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Urinary incontinence in male dogs under primary veterinary care in England: prevalence and risk factors

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Structured summary

Objective: Estimate prevalence and identify demographic risk factors for urinary incontinence (UI) in male dogs.

Methods: The study population included all dogs within the VetCompass database from September 2009 to July 2013. Electronic patient records were searched for UI cases; demographic and clinical information was extracted and analysed.

Results: Of 109,428 male dogs attending 119 clinics in England, an estimated 1027 dogs were diagnosed with UI, giving a UI prevalence of 0.94% (95% CI: 0.88-1.00). Breeds with highest

odds of UI compared with crossbreds included the bull mastiff (OR 17.21, 95% CI 6.65-44.56, case=5, non-case=314, P < 0.001), Irish red setter (OR: 12.79, 95% CI 4.83-33.84, case=5, non-case=142, P < 0.001), fox terrier (OR: 9.60, 95% CI 3.68-25.05, case=5, non-case=176, P < 0.001), bulldog (OR: 5.72, 95% CI 2.24-14.59, case=5, non-case=929, P < 0.001) and boxer (OR: 3.65, 95% CI 1.84-7.25, case=10, non-case=1470, P < 0.001). Increased odds of UI were associated with increased age (age 9 to 12 years OR: 10.46, 95% CI 6.59-16.62, n= 12348, P < 0.001) and being insured (OR 1.96 ;95% CI 1.53-2.51, n=26202, P < 0.001). There was no association with castration or bodyweight.

Clinical impact: Overall prevalence of UI in male dogs is approximately 1%, which may be higher than expected given the sparsity of literature describing this problem. At-risk breeds (some previously unrecognised) have a higher prevalence of 2-9%. In contrast to bitches, neutering and bodyweight did not increase odds of UI, which is valuable information for general practitioners giving neutering advice.

Key Words:

epidemiology, dog, urinary incontinence, male

Abbreviations

CI; confidence intervals, EPR; electronic patient record, KC, Kennel Club; OR; odds ratio, PMS: practice management system, UI; urinary incontinence, USMI; urethral sphincter mechanism incompetence

Introduction

Urinary incontinence (UI) is defined as involuntary leaking of urine from the bladder during the storage phase of micturition (Abrams and others 2002). This condition has been extensively investigated in bitches but there are few studies that report the prevalence and risk factors for UI in male dogs (Aaron and others 1996, Holt 1990, Palerme and others 2017, Power and others 1998). Whilst it is reportedly uncommon, with males representing under 4% of 563 incontinent dogs in one UK study (Holt 1990), UI in male dogs can often be a distressing disorder for owners and their pets, negatively impacting the interaction between them (de Bleser and others 2011) and is therefore of major importance on an individual case level. Accurate diagnosis and effective management improves patient and owner welfare by avoiding sequelae such as ascending urinary tract infection, urinary scalding of the skin and euthanasia of affected dogs (O'Neill and others 2017, Schaer 2010).

Similar to bitches, male UI can result from congenital (generally anatomical) or acquired (generally functional) conditions (Coit and others 2008, Schaer 2010). However, sex-associated differences in the features, presentation and response to treatment of UI are reported. Anatomical disorders in juvenile males can include urethral diverticulae and dilations (Aaron and others 1996, Holt 1990). Male dogs with ureteral ectopia resulting in UI are more commonly diagnosed as young (23% of juvenile UI) rather than older dogs (4% of adult UI), which is similar to bitches, but generally at an older median age (24 months in males compared with 10 months in the bitch, (Holt 1990). Acquired urethral sphincter mechanism incompetence (USMI) is often diagnosed in adult dogs of both sexes by exclusion of other causes in the absence of urethral pressure profilometry (Aaron and others 1996, Holt 1990, Palerme and others 2017) and represents an assortment of anatomical and functional problems that ultimately result in poor resistance of the urethra to urinary leakage from the bladder. The specific underlying anatomical, histological and hormone receptor abnormalities

have been found to differ between the sexes (Ponglowhapan and others 2007). Neutering also has a different effect on the histology and function of the male and female bladder (Coit and others 2008)and lower urinary tract (Ponglowhapan and others 2008). These sex specific differences have been suggested to explain the reduced efficacy of medical management for USMI in males (<50%; (Aaron and others 1996, Palerme and others 2017, Richter and Ling 1985) compared to females (between 75 and 90%;(Byron and others 2017, Scott and others 2002, White and Pomeroy 1989)).

