

‘Don’t pee on that!’ Comparing environmental modification and medical management in cats with FIC

A Knowledge Summary by

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ISSN: 2396-9776

Published: 11 Mar 2021

in: The *Veterinary Evidence* journal Vol 6, Issue 1

DOI: [10.18849/VE.V6I1.337](https://doi.org/10.18849/VE.V6I1.337)

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Next Review Date: 03 Jun 2022



PICO question

In cats with feline idiopathic cystitis (FIC) is environmental modification superior than medical management in preventing reoccurrence?

Clinical bottom line

Category of research question

Treatment

The number and type of study designs reviewed

16 papers were critically reviewed; 14 randomised trials and two case studies

Strength of evidence

Critical appraisal of the selected papers meeting the inclusion criteria collectively provide weak evidence in terms of their experimental design and implementation

Outcomes reported

There is weak evidence that any medication or environmental modification is successful in reducing the reoccurrence of FIC when compared to a placebo. Short-term use of amitriptyline can contribute to an increase in occurrence of FIC

Conclusion

In view of the strength of evidence and the outcomes from the studies the following conclusion is made; in cats with feline idiopathic cystitis there is weak evidence that environmental modification or medication are effective at preventing reoccurrence. Further research is required into the cause of FIC before comparisons on treatment options can be made, however, with the exception of short-term use of amitriptyline, environmental modification and systemic treatment of clinical signs did not contribute to an increase in occurrence of FIC

[How to apply this evidence in practice](#)

The application of evidence into practice should take into account multiple factors, not limited to: individual clinical expertise, patient's circumstances and owners' values, country, location or clinic where you work, the individual case in front of you, the availability of therapies and resources.

Knowledge Summaries are a resource to help reinforce or inform decision making. They do not override the responsibility or judgement of the practitioner to do what is best for the animal in their care.

Clinical Scenario

A 4-year-old, male neutered cat is being presented for the third time for cystitis. After a thorough work up, a diagnosis of idiopathic cystitis has been made. The patient is already on a gastrointestinal prescription diet, and the owner does not want to change this. The owner asks if other treatments are available to reduce the occurrence of his clinical signs.

The evidence

The literature searches uncovered 13 papers that addressed pharmaceutical treatment for cats with feline idiopathic cystitis (FIC) and three papers addressing environmental modification as a treatment. Pharmaceutical treatments included oral preparations of non-steroidal anti-inflammatory Drugs (NSAIDs) (Dorsch et al., 2016), steroids (Osbourne et al., 1996), tricyclic antidepressants (Chew et al., 1998; Kruger et al., 2003; and Kraijer et al., 2003), glucosamine (Gunn-Moore and Shenoy, 2004) and prazosin (Reineke et al., 2017). Parenteral treatments include intravesical glycosaminoglycan (GAGs) (Bradley et al., 2013), pentosan polysulphate and lidocaine (Zezza et al., 2012) and subcutaneous pentosan polysulphate (Wallius et al., 2009). Of these studies, only one paper (Chew et al., 1998) found that long-term (12 months) use of amitriptyline successfully decreased clinical signs of recurrent cystitis in 9/15 cats treated, however this improvement was only apparent in the last 6 months. Three studies included environmental modification as a treatment option, which included the use of feline facial pheromones (FFPs) (Gunn-Moore and Cameron, 2004). The use of FFPs did not have a statistical difference in reoccurrence of signs when compared to the placebo, however there was a clinical difference shown, with those exposed to FFP having a reduced occurrence and reduced severity of FIC. A case study by Seawright et al. (2008) followed a case with environmental modification for an extended period of time, which showed that episodes of cystitis only occurred during extraordinary stressful situations such as building works. A study into multimodal environmental modification (Buffington et al., 2006) showed a resolution in signs for 75% for 10 months. Each study into environmental modifications had a number of uncontrollable variables due to each cat's condition and environment, so further studies are required to confirm any success.

Summary of the evidence

Osborne et al. (1996)	
Population:	Male and female cats with idiopathic cystitis
Sample size:	12 cats
Intervention details:	<ul style="list-style-type: none">• Cats split in two groups• Group 1 (n=6) received oral prednisolone 1 mg/kg twice daily for 10 days (two female, four male)• Group 2 (n=6) received placebo with the same dosing schedule for 10 days (two female, four male)• Hospitalised for 10 days
Study design:	Double blinded clinical study
Outcome studied:	<ul style="list-style-type: none">• For first 10 days urine analysis was completed daily• 4 and 18 days after discontinuation of therapy urinalysis and bacterial urine cultures were performed• Daily observation of clinical signs for first 10 days to look for a reduction in dysuria, haematuria and struvite presence in urine

