assigned to either 0.2 mL/kg lidocaine and 0.06 mL/kg 8.4% sodium bicarbonate (n = 8) or the same volume of alkalised placebo (n = 8), and an untreated control group of six cats who were either unsuitable for intravesical infusion or whose owners were reluctant to allow infusion. The main outcomes were recurrence of obstruction during a 12-month follow-up period and owner scoring of clinical signs associated with FLUTD (using a 0–10 visual analogue scale). Zeza *et al.* (2012) reported that recurrence rates were similar between cats treated with lidocaine and cats not given lidocaine (7/12 vs. 8/14, respectively), with relative risk, calculated for this review, of obstruction after lidocaine (compared to no lidocaine) being 1.02 (95% CI = 0.53–1.97). Only data from cats with no recurrence of obstruction in the first 2 months after catheterisation were used for the clinical sign analysis (five lidocaine-treated and six no-lidocaine treatment cats). Of the multiple assessments,

only straining at 2 weeks post-discharge was different between groups (less in lidocaine-treated cats;  $p = 0.01$ ). However, no data on clinical signs were presented, and it is highly likely that the small number of cats analysed could mean that large differences between groups may have been missed (type I error), although the multiple analysis of related outcomes could have resulted in type II errors.

## Discussion

The aim of this scoping review was to locate and describe the evidence available for managing FIC. Twenty-two studies relating to the treatment of FIC were located and grouped according to management strategy. The degree of variation across the studies, including type of management, presenting condition, patient demographics, the heterogeneity of the outcomes assessed and reported, and variations in the statistical analyses performed, limited our ability to combine results across studies. Thus, this review focused on the overall picture within each management strategy.

Although 16 of the studies included in this review were randomised controlled trials, all of these trials were relatively small and thus many lacked the power to detect clinically meaningful differences (Button *et al.* 2013). Even where a pre-study power analysis was undertaken (e.g. Hanson *et al.* 2021), the chosen target was much larger than a clinically acceptable effect, meaning that failure to meet the target did not mean that a potential treatment would not be clinically useful. This lack of power was exacerbated by focusing on statistical tests where the principal outcome is a  $p$ -value (such as  $\chi^2$ ) rather than equally simple but more informative analyses (such as relative risk). This meant that in many studies, claims were made of no effect (because  $p > 0.05$ ) when analysis of relative risk would have shown that the data did not exclude a marked benefit (or negative effect) of treatment.

Small sample size was also an issue across almost all of the remaining non-randomised studies, with only Hetrick and Davidow (2013) and Conway *et al.* (2022) including more than 100 cats. Both studies were retrospective with limited control over factors other than the specific FIC treatment being analysed. This is particularly the case for Hetrick and Davidow (2013), where a change in anti-spasmodic was confounded by a large change in the protocol, and it is plausible that the change in protocol was responsible for some (perhaps even all) of the apparent benefit of prazosin against phenoxybenzamine. However, although less obviously confounded, the data used by Conway *et al.* (2022) confounds veterinarian/veterinary practice with use of prazosin, so even though the treated and un-treated cats seem relatively equivalent (except for

age), we cannot be sure that the differences were driven solely by prazosin.

Indeed, multiple uncontrolled variables, such as diet, home environment, unexpected influences of owner-cat interactions and use of other medications, are an issue across a lot of the studies, potentially limiting treatment impact or resulting in spurious benefits. A lot of this is driven by the complex and incompletely understood aetiopathogenesis of FIC. The most obvious manifestation of this is the diagnosis of the disease itself, which, as a diagnosis of exclusion, is not simple. All the studies included in this review tried to exclude causes of FLUTD other than FIC, with many studies expending significant effort to do so. This review assumed the effectiveness of these exclusion procedures, but if other diseases were present, it would clearly affect the value of a study as a determinant of FIC management.