A recent large epidemiological analysis, that did not differentiate between congenital and acquired causes, has reported a UI prevalence of 3.14% in bitches (3108 out of 100,397) and identified increased risk of UI with neutering, increased age, increased total bodyweight and increased within breed bodyweight. The majority of historical studies investigating risk factors for incontinence have concentrated on USMI in the bitch, particularly focusing on at-risk sub-groups such as neutered females (Angioletti and others 2004, Beauvais and others 2012, de Bleser and others 2011, Forsee and others 2013, Gregory 1994, Holt 1985, Holt and Thrusfield 1993, Holt 2012, Noël and others 2010, Okkens and others 1997a, Spain and others 2004, Stöcklin-Gautschi and others 2001, Thrusfield and others 1998). Breeds predisposed to UI in bitches included the Irish setter, dobermann, bull mastiff, rough collie, Dalmatian and boxer (O'Neill and others 2017). The findings regarding risk factors in male dogs are conflicting and based on lower numbers of animals. The largest retrospective study to date focusing on referred clinically affected male dogs reviewed 54 cases (identified from 121 incontinent males diagnosed over 20 years) and reported that larger breeds (particularly boxers), and possibly neutering, were associated with increased risk of acquired USMI (n=37/54) beginning a median of 10 days postoperatively (Aaron and others 1996). A numerically larger longitudinal cohort study designed to assess the potential implications of

early neutering (<3m age) found no association between early neutering and the development of incontinence in male dogs (Spain and others 2004). A third radiographic study of 37 incontinent male dogs identified bladder neck position and castration to be independent risk factors, whilst proximal urethral length appeared unimportant when adjusted for bodyweight (Power and others 1998). The lack of current data assessing risk factors in male dogs and the contradictory information regarding neutering demonstrate the requirement for more research in this area.

The primary objectives of this study were to estimate the prevalence of UI in the general population of male dogs presented to primary care veterinary practices in England and to evaluate demographic risk factors for diagnosis with UI, with a particular focus on breed effects. This knowledge can assist clinicians to identify individuals at risk in order to improve the diagnosis and management of this condition and to support decision-making advice to owners of at-risk individuals regarding neutering and weight management.

Based on results from an earlier study of risk factors in bitches, we hypothesised that Irish setter, doberman, bull mastiff, rough collie, Dalmatian and boxer breeds, increased age, neutering, increased total bodyweight and increased within breed bodyweight would be similarly associated with increased odds of UI in male dogs (O'Neill and others, 2017).

Materials and methods

The VetCompass Animal Surveillance System collates anonymised electronic patient record (EPR) data from primary-care veterinary practices in the UK for epidemiological research

(O'Neill and others 2014b). Collaborating practices were a convenience sample selected by their willingness to participate and their recording of clinical data within an appropriately configured practice management system (PMS). Practitioners could record summary diagnosis terms from an embedded VeNom Code list during episodes of care (The VeNom Coding Group 2017). Information collected relates mainly to the owned dog population and includes patient demographic (species, breed, date of birth, sex, neuter status, insurance status and bodyweight) and clinical information (free-form text clinical notes, summary diagnosis terms, treatment and deceased status with relevant dates) data fields. EPR data are extracted from PMSs using integrated clinical queries and uploaded to a secure VetCompass relational database (O'Neill and others 2016a).

A cohort study design with a cross-sectional analysis was used to estimate UI prevalence and to evaluate risk factors for UI diagnosis (Pearce 2012). The sampling frame included all male dogs with at least one EPR (clinical note, VeNom summary term, bodyweight or treatment) uploaded to the VetCompass database from September 1st, 2009 to July 7th, 2013 and that were deemed to be under veterinary care during this period. The epidemiological unit for this study was the male dog; each male dog was included only once in the analysis by linking to its unique ID code in the PMS. Sample size calculations estimated that a sample of 27,552 male dogs would need to be evaluated from a population of 100,000 dogs in order to estimate the prevalence of a disease with an expected frequency of 1% within 0.1% precision limits with a 95% confidence level (Epi Info 7 CDC 2015). Ethical approval of the project was granted by the RVC Ethics and Welfare Committee (reference number 00/2014).

The inclusion criteria for a UI case required a veterinary diagnosis of urinary incontinence recorded in the EPR or prescription of a specific urinary incontinence therapy (product containing phenylpropanolamine, oestriol, estriol). UI recorded as occurring secondary to seizure activity was excluded. Case-finding involved initial screening of all EPRs for

candidate UI cases by searching the clinical free-text field (search terms included *incont, usmi, incompet, urethral sp, nocturia, wetting, wet the bed, dribbling urin, leaking urin*), the VeNom term field (*incont*) and the treatment field (*propal, incurin, enurace, urilin, proin*). Findings from these searches were merged and the full clinical notes of a random subset were manually reviewed for case inclusion by an experienced qualified veterinary surgeon familiar with EPR and with an extensive epidemiological research portfolio (D.G.O.). Randomisation used the *RAND* function in Microsoft Excel (Microsoft Office Excel 2007, Microsoft Corp.). The count of candidate cases that were manually reviewed was based on the power analysis. Logistic constraints precluded manual review of all candidate cases. Additional data were extracted on all confirmed UI cases to define each case as pre-existing (first recorded prior to the study period) or incident (first recorded during the study period), whether the animal died during the study period and, if so, the date and method of death (euthanasia or unassisted) and whether UI was recorded as a contributory factor for the death. For incident cases, the date of the first diagnosis and whether medication was prescribed to control UI were also extracted. Prevalence was calculated based on all study dogs. The risk factor analysis classified all male dogs that were not identified as candidate UI cases during the initial screening as confirmed non-cases.

