LATER-AGE NEUTERING OF BITCHES REDUCES RISK OF URINARY INCONTINENCE

In this article, Dr Camilla Pegram BVetMed MRes PhD MRCVS, Lecturer in Veterinary Epidemiology, Royal Veterinary College, University of London, discusses recent research examining the impact of neutering age on the risk of early-onset urinary incontinence (UI) in bitches, using a novel "target trial emulation" approach applied to real-world clinical data from the VetCompass programme

While surgical neutering is widely recognised for its role in population control and potential health and behavioural benefits, it is also associated with adverse outcomes, including UI. The featured study compared bitches neutered at three to <7 months with those neutered at ≥7 to ≤18 months, analysing anonymised records from 1,500 dogs attending UK primary-care veterinary practices. The findings indicated that bitches neutered later (seven to 18 months) had a 20 per cent reduced risk of developing early-onset UI compared to those neutered earlier (three to six months). By using causal inference methodology, the study provides strong evidence that age at neuter influences UI risk. These findings suggest that clinical decision-making to undertake early-age neutering (< 7 months) should be carefully considered and be well-justified.

Background

Surgical neutering of bitches is generally viewed as an important means of population control, offering both health-related and behavioural benefits. The benefits include reduced risk of mammary tumours, pyometra, and problem behaviours associated with oestrus or pseudopregnancy (Warnes, 2018). However, neutering has also been linked to adverse health-related effects in bitches, including the development of obesity, joint disease, neoplasia, and urinary incontinence (UI) (Kustritz *et al*, 2017, Warnes, 2018, Pegram *et al*, 2019a). Given an estimated 75 per cent of the estimated six million bitches in the UK are neutered during their lifetime (PDSA, 2022), the associated risks from neuter decision-making are magnified at a population level. Evidence for the optimal age to neuter bitches to minimise the risk of negative health-related and behavioural effects remains inconsistent, although it has been suggested this decision should be made on a bitch-by-bitch basis, factoring in breed-specific considerations (Hart and Hart, 2021).

UI is defined as the involuntary loss of urine during the filling phase of the bladder (Abrams, 2002) and is commonly diagnosed in bitches, affecting approximately one in thirty bitches in the UK (O'Neill *et al*, 2017). The most common cause of UI in puppies (< 6 months) is ureteral ectopia (Owen, 2019), whilst in adult dogs, urethral sphincter mechanism incompetence (USMI) is the most common, with neutered females reported at particular risk (O'Neill *et al*, 2017, Pegram *et al*, 2019b). In bitches, clinical history and pattern recognition often lead to a presumptive diagnosis of UI. To assist practitioners, the latest American College of Veterinary Internal Medicine (ACVIM) consensus statement offers a helpful visual aid outlining the recommended pathway for diagnosing and managing UI in dogs (Figure 1) (Kendall *et al*, 2024).

Previous RVC VetCompass research identified that Irish setters, Dalmatians, Hungarian vizslas, Dobermans, Weimaraners, Shar-peis and Boxers are the breeds at greatest risk of UI with increasing bodyweight also resulting in increased UI risk (Pegram *et al*, 2019a). From a pathophysiological perspective, the associations between

Evidence from VetCompass research indicates that bitches neutered later had a 20 percent reduction in the risk of early-onset UI.