The complex, multifactorial nature of FIC further limits our ability to perform controlled studies. For example, undertaking studies in a hospital or experimental facility, where more complete control of variables is possible, may appear a tempting option. However, the stress induced by this environment may affect outcomes and reduce our ability to extrapolate the data from such studies to individuals in their natural environment. In comparison, where studies are performed on client-owned cats housed at home, absolute control of variables is more complicated. In such a situation, we are unlikely to be able to dictate the exact environmental set-up, social interactions and sometimes even diet, even though failing to do so limits the external validity of our results.

## Environmental modification

There is a clear consensus that stress, particularly that related to the cat's environment (Ellis *et al.* 2013), is a crucial part of the development of FIC. Thus, minimising stress would seem to be a useful approach for reducing symptoms. However, this review has shown that there are only limited data on this approach. Although the use of FFP has been shown to reduce some anxiety-related behaviours (Frank *et al.* 2010), this review identified only one small-scale study of its use in management of FIC (Gunn-Moore and Cameron 2004). Those authors stated that the results of their pilot study, although statistically not significant, warranted further investigation. However, there have been no published peer-reviewed studies of FIC and FFP in the 20 years since it was published.

A similar situation also applies to multimodal environmental modification. This has long been recommended for cats with FIC (Gunn-Moore 2000; Westropp and Buffington 2004), but this review identified only one published peer-reviewed study of such

modification (Buffington *et al.* 2006). The authors of that study (like Gunn-Moore and Cameron 2004) suggested that their approach was “a promising adjunctive therapy” for FIC and “should be followed up with prospective controlled clinical trials.” However, there have been no subsequent published peer-reviewed studies. Buffington *et al.* (2006) did show a statistically significant benefit (for pre-treatment compared to post-treatment) so there is better support for multimodal environmental modification than FFP, but without properly controlled trials, we do not know how much of the benefit was due to the environmental modification and how much to being part of the study. Nevertheless, these results do reinforce the current expert opinion that owners should be provided with detailed information regarding the role of stress in cats with FIC (Westropp *et al.* 2019), alongside demonstrating that we need more studies of the benefit of reducing stress in cats with FIC.

### **Dietary manipulation**

Dietary manipulation has been a mainstay of FIC management for many years (Gunn-Moore 2000; Westropp and Buffington 2004). However, this review has identified only five peer-reviewed studies of the effect of diet on FIC. One of those was a very small-scale study of a cranberry-based supplement, which, although apparently successful in reducing recurrence, was too small to draw strong conclusions (Colombino *et al.* 2022). The other four studies used specialised diets that reduce the risk of FLUTD by producing urinary acidification and controlling calcium, magnesium and phosphorous intake (alongside providing increased amounts of other nutrients such as antioxidants). The first of these four studies (Markwell *et al.* 1999) was an uncontrolled non-randomised comparison of a dry and a canned specialised diet with limited external validity, in which the main finding was that the canned diet might be more effective than the dry diet at preventing recurrence. This suggestion is consistent with the frequent recommendation to increase the moisture content of food and encourage water intake in cats with FIC (Forrester and Towell 2015; Breheny *et al.* 2022). However, this review found no randomised studies comparing dry and moist urinary diets in cats with FIC, with the best published support for Markwell *et al.* (1999) coming from Naarden and Corbee (2020), who reported, in a study where owners chose which diet they gave their cats, that cats whose owners chose moist diets had the lowest recurrence rate (although this was not statistically significant); and Gunn-Moore and Shenoy (2004), who believed that the frequency of clinical signs of FIC in both of their treatment groups (glucosamine and control) reduced markedly over time because 36/40 owners greatly increased the

proportion of their cat’s diet that was moist. More research is required to establish the benefits of changing to moist food in relation to FIC, for both specialised and non-specialised diets.

The evidence that therapeutic diets are effective is more conclusive. Kruger *et al.* (2015) showed in a randomised control trial, that on the control diet the risk of recurrent episodes of FLUTD during the 12-month study was ~8 times higher than on the therapeutic diet, consistent with Naarden and Corbee (2020), who reported that compared to cats fed a therapeutic diet, the risk of FLUTD during their 5-week study was ~3 times higher in cats fed non-therapeutic diets. Thus, although more data would be beneficial, especially in relation to long-term benefits, the published data support the use of specialised urinary diets. However, this does not apply to added anti-stress ingredients such as L-tryptophan, for which there is no peer-reviewed evidence that their addition improves FIC-related outcomes.