Main findings: (relevant to PICO question):	<ul style="list-style-type: none"> • Dysuria subsided after a mean of 1.5 days in both groups • Haematuria reduced after a mean of 3.2 days in prednisolone treated cats and 3.5 days in placebo treated cats • A 10 day course of prednisolone had no clinical benefit over the placebo
Limitations:	<ul style="list-style-type: none"> • Patients were hospitalised throughout, potentially increasing stress and exacerbating any clinical signs • Act of collecting urine daily and medicating everyday has potential to increase stress and exacerbate clinical signs. • Study had a small sample size and was performed over a short period of time

Chew et al. (1998)	
Population:	Cats with idiopathic cystitis that failed to respond to other treatments
Sample size:	15 cats
Intervention details:	Cats received 10 mg of amitriptyline per os (PO), every (q)24 hours in the evening for 12 months, or until signs reoccurred
Study design:	Prospective study
Outcome studied:	<ul style="list-style-type: none"> • Urinalysis, complete blood count, serum biochemical analysis, urine bacteriologic culture and cystoscopy were performed initially and after 6 and 12 months • Owner-observed severity scores of lower urinary tract signs were recorded
Main findings: (relevant to PICO question):	<ul style="list-style-type: none"> • During first 6 months 11/15 cats had no owner observed signs • In the last 6 months 9/15 cats had no owner observed signs. • Cystoscopic abnormalities persisted in all cats • Haematuria and proteinuria were decreased in all cats at 12 month evaluation • Treatment with amitriptyline decreased signs and occurrence of FIC in 9/15 patients over the 12 month period • Urinary calculi presented in 4/15 cats in the first 6 months
Limitations:	<ul style="list-style-type: none"> • Owner evaluation can be inaccurate • Not a controlled study so external factors could have contributed • Small sample size • Paper did not include any CI or p-values

Kruger et al. (2003)	
Population:	Cats with acute, non-obstructive idiopathic lower urinary tract disease
Sample size:	31 male and female cats
Intervention details:	<ul style="list-style-type: none"> • Split into two groups • Group 1 (n=16) treated with 5 mg amitriptyline daily for 7 days – two cats then excluded from this group due to acquired urinary tract infection • Group 2 (n=15) given placebo for 7 days • Re-examined after 1 month of treatment • Owners interviewed by telephone 6, 12 and 24 months of treatment
Study design:	Randomised controlled trial
Outcome studied:	Incidence of pollakiuria and haematuria
Main findings: (relevant to PICO question):	<ul style="list-style-type: none"> • Group 1 – Pollakiuria and haematuria resolved by day 8 in cats treated with amitriptyline • Group 2 – Pollakiuria and haematuria resolved by day 10 in cats treated with placebo • Pollakiuria and haematuria recurred faster and more frequently in amitriptyline treated cats • Results suggested that short-term amitriptyline treatment has no benefit in terms of resolution of pollakiuria and haematuria in cats with idiopathic lower urinary tract disease and may be associated with an increased risk of reoccurrence
Limitations:	<ul style="list-style-type: none"> • Small sample size • Owner evaluation can be inaccurate • External factors could have contributed • Potential for wide number of variables in each cat's environment • No p-value available

Kraijer et al. (2003)	
Population:	Cats with idiopathic cystitis in the Netherlands
Sample size:	24 cats
Intervention details:	<ul style="list-style-type: none"> • Treatment group (n=11) amitriptyline 10 mg/cat given orally once daily in the evening for 7 days • Control group (n=13) received a placebo tablet with the same dosing schedule • 10 mg/kg amoxicillin trihydrate orally twice daily given to all cats
Study design:	Double blind, placebo controlled study
Outcome studied:	<ul style="list-style-type: none"> • Severity of symptoms marked by a practitioner on a visual analogue scale at days 0, 7 and 14

	<ul style="list-style-type: none"> • Owners monitored urination frequency, duration and volume, level of activity and general attitude of the patient
Main findings: (relevant to PICO question):	<ul style="list-style-type: none"> • No statistical differences between the treatment group and placebo group by practitioner (p=0.2) or owner (p=0.5) • The treatment was associated with a change in general attitude and decreased level of activity (p=0.02) • Treatment group experienced a reduction in microscopic haematuria and proteinuria after 5 days • Placebo group experienced a reduction in proteinuria after day 2
Limitations:	<ul style="list-style-type: none"> • Environment not controlled, so cats had other variables that could have affected results • Owner evaluation of signs can be inaccurate • No p-values for the reduction in microscopic haematuria or reduction in proteinuria