A *breed* variable included any individual breeds with 5 or more UI cases, a grouped category of all remaining breeds and a general grouping of crossbred male dogs. A *purebred* variable categorised all male dogs with a recognisable breed name as 'purebred' and the remaining male dogs as 'crossbred' (Irion and others 2003). A Kennel Club (KC) *KC breed group* variable classified breeds recognised by the KC into their relevant breed groups (gundog, hound, pastoral, terrier, toy, utility and working) and all remaining male dogs were classified as non-KC recognised (The Kennel Club 2017). *Neuter* described the recorded status of the dog (neutered or entire) at the final EPR. *Insurance* described whether a dog was recorded as

insured at any point during the study period. *Age* described the age at the date of first recorded diagnosis for incident UI cases so that the interpretation from the logistic regression results would reflect associations between age and 'becoming' a UI case rather than 'being' a UI case. It was assumed that the dates for first diagnosis of UI cases would be randomly spread throughout the period of study data for the UI cases and therefore *Age* for the non-cases described the age at the mid-point between the dates of the first and final EPRs recorded during the study period so that these ages would be as representative as possible of the expected ages for these dogs if they had received a diagnosis of UI. *Age* (years) was categorised into six groups (< 3.0, 3.0-5.9, 6.0-8.9, 9.0-11.9, ≥ 12.0, not recorded). *Adult bodyweight* described the maximum bodyweight recorded during the study period for male dogs older than nine months and was categorised into six groups (0.0-9.9 kg, 10.0-19.9 kg, 20.0-29.9 kg, 30.0-39.9 kg, ≥ 40.0 kg, not recorded). Within-breed bodyweights were graphically assessed for normality and hence summarised using the mean and standard deviation. Mean adult bodyweight was calculated for each breed in the study and used to generate a *breed relative bodyweight* variable that characterised male dogs as either below or equal/above the mean adult bodyweight for their breed. This variable allowed the effect of adult bodyweight *within* each breed to be assessed.

Following data checking and cleaning in Excel to assess the completeness, internal data consistency and validity of the demographic and clinical data extracted from the VetCompass database (Microsoft Office Excel 2013, Microsoft Corp.) (O'Neill and others 2016b), analyses were conducted using Stata Version 13 (Stata Corporation). The period prevalence with 95% confidence intervals (CI) described the probability of having UI at any time during the study period and included both pre-existing cases and incident cases. The case count that would have been identified if the entire set of candidate cases had been manually verified was calculated by weighting the verified case numbers by the inverse of the

proportion of candidate cases that was manually verified (O'Neill and others 2016a). The overall period prevalence of UI was estimated based on a denominator of all study male dogs and the breed-specific period prevalence of UI was estimated for each breed based on a denominator of all male dogs of that breed in the study. The CI estimates were derived from standard errors, based on approximation to the normal distribution (Kirkwood and Sterne 2003). Descriptive statistics characterised the breed, neuter status, insurance status, age and adult bodyweight for the incident cases and non-case male dogs. The medical management regimes were reported for incident cases only because clinical records extending back to the original date of first diagnosis of UI may not have been available for many pre-existing cases. Mortality results were reported on all UI cases.

Binary logistic regression modelling was used to evaluate univariable associations between risk factors (*breed, purebred, KC breed group, adult bodyweight, breed relative bodyweight, age, neuter* and *insurance*) and incident cases of urinary incontinence. Inclusion of all cases (pre-existent and incident) into risk factor analysis has the effect of evaluating risk factors for 'being' a case rather than for 'becoming' a case and therefore biases towards higher odds ratios for factors associated with longer survival with UI. For example, long-lived breeds are more likely to be included compared with short-lived breeds. The current study aimed to evaluate risk factors for 'becoming' a case and therefore elected to include only incident cases that were diagnosed with UI during the study period. Breed was a factor of primary interest for the study. The *purebred*, *KC breed group* and *adult bodyweight* variables were correlated with the *breed* variable and were therefore not simultaneously considered in multivariable modelling. Instead, the results for these correlated variables were derived by individually replacing the *breed* variable from the final breed multivariable model.

Risk factors with liberal associations in univariable modelling ($P < 0.2$) were taken forward for multivariable evaluation. Multivariable model development used manual backwards

stepwise elimination (P < 0.05 cut-off). Clinic attended was evaluated as a random effect and pair-wise interaction effects were evaluated for the final model (Dohoo and others 2009). The Hosmer-Lemeshow test statistic and the area under the ROC curve were used to evaluate the quality of model fit (non-random effect model) (Dohoo and others 2009, Hosmer and Lemeshow 2000). Statistical significance was set at $P < 0.05$.