### **Anti-inflammatory drugs**

Although inflammatory change plays an important role in FIC (Dorsch *et al.* 2016; Nivy *et al.* 2019; He *et al.* 2022), evidence to support the use of anti-inflammatory drugs in cats with FIC is lacking. In non-obstructive FIC, there is only one study of any class of anti-inflammatory drug (Osborne *et al.* 1996). This study of prednisolone reported no effect on the severity or duration of clinical signs. However, this was a very small study (six cats per group) undertaken in hospitalised cats undergoing a dietary change, so was both stressful and lacked the power to detect clinically meaningful effects. Nevertheless, the lack of analgesia provided by prednisolone combined with its association with urinary tract infection (Epstein *et al.* 2015) means that it is difficult to support the use of prednisolone in cats with FIC.

Meloxicam is the only non-steroidal anti-inflammatory drug (NSAID) for which there is published peer-reviewed data in cats with FIC. All three studies (Hetrick and Davidow 2013; Dorsch *et al.* 2016; Nivy *et al.* 2019) examined short-term use of meloxicam in cats with obstructive FIC around the time of urinary catheter placement and removal. None reported a benefit in reducing the recurrence of urethral obstruction; however, all were small studies so this lack of “significant effect” does not preclude clinically important benefits or important negative effects.

Meloxicam is an effective analgesic in cats (Epstein *et al.* 2015), so the lack of a benefit regarding the recurrence of urethral obstruction does not preclude its use in such cats. However, increased risk of adverse events associated with meloxicam and other NSAID can occur in cats with acute ischaemic kidney injury, hypotension and hypovolaemia, all of which may be present in

obstructive FIC (Dorsch *et al.* 2016). Thus, without strong evidence of an additional FIC-related benefit, other analgesics such as opiates may be more appropriate in cats with obstructive FIC (although further research is required on how best to use opiates in such cats). The same is likely also to apply to NSAID in cats with non-obstructive FIC, i.e. without benefits beyond simple analgesia, they should be used with caution. As there is currently no published evidence on the impact of NSAID on non-obstructive FIC, their routine use cannot be recommended (Taylor *et al.* 2024).

### **Amitriptyline**

The use of amitriptyline in human patients with interstitial cystitis led to the initial interest in amitriptyline use for cats with FIC (Chew *et al.* 1998). The first study of amitriptyline for FIC was an observational study of daily administration over 12 months (Chew *et al.* 1998), which found that 9/15 previously refractory cases showed complete resolution of clinical signs over the 12-month period. Although these data are promising, the lack of a control group combined with limited control of other factors that could influence recurrence means it is difficult to extrapolate these results to the general population, and the results need further confirmation. This has not happened in the past 25 years, with both subsequent studies of amitriptyline (Kraijer *et al.* 2003; Kruger *et al.* 2003) only evaluating its use for FIC over the short term. Kraijer *et al.* (2003) reported no significant benefits of amitriptyline treatment but lacked the power to distinguish between a significant benefit and a significant negative effect. Most of the outcomes evaluated by Kruger *et al.* (2003) were also not significantly affected by amitriptyline treatment except for the hazard of recurrence of all clinical signs, which was lower in placebo-treated cats than in amitriptyline-treated cats. Taken together, these results suggest that over the short term, the use of amitriptyline in cats with FIC is unlikely to be beneficial, while in the long term, we lack the data to make robust conclusions. Combined with the adverse effects of somnolence and a possible increased risk of incomplete bladder emptying (Chew *et al.* 1998; Kruger *et al.* 2003), the published results indicate that care should be taken before amitriptyline is recommended for use in cats with FIC.