Gunn-Moore & Cameron (2004)	
Population:	Cats with a recent history of dysuria pollakiuria and haematuria; at least two episodes in 6 months. Referred to the Feline Clinic of the University of Edinburgh Small Animal Hospital
Sample size:	12 cats (male neutered n=6; female neutered n=6)
Intervention details:	<ul style="list-style-type: none"> • Group 1 (n=6) – Six cats exposed to feline facial pheromone (FFP) for 2 months, then placebo for 2 months • Group 2 (n=6) – Six cats exposed to placebo for 2 months, then FFP for 2 months • One depression of spray 10 cm away from any object that protruded into areas where the cats walked • The spray was applied daily in households with one or two cats, and twice daily in households with three or more cats
Study design:	Randomised double blinded, placebo controlled crossover study
Outcome studied:	<p>Using linear visual analogue scales, the owners were asked to daily define the severity of the cat's clinical signs:</p> <ul style="list-style-type: none"> • increased frequency of urination • straining while urinating • crying out while urinating • blood in urine • urination outside of litter box • increased grooming around perineum <p>A further visual analogue scale was used to assess whether the cats behaviour had changed. This was used on a weekly basis:</p> <ul style="list-style-type: none"> • increase or decrease in negative behaviours • increase or decrease in positive behaviours • increase or decrease in spraying in the house • increase or decrease in eating
Main findings: (relevant to PICO question):	No statistical differences between the two treatment groups (p=0.5). However, a clinical difference showing a trend for the six cats

	<p>exposed to FFP to have less severe episodes and fewer recurrences of FIC</p> <p>FFP total, mean \pm standard deviation:</p> <ul style="list-style-type: none"> • FFP – 30, 4.3 ± 6.7 • Placebo – 69, 9.9 ± 19.1
Limitations:	<ul style="list-style-type: none"> • Three cats did not complete the study, and data for two cats were lost by the owners, so the sample size was small • Those recruited to the study were dedicated owners who had opted for referral, so not a representative sample • Owner evaluation can be inaccurate

Gunn-Moore & Shenoy (2004)	
Population:	Cats with recurrent cystitis due to FIC recruited from the referral cases of the Feline Clinic of the University of Edinburgh Small Animal Hospital between Feb 2001 and May 2002
Sample size:	40 cats
Intervention details:	<ul style="list-style-type: none"> • Treatment group (n=20) – cats received 125 mg of N-acetyl glucosamine PO once daily (UID) for 6 months • Placebo group (n=20) – cats received a placebo PO UID
Study design:	Randomised, double- blinded, placebo controlled
Outcome studied:	<p>Owners asked to grade the severity of their cats' signs at both start and end of study using a health score scale of 0 (very severe cystitis) to 5 (normal cat). Owners also kept a cystitis diary every day (for 6 months), recording the following signs:</p> <ul style="list-style-type: none"> • increased frequency of urination • straining while urinating • crying while urinating • blood in urine • urination outside litter tray • increased grooming around perineum • altered behaviour <p>Mean urine specific gravity after 1 month was compared with the initial urine sample</p>
Main findings: (relevant to PICO question):	<ul style="list-style-type: none"> • Owner assessment suggested that those treated with glucosamine achieved a slightly greater improvement, however there was no significant difference ($p > 0.5$) • The majority of cats in both groups improved significantly ($p < 0.001$, mean health score of each group at the start was $0.5 \pm SD 0.5$, compared to glucosamine 4.4 ± 0.7 and placebo 3.9 ± 1.6 at the end), however this was believed to have occurred due to the concurrent introduction of wet food • The urine specific gravity at the start was significantly higher (mean $1.050 \pm SD 1.007$) than when reassessed after 1 month (1.036 ± 1.010 $p < 0.01$)
Limitations:	<ul style="list-style-type: none"> • Small sample size • Oral medication could increase stress

	<ul style="list-style-type: none"> • Owner evaluation can be inaccurate • Number of variables in different home environments. • Owners concurrently increased cats water intake during study • Potential placebo effect and reduction in stress due to owners increased understanding of condition
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Buffington et al. (2006)	
Population:	Cats with obstructive idiopathic cystitis
Sample size:	<ul style="list-style-type: none"> • 46 client owned indoor housed cats with idiopathic cystitis, specifically suffering from at least two bouts in the previous 10 months • Male (n=24) and female (n=22) from single (n=12) and multicat (n=34) households • Aged between 2 and 5-years-old
Intervention details:	<ul style="list-style-type: none"> • Cases were offered recommendations for multimodal environmental modification (MEMO) based on a detailed environmental history • MEMO included: not punishing the cat, increasing water intake, changing to an unscented clumping litter, improved litter box management, vertical enrichment, increased interaction, resolution of multicat conflicts and audit and video sensory stimulation
Study design:	Prospective observational study
Outcome studied:	Client reported reoccurrence of lower urinary tract signs, and any other signs
Main findings: (relevant to PICO question):	<ul style="list-style-type: none"> • After 10 months, no lower urinary tract signs (LUTS) were observed in 70–75% of the cats ($p<0.0001$) • Of those that did suffer from recurrent episodes, clients reported they resolved spontaneously without veterinary intervention • Reductions in fearfulness ($p<0.0002$), nervousness ($p<0.002$) and upper respiratory signs were seen ($p<0.03$) • Trends towards reductions in aggressiveness ($p<0.09$) and lower intestinal tract signs ($p<0.20$) were also reported
Limitations:	<ul style="list-style-type: none"> • Owner evaluation can be inaccurate • Number of different variables changing for each cat • No concurrent control groups