Results

The overall dataset comprised 109,428 male dogs attending 119 clinics in England. Overall, 2,307 animals were identified as candidates for urinary incontinence. From 860 (37.3% of the candidates) candidates that were manually checked, 383 male dogs met the case definition for UI. These confirmed UI cases comprised of 345 (90.1%) incident and 38 (9.9%) pre-existing cases. Data on all 383 UI cases were included in the demographic descriptive evaluation. Data on just the 345 incident UI cases were included in the medical management evaluation and the risk factor analysis. An estimated 1,027 cases would have been identified if all candidate animals were checked. After accounting for the sampling approach, the estimated prevalence for UI in male dogs overall was 0.94% (95% CI 0.88-1.00). Breeds with the highest prevalence of male UI included the Irish red setter (8.44%, 95% CI 4.57-14.00), fox terrier (6.95%, 95% CI 3.76-11.59), bull mastiff (4.02%, 95% CI 2.16-6.78), boxer (2.49%, 95% CI 1.77-3.40) and English springer spaniel (2.25%, 95% CI 1.68-2.94). The prevalence in crossbreds was 0.71% (95% CI 0.61-0.83) (Table 1).

Data completeness overall were: breed 99.95%, age 99.82%, adult bodyweight 65.70%, insurance 66.38% and neuter status 46.06%. Descriptive evaluation included 383 confirmed UI cases (pre-existing and incident cases) and 107,121 non-cases. The median (interquartile range [IQR], range) time between the first and final EPR across all study male dogs was 0.6 years (0.0-2.2, 0.0-5.0). Of the UI cases with information available, 319/383 (83.29%) were

purebred, 223/263 (84.79%) were neutered and 173/321 (53.89%) were insured. The median

adult bodyweight was 18.80 kg (IQR: 10.65-31.60, range 1.90-100.60) and the median age at

diagnosis was 11.60 years (IQR: 7.95-14.10, 0.20-19.00) (Figure 1). The most common breed

types diagnosed with UI (pre-existing and incident) were the Labrador retriever (n = 23,

6.01% of dogs overall), Staffordshire bull terrier (n=22, 5.74%), West Highland white terrier

(n=21, 5.48%), Jack Russell terrier (n=20, 5.22%) and English springer spaniel (n=19,

4.96%), along with 59 (15.40%) crossbreds (Table 1).

 Of the non-case male dogs with information available on that specific variable,

83,333/107,065 (77.83%) were purebred, 36,956/48,847 (75.66%) were neutered and

26,049/61,917 (42.07%) were insured. The median adult bodyweight was 18.90 kg (IQR:

9.80-31.00, range 1.15-112.00) and the median age was 3.90 years (IQR: 1.30-8.00, range

0.00-23.00). The most common breeds among the non-case male dogs were the Labrador

retriever (n= 9,175, 8.57% of dogs overall), Staffordshire bull terrier (n= 8,333, 7.73%), Jack

Russell terrier (n= 6,773, 6.32%) and cocker spaniel (n = 3,915, 3.65%) along with 20,312

(18.96%) crossbreds.

Medical therapy directed specifically at managing UI was prescribed to 60/345 (17.39%) of

the incident UI cases. During the study period, 212/383 (55.35%) of the overall UI caseload

died. The median age at death was 13.20 (IQR 11.20-15.10, range 1.10-19.00) years and

190/195 (97.44%) deceased male dogs with a recorded mechanism of death were euthanased.

UI was recorded as either contributory or the main reason for the euthanasia decision in

79/190 (41.58%) of incontinent male dogs that died via euthanasia and where information

was recorded.

Risk factor analysis included 345 incident UI cases and 107,121 non-cases. Univariable

logistic regression modelling identified seven variables liberally associated ($P < 0.20$) with

urinary incontinence: (*purebred status, breed, KC breed group, breed relative bodyweight, age, neuter* and *insurance*) (Table 2). Following evaluation using multivariable logistic regression, the final breed model comprised four risk factors: *age, breed, neuter* and *insurance*. The *neuter variable* was retained in the final model as a confounder. No biologically significant interactions were identified. Modelling was improved by inclusion of the clinic attended as a random effect ($P < 0.001$, rho = 0.046, indicating that the clinic attended accounted for 4.6% of variation) and the clinic random effect was retained in the final model. For the final non-clustered breed model, the Hosmer-Lemeshow test did not identify poor model fit ($P = 0.089$) and the area under ROC curve (0.851) indicated excellent UI discrimination (Hosmer and Lemeshow 2000).

After accounting for the effects of the other variables evaluated, 10 breeds showed increased odds of UI compared with crossbred male dogs in the multivariable model (just for clarity). Breeds with the highest odds included the bull mastiff (cases = 5, non-cases = 314), OR: 17.21, 95% CI 6.65-44.56, $P < 0.001$), Irish red setter (cases=5, non-cases=142, OR: 12.79, 95% CI 4.83-33.84, $P < 0.001$), fox terrier (cases= 5, non-cases=176), OR: 9.60, 95% CI 3.68-25.05, $P < 0.001$), bulldog (cases= 5, non-cases=929), OR: 5.72, 95% CI 2.24-14.59, $P < 0.001$), and boxer (cases=10, non-cases=1470), OR: 3.65, 95% CI 1.84-7.25, $P < 0.001$). Castrated male dogs (cases=204, non-cases=36,956) were not significantly more likely to develop UI compared with entire dogs (cases= 35, non-cases=11,891), $P=0.427$). Increasing age was associated with increasing risk of developing UI; the odds of UI increased sequentially with each category of increasing age. Male dogs aged 9 to less than 12 years showed 10.46 (cases= 83, non-cases= 12,265), 95% CI 6.59-16.62, $P < 0.001$) times the odds of UI compared with those aged less than 3 years (cases=24, non-cases=45,395). Insured

male dogs had 1.96 (cases=153, non-cases=26,049), 95% CI 1.53-2.51, $P < 0.001$) times the odds compared with uninsured male dogs (cases=135, non-cases=35,868), Table 3).