### **Glycosaminoglycans**

Alterations in the urinary glycosaminoglycan layer may play a role in FIC pathogenesis (Forrester and Towell 2015), leading to the hypothesis that restoration of a normal layer may result in an improvement in the clinical picture of cats with FIC. None of the studies identified by the review reported statistically significant

effects of glycosaminoglycans over placebo. However, all of them lacked the power to identify clinically relevant benefits or negative effects. We thus lack sufficient evidence to conclude whether glycosaminoglycans are likely to be beneficial in cats with FIC.

### **Prazosin**

It has been postulated that urethral spasm contributes to the pathogenesis of initial and recurrent obstruction of cats with FIC, leading many veterinarians to recommend antispasmodic drugs in such cats, particularly prazosin (Reineke *et al.* 2017). The initial study on prazosin, by Hetrick and Davidow (2013), concluded that cats administered prazosin had a lower risk of recurrent obstruction than those given phenoxybenzamine. This was, however, a retrospective study where multiple changes occurred alongside the change in antispasmodic drug, and it is plausible that it was these changes that reduced recurrence, rather than prazosin. Two subsequent prospective double-blind studies of prazosin vs. a placebo (Reineke *et al.* 2017; Hanson *et al.* 2021) failed to find a statistically significant benefit of prazosin, but both studies lacked the power to identify clinically important effects. The most recent study of prazosin (Conway *et al.* 2022) was a retrospective observational study that showed a negative effect of prazosin on recurrence. The confounding of prazosin use with veterinary practice means that interpretation of these results is not simple, especially as there were no standardised treatment protocol or follow-up, but the results do suggest that the use of prazosin (and perhaps any antispasmodic) is not likely to be beneficial in cats with obstructive FIC, especially as the evidence for the importance of urethral spasm in FIC-related obstruction is far from strong (Conway *et al.* 2022).

### **Intravesical lidocaine**

As with many treatments for FIC, the use of intravesical alkalinised lidocaine stemmed from positive effects of its use in humans with interstitial cystitis (Zezza *et al.* 2012). However, the study by Zezza *et al.* (2012) failed to show any significant benefit on the recurrence rate or severity of clinical signs in cats with obstructive FIC. Although this study, like many others, was underpowered to detect clinically meaningful differences, the lack of a large benefit from a treatment regime that can be difficult to achieve (Zezza *et al.* 2012), suggests that intravesical alkalinised lidocaine should not be recommended for cats with FIC.

### **Conclusion**

This systematic review aimed to identify and describe the current evidence for commonly recommended management techniques for feline idiopathic cystitis.

The results indicate that very few of the management techniques included in the 22 papers had good evidence to support their use (or indeed good evidence to recommend that they were not used). Currently, multimodal environmental management to reduce stress/conflict, and therapeutic urinary foods (particularly if combined with an increase in moisture content of the diet) have the best evidence for use and should, together, be considered the primary treatment approach. The evidence for other modalities, especially oral medicines such as NSAID, anti-depressants, glycosaminoglycans and sprays containing pheromones, is insufficient to support their use, but larger-scale studies are needed to better characterise their benefit and to identify whether there are sub-populations of cats with FIC that may benefit. The overall lack of high-quality demonstrations of effective treatments, even for widely used treatments such as specialised urinary diets, emphasises the need for clinicians to be critical in their evaluation of the published literature on FIC management and to keep themselves up-to-date with the latest research on this perplexing and difficult to manage condition.

As an example of this, during the process of this review, initial findings of a pilot study using low-dose radiation therapy to treat FIC were presented at the 2023 American College of Veterinary Internal Medicine Forum (Kendall *et al.* 2024). As of September 2023, 15 cats had been treated, with no recurrence of their clinical signs (A. Kendall,<sup>1</sup> pers. comm.). This is promising, and a formal study has been announced (Eplin Wheeler 2024), however to-date there are still no peer-reviewed studies available, and, as this review shows, we should not assume a treatment is effective until properly planned, controlled, large-scale clinical trials have been published.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

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