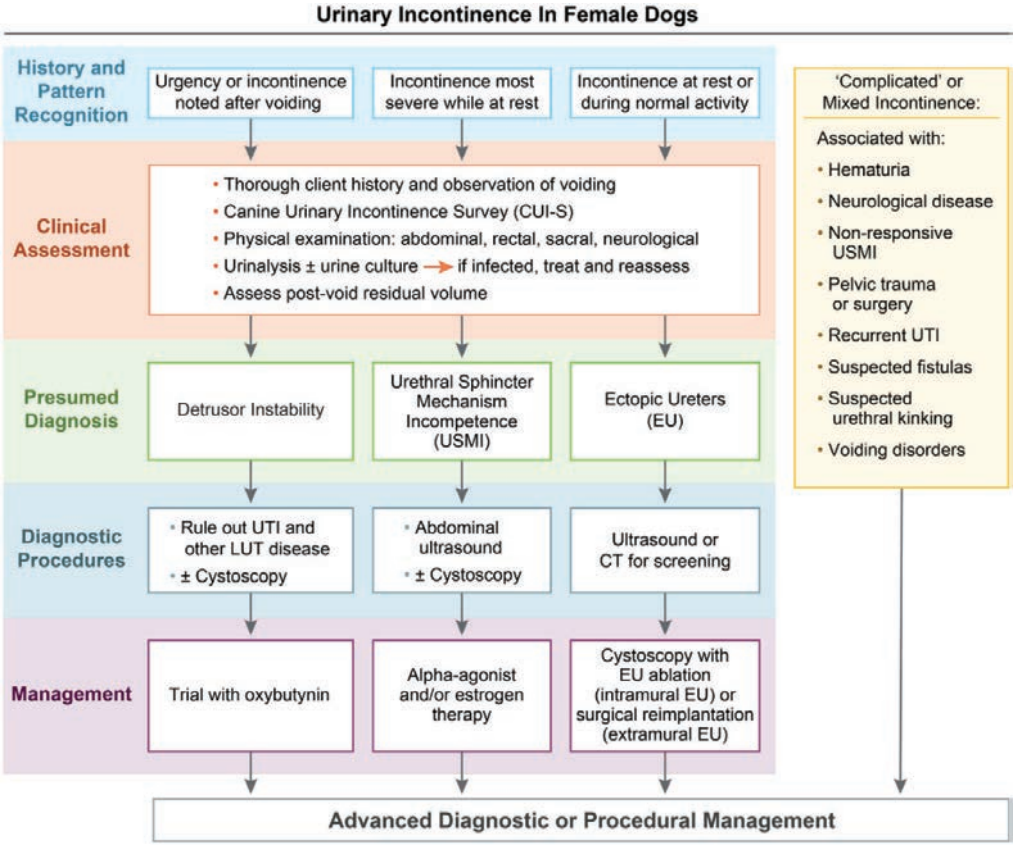

Figure 1: Visual aid for diagnosis and management of urinary incontinence in female dogs based on initial pattern recognition presented by Kendall *et al* (2024). The original image is adopted from the International Continence Society.

neutering and UI are not fully clear, but neurological, vascular, and hormonal changes have been proposed (Gregory, 1994, Pegram *et al*, 2019b). However, the evidence on the timing of neutering relative to urinary incontinence risk has, to date, been less definitive. A systematic review in 2012 reported some weak evidence that the risk of UI in bitches decreases as the age at neutering increases, up until 12 months of age, after which the evidence did not support any remaining effect (Beauvais *et al*, 2012). A more recent observational study based on UK veterinary primary-care data identified an increased risk of early-onset UI (first diagnosed at < 8.5 years) within the first two years following neutering in bitches neutered before six months, compared to bitches neutered at six to <12 months (Pegram *et al*, 2019a).

The age at neutering may be correlated with whether bitches are neutered before or after their first oestrus, which typically occurs between six and 24 months of age, with smaller breeds more likely to have their first oestrus at an earlier age than larger breeds (Da Costa *et al*, 2022). Any associations between the timing of neutering relative to the first oestrus and later development of UI in the bitch remain unclear. A UK study based on veterinary primary-care data attempted to evaluate the association between timing of neuter relative to onset of oestrus and UI but data on the timing of neuter relative to first oestrus were missing in 76.9 per cent of bitches in the study, and therefore this analysis was not carried out (Pegram *et al*, 2019b).

UI has been reported as a major contraindication for neutering bitches by veterinarians (Diesel *et al*, 2010). However, associations between neutering and UI are multifaceted and nuanced. The age at neutering may affect the overall UI risk, although the evidence is currently weak (O'Neill *et al*, 2017, Pegram *et al*, 2019a). Additionally, previous studies that attempted to explore the effects of age at neutering on UI diagnosis were limited to reporting associations rather than causal effects (Pegram *et al*, 2019a).

VetCompass research programme

The Veterinary Companion Animal Surveillance System (VetCompass) is a research programme that collects and analyses anonymised clinical data from veterinary practices. Started by the Royal Veterinary College (RVC) in the UK, VetCompass has expanded internationally, providing a comprehensive picture of disease management in everyday settings. The data collected for the UI study (discussed below) came directly from primary-care veterinary clinics, reflecting real-world scenarios. This provides a more accurate picture of disease management and outcomes compared to controlled or referral studies that might not capture everyday veterinary practice. VetCompass harnesses the power of large datasets and real-world evidence, enhancing understanding of animal health, which can ultimately result in the overall improved health and welfare of animals (RVC, 2023).