Seawright et al. (2008)	
Population:	5-year-old male, neutered Domestic Short Haired (DSH) with FIC
Sample size:	One cat
Intervention details:	<ul style="list-style-type: none"> • Treatment with meloxicam, prazosin, dantrolene and GAG supplementation for 3 weeks

	<ul style="list-style-type: none"> Wet diet introduced as well as a water fountain Patient given a core area with easy access to resources, increased number of hiding places and 3-dimensional space Visual access to outside blocked Cat followed up for 15 months
Study design:	Case-control study
Outcome studied:	<ul style="list-style-type: none"> Reoccurrence of urethral blockage or signs of FIC Behavioural assessment
Main findings: (relevant to PICO question):	<ul style="list-style-type: none"> No recurrence of clinical signs for 6 months One stressful event (owner confined all cats household cats in close proximity) 2 days prior to recurrence of signs No recurrence of clinical signs for another 6 months
Limitations:	<ul style="list-style-type: none"> Number of variables including environment, medication and diet change Owner evaluation can be inaccurate Statistical analysis not available

Wallius et al. (2009)	
Population:	Cats with clinical signs of cystitis, absence of positive urine culture for bacteria, absence of urethral obstruction
Sample size:	18 neutered male (n=9) and female (n=9) cats
Intervention details:	<ul style="list-style-type: none"> Treatment group (n=9) – cats were treated with subcutaneous injections of 3 mg/kg pentosan polysulphate on days 1, 2, 5 and 10 Placebo group (n=9) – isotonic saline solution on days 1, 2, 5 and 10 Cats examined at the time of injections and owners interviewed regarding urination habits Telephone interview at 2 weeks, 2 months, 6 months and 1 year following treatment
Study design:	Double blinded, randomised, placebo controlled
Outcome studied:	Recurrence of lower urinary tract signs
Main findings: (relevant to PICO question):	<ul style="list-style-type: none"> Two cats left the study due to euthanasia No statistical differences between the two groups during treatment or at reevaluation for clinical signs Those that did show clinical signs, had been exposed to stressful events before clinical signs, which was found to be significant ($p=0.0023$)
Limitations:	<ul style="list-style-type: none"> Small sample size High number of variables Owner evaluation can be inaccurate No reported confidence interval

Zeza et al. (2012)	
Population:	Cats with obstructive idiopathic lower urinary tract disease (LUTD), median of 5-years-old, median of 5.5 kg
Sample size:	26 cats – male neutered (n=25) male entire (n=1)
Intervention details:	<ul style="list-style-type: none"> • Case group (n= 12) – treated with 0.2 ml/kg lidocaine (2%) and 0.06 ml/kg sodium bicarbonate (8.4%) intravesical UID for 3 days • Control group (n=14) – treated with placebo of 0.2 ml/kg saline solution and 0.06 ml/kg sodium bicarbonate (8.4%) intravesical UID for 3 days • Cats monitored every 2 hours for 2 days • Amoxicillin-clavulanic acid (20 mg/kg PO q12hr) or amoxicillin (20 mg/kg PO q12hr) started concurrently and continued in cats that did not re-obstruct immediately
Study design:	Randomised placebo controlled prospective clinical trial
Outcome studied:	<ul style="list-style-type: none"> • Recurrence rate and amelioration scores of clinical signs were assessed and compared • Questionnaire follow-up at 2 weeks, 1 month and 2 months. Questionnaire was composed of 8 visual analog scales, with values ranging from 0 (normal cat) to 10 (very severe clinical signs) • Owners asked to look for 8 signs: <ol style="list-style-type: none"> 1. increased frequency of urination 2. straining while urinating 3. crying out while urinating 4. presence of blood in the urine (macroscopic hematuria) 5. urination outside the litter box 6. increased grooming around the perineum 7. altered behaviour (increased aggression, fear, or nervousness) 8. gastrointestinal symptoms (e.g., vomiting, diarrhea)
Main findings: (relevant to PICO question):	<ul style="list-style-type: none"> • Reoccurrence of urethral obstruction was 7/12 (58%) in the case group and 8/14 (57%) in the control group • Amelioration scores were similar between the two groups • No clinical benefit to adding lidocaine • Amelioration of straining after 2 weeks was noted (p=0.01)
Limitations:	<ul style="list-style-type: none"> • Small sample size • High number of variables • Sample restricted to cats with urethral obstruction • No reported confidence interval • Owner observation could be biased or inaccurate