Additionally, *purebred status* and *KC breed group* were significant risk factors when used to replace the breed variable in the final breed model. Purebred male dogs had 1.45 (cases=287, non-cases=83,333), 95% CI 1.09-1.93, $P = 0.012$) times the odds compared with crossbred male dogs (cases=58, non-cases=23,732). Of the KC breed groups, Working (cases= 30, non-cases= 5,913), OR 3.83, 95% CI 2.48-5.94, $P < 0.001$), Hound (cases=21, non-cases= 4,619), OR 2.14, 95% CI 1.31-3.49, $P < 0.001$), Pastoral (cases=37, non-cases=7,705), OR 1.76, 95% CI 1.18-2.62, $P = 0.005$), and Terrier (cases=56, non-cases=14,966), OR 1.57, 95% CI 1.10-2.22, $P = 0.012$) group male dogs showed higher odds of UI compared with male dogs that were not of KC recognised breeds (cases= 77, non-cases= 31,941), Table 4).

Discussion

This study is the first to report the prevalence for UI in male dogs by examining a large number of dogs that are more representative of the wider population. We estimated a UI prevalence of 0.94% in 109,428 male dogs attending 119 primary care practices in England. Given the large size of the group investigated, this is likely to be an accurate and generalisable assessment compared with studies focusing on either high-risk subsets of dogs or referral populations (Bartlett and others 2010, O'Neill and others 2014a). Previous large UI studies have focused on bitches, likely given the general perception that female dogs have a much higher incidence of UI compared to males; we confirm that whilst this is the case (a recent large study reported a female prevalence of just over 3%, (O'Neill and others 2017) the difference in prevalence is not as marked as might be expected.

The predominance of literature concentrating on bitches means that the population risk factors for males have not been previously well described. Irish setter, fox terrier, bull mastiff, boxer and English springer spaniel breeds had the highest UI prevalence in the current study. The fox terrier has not been recognised to be at increased risk of UI in recent epidemiological studies (increased odds of 9.6 compared with crossbreed dogs in our investigation). Fox terriers are often cited to have an increased risk of ectopic ureter although this supposition is the result of historic retrospective analyses in the United States of America (5 out of 54 dogs, 2 of which were male (Hayes 1974) and 7 out of 217 female dogs (Hayes 1984)) and comparison of data from different groups of dogs with UI on different continents may be unreliable (Forsee and others 2013, O'Neill and others 2017). Whilst the other four breeds also have an increased prevalence of UI in females, the within-breed prevalence for males is between a quarter to a third that of bitches (O'Neill and others 2017), consistent with the overall sex associated difference in prevalence we report (1% in males versus 3% in females). Of interest, the odds ratios reported for the at-risk breeds common to both males and females are consistently higher in males than those reported for females (O'Neill and others 2017). Therefore, whilst fewer males are affected than females within each individual at-risk breed (the lower prevalence or absolute risk), the effect of breed has a stronger effect for males compared to females and predisposed breeds generally carried a higher relative risk of developing UI compared with crossbreeds in males (particularly for bull mastiff, Irish setter, fox terrier and bulldogs). Male and female boxer dogs have a similar OR of approximately 3. In a retrospective analysis of cases seen over a 20 year period, 54 male dogs with USMI were identified and described (Aaron and others 1996). Boxer (n=7) and English springer spaniel breeds (n=3) were over-represented, consistent with our findings.

Surprisingly we showed no effect of bodyweight, overall or within breed, on the incidence of UI. Increasing bodyweight has been a consistently recognised and reported risk factor for female USMI (Angioletti and others 2004, de Bleser and others 2011, O'Neill and others 2017, Okkens and others 1997b, Stöcklin-Gautschi and others 2001). This principal difference between males and females may highlight the importance of the anatomical and physiological differences of the lower urinary tract in the pathogenesis of UI between the sexes. Power et al (1998) found an association between shorter urethral length and incontinence in males that was not significant when they allowed for the influence of body size. Further investigation would be necessary to determine whether urethral length and bladder neck position has a different association with body size between males and females. Whilst obesity has not been definitively confirmed as a cause of USMI (Angioletti and others 2004) it may worsen the severity of incontinence and bodyweight loss has been reported to improve clinical signs of incontinence in bitches (Holt 2012). Some studies have found that female dogs are at higher risk of obesity compared to males (Edney and Smith 1986, Krook and others 1960). We were not able to assess the effect of body condition score, but potentially the association of between breed and within breed body weight with female UI (O'Neill and others 2017) and the contrasting lack of association between bodyweight and male UI that we describe may be explained by a sex associated difference in body condition score rather than absolute bodyweight.