While randomised controlled trials (RCTs) are still considered the gold standard for determining treatment effects, they aren't always practical — or ethical — in a clinical setting. That's where VetCompass's use of "target trial emulation" comes into play. This novel approach lets researchers mimic the conditions of an RCT using existing data from routine veterinary records, which means we can draw conclusions on real-world treatment effects without having to rely solely on traditional trials (Pegram *et al*, 2023, Pegram *et al*, 2024a, Pegram *et al*, 2024b).

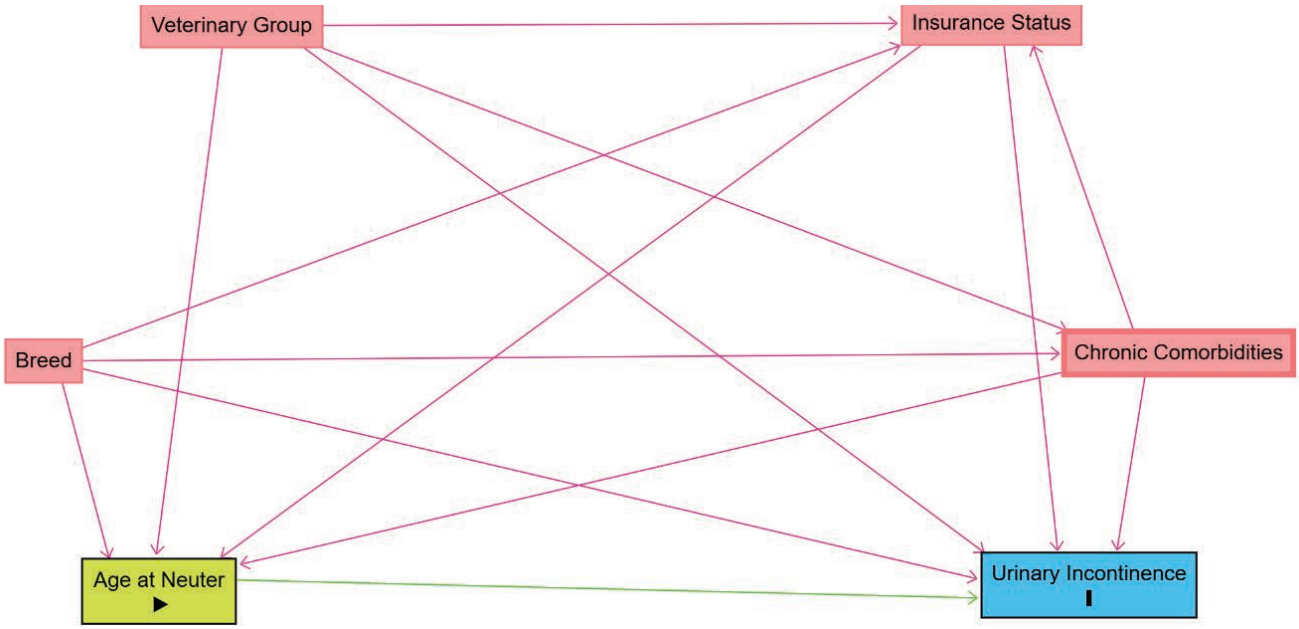

Figure 2: Directed acyclic graph (DAG) based on existing evidence and expert knowledge to estimate beliefs by the research team about the total effect of age at neutering in bitches on early-onset UI diagnosis.

The UI study is the third in a series of VetCompass papers using the "target trial emulation" approach. The first study evaluated whether antimicrobial or gastrointestinal nutraceutical treatment in acute, uncomplicated canine diarrhoea causes improved clinical outcomes (Pegram *et al*, 2023). The second study evaluated whether surgical or non-surgical management for cranial cruciate ligament rupture in dogs causes improved clinical outcomes (Pegram *et al*, 2024a).

This third study used the "target trial emulation" method to compare the causal effects between neutering at three to < 7 months and neutering at ≥ 7 to ≤ 18 months on subsequent diagnosis with early-onset UI in bitches. Early-onset UI was explored (i.e., diagnosed before 8.5 years of age) because older or geriatric bitches may have comorbidities resulting in urination disorders and degenerative changes that may be more age-related and less influenced by neuter status and the neutering choices that owners and veterinary surgeons make for bitches in early life (Pegram *et al*, 2019a).