Bradley et al. (2013)	
Population:	Veterinary referred male cats with urethral obstruction from suspected FIC
Sample size:	14 cats
Intervention details:	<ul style="list-style-type: none"> All cats received bladder lavage and received fluid therapy Treatment group (n=7) received intravesical GAGs at the time of urinary catheter placement and again 12 and 24 hours later Placebo group (n=7) received intravesical saline at the time of urinary catheter placement and again 12 and 24 hours later Three of the cats in the placebo group suffered obstruction within 7 days, and two were then crossed over to the treatment group Patients were monitored for 7 days, including urinalysis at 0, 3 and 7 days, urine culture at 0 and 7 days, daily pain scoring and re-check at 3 and 7 days
Study design:	Randomised, blind placebo controlled clinical trial
Outcome studied:	<ul style="list-style-type: none"> Repeat urethral obstruction Urine specific gravity Pain score Aerobic bacterial urine culture
Main findings: (relevant to PICO question):	<ul style="list-style-type: none"> Repeat obstruction rates were 3/7 (42.9%) placebo group cats and 0/9 (0%) treatment group cats (p= 0.06) Mean urine protein content of the treatment group was 2.9 vs 1.6 for the placebo group (p=0.03) Mean urine specific gravity of the treatment group was 1.028 vs 1.043 for the placebo group (p=0.02)
Limitations:	<ul style="list-style-type: none"> Study limited to males with urethral obstruction, not confirmed FIC Study size relatively small Controlled hospital study can increase stress in cats which can lead to urethral blockage

Delille et al. (2016)	
Population:	Cats obstructive FIC
Sample size:	35 cats
Intervention details:	<ul style="list-style-type: none"> All cats received intravenous fluids and buprenorphine Once clinically stable an indwelling urinary catheter was placed and the bladder drained and flushed with warm sterile solution of sodium chloride until the urine appeared macroscopically clear Treatment group (n= 18) received 30 mg pentosan polysulfate in 10 mls of saline. This was instilled into the

	<p>bladder via urinary catheter, and the urinary catheter clamped for 30 minutes before connection to a closed system collection set</p> <ul style="list-style-type: none"> • Placebo group (n= 17) only had saline instilled into the bladder • All cats were treated with 0.01 mg/kg buprenorphine q8hours for day 1 to 5, 0.5 mg phenoxybenzamine q24 hours from day 3 to 14 and 0.05 mg of acepromazine q8–12hours for day 1 and 2
Study design:	Prospective, randomised, placebo controlled, double-blinded study
Outcome studied:	<ul style="list-style-type: none"> • Daily physical examinations and urinalyses were compared • Patients monitored for repeat urinary obstruction
Main findings: (relevant to PICO question):	<ul style="list-style-type: none"> • No statistical differences between the treatment group and placebo group on physical exam (p=0.99) • No statistical differences between the treatment group and placebo group for repeat urethral obstruction (p=1.00) • Treatment group experienced a reduction in microscopic haematuria and proteinuria after 5 days (p<0.05) • Placebo group experienced a reduction in dipstick haematuria on day 5 (p<0.05) and reduction in proteinuria after day 2 (p<0.05) and day 3 (p<0.01)
Limitations:	<ul style="list-style-type: none"> • Limited to those with obstructive idiopathic cystitis • Cats were hospitalised, potential for external stressors to affect results • No reported confidence interval

Dorsch et al. (2016)	
Population:	Cats with obstructive idiopathic cystitis
Sample size:	37 cats
Intervention details:	<ul style="list-style-type: none"> • Cats received supportive treatment and an indwelling urinary catheter for 48 hours, concurrent to intervention treatments • Group 1 (n=18) received meloxicam orally at 0.1 mg/kg on day one, then 0.05 mg/kg on days 2–5 • Group 2 (n=19) received placebo alongside same schedule • Sent home after able to urinate for 24 hours by self
Study design:	Double blinded controlled clinical study
Outcome studied:	<ul style="list-style-type: none"> • Physical exams and urinalysis repeated daily for 5 days, then owner reported demeanor for 5 days and repeat telephone interview after 3 months • Parameters for evaluation were occurrence of urethral obstruction, results of physical exams and demeanor
Main findings: (relevant to PICO question):	<ul style="list-style-type: none"> • Recurrent urethral obstruction occurred after 5 days in 4/18 (22%) of cats in meloxicam group and 5/19 (26%) in Group 2 (p=1.00)