The odds of developing UI rise progressively and substantially with age in male dogs. Previous reports for bitches (de Bleser and others 2011, O'Neill and others 2017) have reported similar odds for age categories younger than 9 years to those reported for males in the current study, but males older than 9 years have a 3 times higher magnitude of odds compared with females in those reports. Advancing age therefore seems to have a greater

effect on the risk of UI in males compared with females. This may be a direct effect of changes in anatomy, physiology or increasing incidence of concurrent disease that may either directly cause UI (e.g. neurological disease, neoplasia) or challenge a previously subclinical UI (e.g. polydipsia / polyuria secondary to endocrinopathy, renal disease etc). UI cases with congenital and anatomical aetiologies tend to present at younger ages (Aaron and others 1996, Holt and Moore 1995). Our study included all UI cases with any cause and the association with increased age may suggest that the majority of UI in male dogs is acquired and likely to be USMI. However, normal male anatomy may be protective against clinical signs of both congenital and acquired causes of UI; early mild USMI and even anatomic abnormalities may be masked until the animals are older and the underlying disease more progressed (e.g. a longer urethra, greater ratio of muscle to collagen in the proximal urethra, the prostate gland surrounding the urethra and helping to hold the bladder neck cranial to the pubic brim and the muscles of the penis applying some pressure adjacent to the urethra). This would artificially increase the odds of UI in older patients for progressively developing or mild underlying disease that began much earlier in life. Smooth muscle degeneration over time has been proposed to lead to increased incidence of UI with age in females (Krawiec and Rubin 1985), and should this be the case in males, may be a reason for our findings.

Castration was not associated with increased odds of UI in our study using multivariable analysis taking into account additional factors. Castration was suggested to contribute to the development of UI by Aaron et al (1996), with the proposed reasoning that a smaller prostate would provide less peri-urethral support and constriction, and may allow a more caudally positioned bladder, with less support of the bladder neck provided by the pubic brim during periods of raised intra-abdominal pressure. Power et al (1998) subsequently reported that castration predicted USMI (diagnosed by exclusion rather than urethral pressure

profilometry) with a sensitivity and specificity of 56.8% and 78.6% by comparing 37 incontinent dogs with 28 controls. Bladder neck position was significantly related to prostate size, and incontinent male dogs were more likely to have a caudally displaced bladder. They therefore suggested that castration would reduce prostate size and cause UI but, in contradiction, their statistical analysis did not show a relationship between castration and bladder neck position. Possible reasons that we did not find an association between castration and UI could be that our data represented a different population of dogs (e.g. first opinion rather than a selection biased referral population), that multivariable analysis has eliminated castration as a confounding factor or that an association between UI and castration has been masked by other more influential factors. Alternatively, relatively low completeness (46.06%) of neuter status data in the available clinical records could have meant that a genuine association was missed because of reduced study power, although the large number of dogs for which neuter status was still available (n = 50,400) means that the study was still highly powered to assess neuter status.

As a consequence of previously published associations between female USMI and neutering (de Bleser and others 2011, Forsee and others 2013, Spain and others 2004, Stöcklin-Gautschi and others 2001, Thrusfield and others 1998), and the previous investigations implicating castration to be associated with male USMI (Aaron and others 1996, Power and others 1998), subsequent studies have tried to elucidate the mechanism by which neutering may affect continence. Male and female bladder walls have been shown to be less responsive to muscarinic agonists following neutering, although only females showed an increase in the collagen to muscle ratio of the bladder, suggesting that multiple factors are involved and therefore implying that there may be different therapeutic targets in males and females (Coit and others 2008). Ponglowhapan et al 2008 reported that the proximal female urethra has

significantly less muscle to collagen content compared with males, and that both sexes show an increase in urethral collagen following gonadectomy. Male USMI is generally reported to be considerably less responsive to medications shown to be effective and widely used in females (e.g. phenylpropanolamine (Aaron and others 1996, Coit and others 2008, Palerme and others 2017, White and Pomeroy 1989)), and there was little therapeutic benefit found in studies supplementing testosterone (Barsanti and others 1981, Palerme and others 2017). This may be consistent with castration only playing a minor role in revealing subclinical USMI in males and is supported by our findings that castration was not a risk for UI in our population. Alternatively, UI in males may represent the most severe cases of USMI that have been masked until the sex specific protective anatomy and physiology can no longer compensate and prevent urinary leakage. This is consistent with our findings that the OR of incontinence in older male dogs is higher than that reported for older females in the same age categories (O'Neill and others 2017). Clinically evident UI in males may therefore be more analogous to the most severe USMI cases in females that can progressively worsen with time and fail to respond to pharmacological management.