VetCompass study summary

In this study, we explored how age at neuter affects early-onset UI risk by using causal inference methods to analyse data from a random sample of 1,500 bitches, neutered between three and 18 months old. This approach aimed to replicate a randomised clinical trial. To guide our analysis, we created a causal diagram (also called a directed acyclic graph, or DAG) that laid out our understanding of the possible causal relationships at play. This helped us identify the key factors we needed to account for during the study. So, we collected data on the following factors: breed, veterinary group, insurance status, and chronic comorbidities (as shown in Figure 2). By doing so, we aimed to build a comprehensive picture of how these variables might interact with each other and influence the outcome.

The trial emulation included 612 (40.8 per cent) bitches neutered between three and six months and 888 (59.2 per cent) at seven to 18 months. The analytic methods used in the study balanced the two groups of bitches across other characteristics (as identified in Figure 2) namely breed, veterinary group, insurance status, and chronic comorbidities. This meant that the only remaining difference between the two groups was when they were neutered.

The results showed that bitches neutered between seven and 18 months had 0.80 times the odds of developing early-onset urinary incontinence compared with bitches neutered between three and six months. This means the bitches neutered later had a 20 percent reduction in the risk of early-onset UI. Although neutering itself has consistently been reported as an important risk factor for UI diagnosis in bitches (Pegram *et al*, 2019a), until now, the literature has offered much less evidence about the effects of age on neutering. To date, there has been some limited evidence that neutering < 7 months increases the risk of UI in bitches (Pegram *et al*, 2019b), in line with the current study findings. That said, the effect for neuter itself (as a binary yes/no variable) appears stronger than the effect for age at neutering, with neutered bitches under primary-care in the UK at 3.01 times the odds of UI compared with entire bitches in a previous study (Pegram *et al*, 2019b).

Previous observational studies using VetCompass data have explored the effect of age at neutering on early-onset UI diagnosis in bitches but these were limited to reporting associations rather than causal effects (Pegram *et al*, 2019b, Pegram *et al*, 2019a). The current study used causal inference methodology to overcome this limitation by aiming to determine cause rather than just reporting association.

The decision to neuter a bitch is based on many other factors as well as UI risk, but these results suggest that clinical decision-making to undertake early-age neutering (< seven months) should be carefully considered and be well-justified.

The full study is available open access: https://pubmed.ncbi.nlm.nih.gov/38959183/

with an accompanying research infographic:

https://www.rvc.ac.uk/Media/Default/VetCompass/240412_UI_Infographic%20(5)%20(1).pdf