	<ul style="list-style-type: none"> • General abdominal pain and demeanour improved significantly during hospitalisation for both groups ($p < 0.001$) • General demeanour, food intake and voiding behaviour were no different in both groups during the 3 months • No significant difference between groups at different time points
Limitations:	<ul style="list-style-type: none"> • Patients receiving supportive treatment concurrently to meloxicam and placebo. This could affect results as you cannot credit any success to one treatment alone • Owner questionnaire was with a visual analog scale which can be inaccurate depending on owner interpretation and understanding • Study was performed on FIC cats with only obstructive FIC with the measured outcome being repeat obstruction. Some cats show other signs before obstructing, with others not obstructing at all, so this study may not show any relevance to them • Cats were then observed at home, which although is a more natural environment, has uncontrollable external factors that will affect results

Reineke et al. (2017)	
Population:	Male cats with urethral obstruction with urinary calculi >2 mm in diameter
Sample size:	47 cats
Intervention details:	<ul style="list-style-type: none"> • Cats (n=27) were chosen at random to receive prazosin 0.25 mg/cat PO q12hours for 1 month following obstruction • Remaining cats (n=20) received a placebo for 1 month • Owners reported signs at 1, 2, 3 and 4 weeks follow-up periods, and again at 6 months
Study design:	Double blinded, prospective, interventional study
Outcome studied:	Cats were monitored for: <ul style="list-style-type: none"> • repeat urethral obstruction (rUO) • severity of lower urinary tract signs
Main findings: (relevant to PICO question):	<ul style="list-style-type: none"> • No difference in the rUO rate with prazosin or placebo prior to hospital discharge: (2/26 (7%) vs 1/19 (5%), $p=1.00$) • No difference in the rUO rate with prazosin or placebo during the 1 month medication period: (4/26 (15%) vs 3/18 (17%), $p=0.776$) • No difference in the rUO rate with prazosin or placebo at 6 months following treatment: (7/19 (37%) vs 4/13 (31%), $p=0.811$) • Following randomisation two cats (one from each group) were withdrawn

Limitations:	<ul style="list-style-type: none"> • Study limited to males with urethral obstruction, not confirmed FIC • Study size relatively small • Owner evaluation can be inaccurate
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Nivy et al. (2019)	
Population:	Male cats with FIC associated urethral obstruction
Sample size:	51 cats
Intervention details:	<ul style="list-style-type: none"> • Group 1 (n=24) – cats after hospitalisation were treated with phenoxybenzamine, alprazolam and meloxicam (0.025 mg/kg/day) for 2 weeks • Group 2 (n= 27) – cats after hospitalisation were treated with phenoxybenzamine and alprazolam for 2 weeks
Study design:	Prospective, randomised clinical trial
Outcome studied:	Recurrent urethral obstruction
Main findings: (relevant to PICO question):	<p>Cumulative number of cats with recurrent urethral obstruction at:</p> <ul style="list-style-type: none"> • 10 days = 1 (2%) • 1 month = 2 (4%) • 2 months = 4 (8%) • 6 months = 8 (16%) <p>Overall 12 cats: Eight cats with added meloxicam and four cats without No clinical benefit of adding low-dose meloxicam was detected (p=0.70)</p>
Limitations:	<ul style="list-style-type: none"> • Small sample size • Number of variables in the environment • Owner evaluation can be inaccurate • Study limited to those with urethral obstruction

Sofyan et al. (2019)	
Population:	8-month-old, male neutered Domestic Short Haired (DSH) cat, weighing 4.5 kg, with FIC
Sample size:	One cat
Intervention details:	<ul style="list-style-type: none"> • Doxycycline, diazepam and neurotropic vitamins for 5 days • Probiotic with <i>Lactobacillus casei</i>, <i>L. rhamnosus</i>, <i>L. acidophilus</i> and <i>bulgaricus</i> and <i>Bifidobacterium infantis</i> and <i>B. breve</i> and <i>Streptococcus thermophilus</i> • Dry food prescription for urinary disease
Study design:	Case report
Outcome studied:	Ability to urinate post catheterisation
Main findings: (relevant to PICO question):	Cat was able to urinate once treatments given

Limitations:	<ul style="list-style-type: none"> • Patient was on a number of treatments • Study contributes success to probiotic combination treatment. However, no measurements or scales to analyse this • Does not state how long patient was monitored for
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Appraisal, application and reflection

A number of studies were identified due to the wide variables involved with searching for medication. However, each study focused on a different treatment, allowing for a wide range of results. There was no study that compared medical treatment alone to environmental treatment.

Only one study, Chew et al. (1998), identified medication as having an effect on reducing the occurrence of FIC. This was if the patients were treated with amitriptyline 10 mg/cat SID PO long-term. The study showed that the medication decreased the occurrence in 9/15 (60%) cats, and reduced haematuria and proteinuria in 100% of cats at the 12 month evaluation. However, the sample size of this study was small (n=15) and could have been impacted by a number of variables within the cat's environment. The cessation of haematuria and proteinuria is a positive outcome for the treatment; however, it is not made clear if these patients were tested within the same time period. FIC being a self-limiting disease may indicate that the cats could have been asymptomatic at the time regardless of the treatment. 5 years later, Kruger et al. (2003) found that short-term administration (7 days) of amitriptyline had no statistical benefit over the reduction in pollakiuria and haematuria. Additionally, cats treated with amitriptyline had a faster recurrence rate when compared to the placebo. Much like the study by Chew et al. (1998) there were uncontrollable variables within the cat's environment that could have contributed to these results.