Male dogs with UI that were identified in this study may not be analogous to a female population with respect to the predominant underlying cause being USMI. This could explain the lack of effect of bodyweight or neutering in males compared with previous female studies (O'Neill and others 2017) and the reported poor response to USMI therapies in males. Conversely, the failure to identify risk factors associated with neuter status or bodyweight may actually demonstrate the low prevalence of other underlying diseases that can cause UI (e.g. entire male dogs with hormone responsive prostatic changes or obesity raising intra-abdominal pressure on the bladder with bladder atony or other causes of overflow incontinence). The at-risk breeds identified in the current study of males are almost identical (other than the fox terrier) to those reported in a recent large study of females (O'Neill and

other 2017) which may suggest a common aetiology for UI between the sexes and indeed, the male dogs of the at-risk breeds have higher odds ratios than the females supports there being a genetic predisposition. Urethral pressure profilometry of both sexes would be required to definitively confirm the underlying cause of UI in these at-risk breeds (since USMI is generally a diagnosis made by exclusion, or based on response to medical intervention). Additionally, it should be recognised that the reliability of the odds ratios for the risk factors investigated is limited by the relatively low numbers of incident cases in some breeds; this means that misclassification of breed (for example) of a UI case may have a disproportionately large effect on odds ratio estimation for that risk factor. Interpretation of our findings should therefore be cautious when reported numbers are low.

Cases of UI were first selected when a final diagnosis of UI was entered into an EPR field. Consequently, UI described as a clinical sign of a diagnosed underlying condition (e.g. spinal disease, bladder atony, urolithiasis, urinary tract neoplasia etc) were largely omitted without the requirement for specific exclusion; this was further refined to try and avoid false negative UI case identification by cross-referencing with free text searches for clinical descriptors of UI without a final diagnosis having been recorded, or if USMI specific treatment were administered as a diagnostic aid. Should false negative cases still be included in the control group, this could reduce or eliminate the significance of the risk factors investigated. In cases where incomplete investigations were performed (e.g. urolithiasis), or if there were early subtle underlying disease that was not evident (e.g. urethral neoplasia), dogs may have be classified as UI rather than a more appropriate definitive diagnosis leading to false positive cases; this was largely avoided by a qualified veterinary professional manually checking records. Whilst we feel that the dogs identified in this study are largely representative of USMI, consistent with the breed similarities with affected bitches, we wish to be clear that the limitations of retrospective investigations, the rarity of urethral pressure profilometry, and

the risk of inaccurate or incomplete diagnosis is the reason that we report the prevalence and risk factors for UI generally, and not specific for underlying aetiology.

The data was taken from a broad cross section of first opinion practices in the UK that have previously agreed to encode the information from consultations in a standardised electronic patient record system and share the data. Whilst this could introduce bias in the data, the large numbers of patients and non-selective sampling of all electronic records available (when not searching for a specific EPR which is essential to identify any case in a retrospective study) likely alleviates this and there are policies or protocols in place across corporate groups that would bias the diagnosis, investigation and management of UI in dogs.

A lower proportion of male dogs received medical management than has been recently reported for females (17% versus 46%, O'Neill et al 2017), a greater proportion died during the study period (55% versus 37%) and of those dogs with a recorded cause, approximately 95% were euthanased in both sexes but a greater proportion of males had UI cited as the main or contributory cause (42% of males versus 17% of bitches). The median age of death was similar for both sexes. It therefore seems that owners or veterinary surgeons are less inclined to treat incontinence in males, which may in turn explain why the mortality rate associated with this condition (when electively performed) is higher for males than females. Explanations for this may be that male dogs are older at presentation, although the mean age of death is the same for both sexes (approximately 13.5 years), an expectation that male dogs will respond poorly to treatment, the underlying cause of UI is not perceived or diagnosed to be USMI or a more subtle societal reason.

Conclusions

The novel breed prevalence and odds ratios described in this study are the most accurate data available for male UI to date and highlight important distinctions between dogs and bitches affected by this condition. Accurately identifying affected dogs, facilitated by precise epidemiological data, allows targeted investigations and the development of more effective therapeutic interventions. There are clearly some consistent factors, as highlighted by increased prevalence in dogs and bitches of the same breed suggesting a likely genetic component, but equally some important differences that may have a sex linked genetic association or be more associated with contrasting male and female anatomy, physiology or underlying cause. The low treatment and high mortality rate in male dogs with UI highlight the welfare importance and requirement for further research into the aetiology and treatment of this condition.