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References

Abrams, P. 2002. Standardisation Sub-Committee of the International Continence Society. The standardization of terminology of lower urinary tract function: Report from the standardization sub-committee of the International Continence Society. Neurourol. Urodyn., 21, 167-178.
Beauvais, W., Cardwell, J. M. & Brodbelt, D. C. 2012. The effect of neutering on the risk of urinary incontinence in bitches - a systematic review. J Small Anim Pract, 53, 198-204.
Da Costa, R. E., Kinsman, R. H., Owczarczak-Garstecka, S. C., Casey, R. A., Tasker, S., Knowles, T. G., Woodward, J. L., Lord, M. S. & Murray, J. K. 2022. Age of sexual maturity and factors associated with neutering dogs in the UK and the Republic of Ireland. Veterinary Record, 191, e1265.
Diesel, G., Brodbelt, D. & Laurence, C. 2010. Survey of veterinary practice policies and opinions on neutering dogs. Vet Rec, 166, 455-8.
Gregory, S. 1994. Developments in the understanding of the pathophysiology of urethral sphincter mechanism incompetence in the bitch. The British Veterinary Journal, 150, 135 - 150.
Hart, L. A. & Hart, B. L. 2021. An ancient practice but a new paradigm: personal choice for the age to spay or neuter a dog. Frontiers in Veterinary Science, 8, 603257.
Kendall, A., Byron, J. K., Westropp, J. L., Coates, J. R., Vaden, S., Adin, C., Oetalaar, G., Bartges, J. W., Foster, J. D. & Adams, L. G. 2024. ACVIM consensus statement on diagnosis and management of urinary incontinence in dogs. Journal of Veterinary Internal Medicine.
Kustritz, M. V. R., Slater, M. R., Weedon, G. R. & Bushby, P. A. 2017. Determining optimal age for gonadectomy in the dog: a critical review of the literature to guide decision making. Clinical Theriogenology, 9, 167-211.
O'Neill, D. G., Riddell, A., Church, D. B., Owen, L., Brodbelt, D. C. & Hall, J. L. 2017. Urinary incontinence in bitches under primary veterinary care in England: prevalence and risk factors. J Small Anim Pract.
Owen, L. 2019. Ureteral ectopia and urethral sphincter mechanism incompetence: an update on diagnosis and management options. Journal of Small Animal Practice, 60, 3-17.
PDSA. 2022. PAW Report 2022 [Online]. Available: https://www.pdsa.org.uk/what-we-do/pdsa-animal-wellbeing-report/paw-report-2022 [Accessed 06/11/2023 2023].
Pegram, C., Brodbelt, D., Church, D., Hall, J., Owen, L., Chang, Y. M. & O'Neill, D. 2019a. Associations between neutering and early-onset urinary incontinence in UK bitches under primary veterinary care. Journal of Small Animal Practice.
Pegram, C., Diaz-Ordaz, K., Brodbelt, D. C., Chang, Y.-M., Von Hekkel, A. F., Wu, C.-H., Church, D. B. & O'Neill, D. G. 2024a. Target Trial Emulation: Does surgical versus non-surgical management of cranial cruciate ligament rupture in dogs cause different outcomes? Preventive Veterinary Medicine, 106165.
Pegram, C., Diaz-Ordaz, K., Brodbelt, D. C., Chang, Y.M., Hall, J. L., Church, D. B. & O'Neill, D. G. 2024b. Later-age neutering causes lower risk of early-onset urinary incontinence than early neutering-a VetCompass target trial emulation study. PLoS One, 19, e0305526.
Pegram, C., Diaz-Ordaz, K., Brodbelt, D. C., Chang, Y. M., Tayler, S., Allerton, F., Prisk, L., Church, D. B. & O'Neill, D. G. 2023. Target trial emulation: Do antimicrobials or gastrointestinal nutraceuticals prescribed at first presentation for acute diarrhoea cause a better clinical outcome in dogs under primary veterinary care in the UK? PLoS One, 18, e0291057.
Pegram, C., O'Neill, D., Church, D., Hall, J., Owen, L. & Brodbelt, D. 2019b. Spaying and urinary incontinence in bitches under UK primary veterinary care: a case–control study. Journal of Small Animal Practice.
RVC. 2023. VetCompass overview [Online]. Available: https://www.rvc.ac.uk/vetcompass/about [Accessed 21/09/2023].
Warnes, C. 2018. An update on the risks and benefits of neutering in dogs. The Veterinary Nurse, 9, 150-155.

READER QUESTIONS AND ANSWERS

1. WHAT PROPORTION OF BITCHES IN THE UK ARE ESTIMATED TO BE NEUTERED DURING THEIR LIFETIME?

A. 35 per cent
B. 60 per cent
C. 75 per cent
D. 85 per cent

2. WHAT IS THE MOST COMMON CAUSE OF UI IN ADULT BITCHES?

A. USMI
B. Ureteral ectopia
C. Detrusor instability
D. Bladder neoplasia

3. THERE IS STRONG EVIDENCE THAT NEUTERED BITCHES ARE AT GREATER RISK OF UI THAN ENTIRE BITCHES:

A. True
B. False

4. THERE IS STRONG EVIDENCE FOR AN ASSOCIATION BETWEEN THE TIMING OF NEUTERING RELATIVE TO THE FIRST OESTRUS AND LATER DEVELOPMENT OF UI IN THE BITCH:

A. True
B. False

5. BASED ON THE RANDOM SAMPLE OF BITCHES IN THE VETCOMPASS UI TARGET TRIAL, BY WHAT PERCENTAGE DID LATER NEUTERING (≥ 7 TO ≤ 18 MONTHS) REDUCE THE RISK OF EARLY-ONSET UI COMPARED TO NEUTERING AT THREE TO < 7 MONTHS?

A. 5 per cent
B. 10 per cent
C. 20 per cent
D. 40 per cent

ANSWERS: 1C; 2A; 3A; 4B; 5C.