Six of the studies focused specifically on cats with FIC that caused urethral obstruction and the reoccurrence of symptoms if treatment was given at the time of obstruction. Dorsch et al. (2016) identified that there was no significant difference between patients having meloxicam and a placebo for 5 days post obstruction, however due to the nature of the treatment for a urethral obstruction, this was given concurrently with a urinary catheter and fluid therapy, so credit of success cannot be given to one treatment alone. This study does not identify the cause of the obstruction, and whether patients had high amounts of urinary sediment, or inflammation. The measured outcome was a repeat urethral obstruction and does not record whether cats suffered with other generalised symptoms of FIC before becoming obstructed. This was a similar finding to Nivy et al. (2019) with the administration of phenoxybenzamine and alprazolam (n=51) with the addition of meloxicam (n=24). This study had the largest sample size, but no placebo control group, so the results cannot be contributed to any success.

Reineke et al. (2017) completed a longer-term study with the administration of prazosin (n=27) for 1 month following urethral obstruction. Follow-ups for 6 months post-treatment identified no statistical difference between the prazosin and placebo for a repeat urethral obstruction, or a reduction in the severity of clinical signs. Like the previous studies that test oral medication, the variables in the environment cannot be controlled, and may have contributed to the recurrence of clinical signs, alternatively the stress of giving medication on a daily basis could have also contributed to clinical signs.

Three studies focused on the administration of medication through intravesical means, one with intravesical GAGs (Bradley et al., 2013), pentosan polysulphate (Delille et al., 2016) and the other with intravesical sodium bicarbonate ± lidocaine (Zezza et al., 2012). Bradley et al. (2013) found that those treated with GAGs had a reduced recurrence of obstruction when compared to the placebo group (p=0.06), however the study size was small (n=14) and performed within a hospital environment with concurrent treatment of fluid therapy. When given intravesical pentosan polysulphate (Delille et al., 2016), obstructed cats suffered with repeat obstruction at the same rate as those with a placebo (p=1.00). Zezza et al. (2012) found no clinical benefit to the addition

of lidocaine, however although the sample size was larger than Bradley et al. (2013), it was again restricted to hospitalised patients (n=26) with concurrent treatments of amoxicillin-clavulanic acid for 2 days before discharge.

Wallius et al. (2009) combined owner interviews with clinical examination for treatment with subcutaneous injections of pentosan polysulphate, treatment used in human interstitial cystitis. The sample size was small (n=18) and was made smaller due to two cats being euthanised due to their clinical signs during the study. No statistical difference was found between the treatment and the placebo, despite the differing variables within the cat's environment.

Giving other treatment concurrently to medication was common in these studies. Those owners that participated in the studies were obviously keen to treat their cats, so tried all forms of treatment to alleviate symptoms. Although beneficial for the patient, is not helpful in regard to studies as any results cannot be related directly to the medication. This was the case with Gunn-Moore & Shenoy (2004) and grading the severity of FIC signs alongside the administration of N-acetylglucosamine (n=40). Participants for the study were recruited from those referred directly to the university so had an invested interest in the cat's success. Although owner assessment suggested that those treated had a greater improvement, there was no significant difference, and it was identified that owners had concurrently increased the water intake of the cats during the study, probably leading to the improvement seen.

Controlled studies within the hospital took place with the administration of prednisolone UID for 10 days (Osbourne et al., 1996). Although this allows for variables to be controlled, it also introduces the variable of the patient being stressed in an unnatural environment, thus potentially increasing the chance of stress related signs. Osbourne showed that steroid treatment had no benefit for reducing the clinical signs of FIC (n=12), however the sample size was small and was only concentrating on the cessation of signs and not the rate of recurrence.

One study concentrated on environmental modification as a treatment (Buffington et al., 2006), with indoor cats (n=46). A change in environment showed a reduction in the reoccurrence of lower urinary tract signs ($p < 0.0001$) and a general improvement in fearfulness ($p < 0.0002$) and nervousness ($p < 0.0002$). However, the environmental modification for each cat was varied, with a number of options being given to the owner. With a number of different variables, it cannot be identified if one was more successful than the other, or if a variety is required for success. There were also no concurrent control groups.

Seawright et al. (2008) reported on a single case control study of a patient treated with a range of medications for 3 weeks and environmental treatment long-term. The patient was assessed for 15 months and showed only one period of FIC signs, occurring due to a stressful event in the environment. This episode was self-resolving. This study indicates the effect the environment has on one cat suffering from FIC; however, it is only one case with a number of variables in place and cannot be taken as a treatment option for a larger population.

Feline facial pheromones were used in conjunction to environmental therapy for 12 cats for a duration of 6 months. Owners were asked to score their cats on a number of scales to identify not only signs of cystitis, but also signs of stress. Owners were given visual analogue scales and daily diaries to record, and although there was no statistical difference between the treatment period and the placebo period, there was a clinical difference, with reports showing a reduced severity and occurrence of FIC; however, those cats that were to experience stressful situations (such as building or moving house) were removed from the study so it is not known if this is an effective treatment during signs of stress.

There was one paper that tested alternative methods of treating FIC, a mix of medication, vitamins and a probiotic (Sofyan et al., 2019). The case report by Sofyan attributed the success of the cat being able to urinate post urethral obstruction to the probiotic. However, this was given concurrently with muscle relaxants and

antibiotics. With no control study taking place, the evidence to support the probiotics success in this case is weak.

There is limited evidence in this research area, with treatments focusing on reducing inflammation or stress to reduce the clinical effects of FIC. This makes any research difficult, as to control variables cats have to be hospitalised, which increases the stress they experience. If not in the hospital, cats are then in their own home environment, where variables cannot be controlled, reducing the efficacy of the research by allowing other variables, meaning any success cannot be contributed to one treatment. Two of the randomised control studies showed a statistical difference between the treatment group and the placebo, these being MEMO and long-term amitriptyline, with the trial involving FFP not showing a statistical difference but a clinical difference. Two of the case reports based on environmental modification showed patient improvement, however their level of evidence is weak as they both have uncontrolled variables and cannot be repeated under the same conditions. It is clear from the variety of medical treatment options, that the true cause of FIC has not been identified. Further research is required to identify the true cause, to then make true comparisons.

Methodology Section

Search Strategy	
Databases searched and dates covered:	CAB Abstracts on OVID interface (1973 – 2020 Week 21) PubMed accessed via the NCBI website (1910 – June 2020)
Search terms:	<p>CAB Abstracts:</p> <ol style="list-style-type: none"> 1. cat or cats or feline or felines or exp cats/ or exp felis/ 2. cystitis or 'feline interstitial cystitis' or 'feline idiopathic cystitis' or FIC or 'Feline lower urinary tract disease' or FLUTD 3. environment* or behaviour or behavior or enrich* or exp environment/ or exp animal behaviour/ 4. drug* or medicat* or medicin* or pharmaceutical* or opioid* or NSAID or NSAIDs or 'non-steroidal anti-inflammatory' or 'non-steroidal anti inflammatories' or 'non-steroidal anti-inflammatory' or 'non-steroidal anti-inflammatories' or 'nonsteroidal anti-inflammatory' or 'nonsteroidal anti inflammatories' or 'nonsteroidal anti-inflammatory' or 'nonsteroidal anti-inflammatories' or exp anti-inflammatory agents/ or exp non-steroidal anti-inflammatory agents/ or exp opioids/ 5. 1 and 2 and (3 or 4) 6. manag* or treat* or therap* or prevent* 7. 5 and 6 <p>PubMed:</p> <ol style="list-style-type: none"> 1. cat OR cats OR feline OR felines 2. cystitis OR “feline interstitial cystitis” OR “feline idiopathic cystitis” OR FIC OR “Feline lower urinary tract disease” OR FLUTD 3. environment OR environmental OR behaviour OR behavior OR enrichment 4. drug OR medication OR medicine OR pharmaceutical OR opioid OR nsaid OR nsaid OR “non steroidal anti inflammatory” OR “non steroidal anti inflammatories”

	<p>5. 1 AND 2 AND (3 OR 4)</p> <p>6. manage OR management OR treat OR treatment OR therapy OR therapeutic OR prevent OR prevention</p> <p>7. 5 AND 6</p>
Dates searches performed:	03 Jun 2020

Exclusion / Inclusion Criteria	
Exclusion:	No relevance to PICO question (e.g. co-morbidities, cause for urine infection) non-English paper, duplicates, diet
Inclusion:	Any study which involved cats with idiopathic cystitis and medication or environmental treatment. This included obstructed idiopathic cystitis if this was mentioned

Search Outcome							
Database	Number of results	Excluded – Not relevant to PICO question	Excluded – Non-English language	Excluded – Conference abstract	Excluded – Duplicate	Excluded – Diet	Total relevant papers
CAB Abstracts	189	146	21	10	1	2	9
PubMed	315	292	3	1	9	3	7
Total relevant papers when duplicates removed							16

CONFLICT OF INTEREST

I work for RCVS Knowledge as a Project Officer: Quality Improvement and Vets Now as an ECC RVN.
Student at Harper Adams University

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