Figures

Figure 1. Age at diagnosis of urinary incontinence in 344 incident cases of urinary incontinence in male dogs attending primary-care veterinary practices in England.
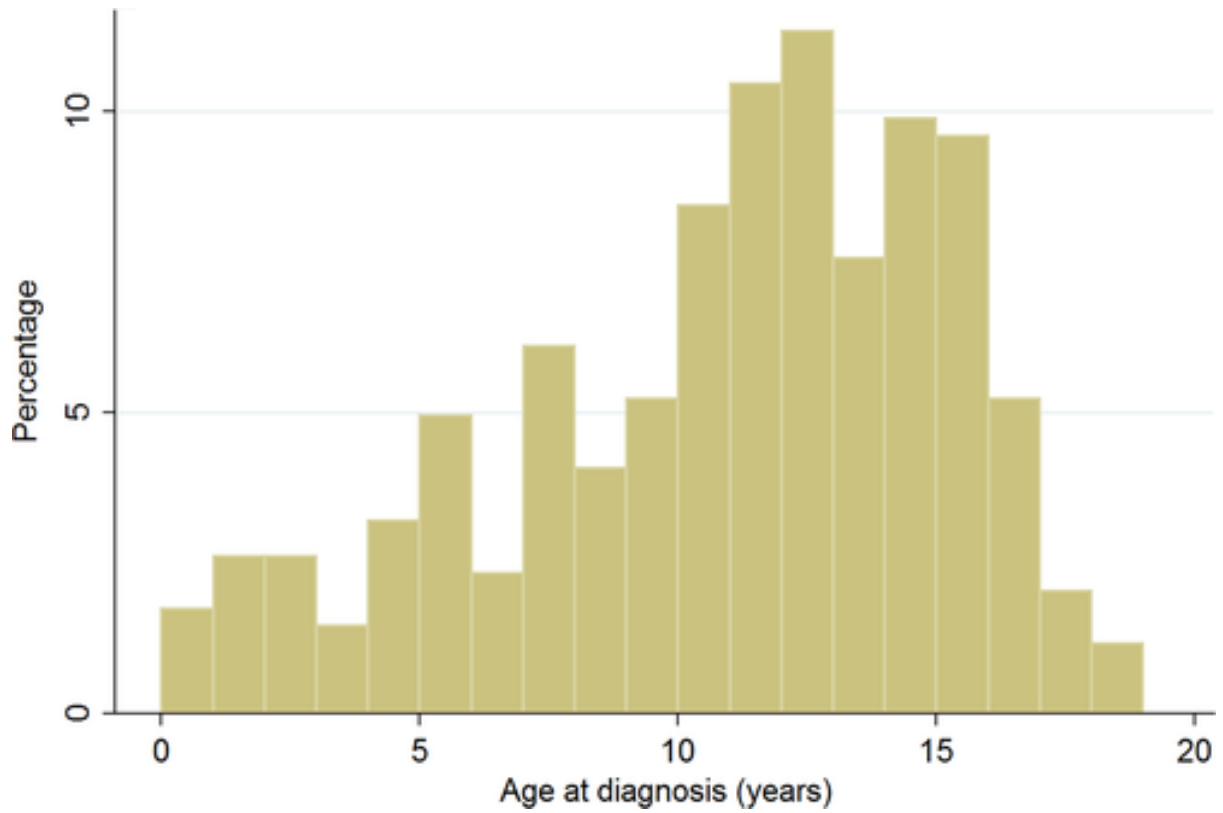
Tables

Table 1: Estimated prevalence and 95% confidence interval (CI) of urinary incontinence in males of commonly diagnosed dog breed types attending primary-care veterinary practices in England.

Breed types	Prevalence (%)	95% CI	Number of UI cases sampled in breed	Estimated overall number of UI cases in breed	Number of breed in overall denominator population
Irish red setter	8.44	4.57 to 14.00	5	13	154
Fox terrier	6.95	3.76 to 11.59	5	13	187
Bull mastiff	4.02	2.16 to 6.78	5	13	323
Boxer	2.49	1.77 to 3.40	14	38	1528
English springer spaniel	2.25	1.68 to 2.94	19	51	2268
West Highland white terrier	2.01	1.52 to 2.60	21	56	2787
Bulldog	1.39	0.74 to 2.36	5	13	938
Border collie	1.27	0.88 to 1.76	13	35	2762
Cavalier King Charles spaniel	1.22	0.82 to 1.75	11	29	2378
Border terrier	1.22	0.70 to 1.97	6	16	1311
Bichon	1.21	0.73 to 1.89	7	19	1564
Greyhound	1.21	0.65 to 2.07	5	13	1070
German shepherd dog	1.18	0.86 to 1.59	16	43	3632
Golden retriever	0.96	0.58 to 1.49	7	19	1983
Rottweiler	0.96	0.51 to 1.64	5	13	1354
Cocker spaniel	0.95	0.67 to 1.30	14	38	4004
Yorkshire terrier	0.89	0.61 to 1.25	12	32	3604
Jack Russell terrier	0.78	0.59 to 1.02	20	54	6885
Crossbreed	0.71	0.61 to 0.83	64	172	24,177
Staffordshire Bull terrier	0.7	0.53 to 0.90	22	59	8426
Labrador retriever	0.66	0.51 to 0.85	23	62	9391
Other breed-types	0.78	0.69 to 0.89	84	225	28,702
Overall	0.94	0.88 to 1.00	383	1027	109,428

Table 2: Univariable logistic regression results for risk factors associated with incidence of urinary incontinence in 107,121 male dogs attending primary-care veterinary practices in England. *P < 0.05.

Variable	Category	Non-case	Case	Odds ratio	95% confidence intervals	Category P value	Variable P value
Purebred status	Crossbred	23,732	58	Base			0.014
	Purebred	83,333	287	1.41	1.06 to 1.87	0.017	
Common breeds	Crossbreed	23,732	58	Base			<0.001
	Irish Red setter*	142	5	14.41	5.69 to 36.45	<0.001	
	Fox terrier*	176	5	11.62	4.61 to 29.33	<0.001	
	Bull mastiff*	314	5	6.52	2.60 to 16.35	<0.001	
	Boxer*	1470	10	2.78	1.42 to 5.46	0.003	
	English springer spaniel*	2186	18	3.37	1.98 to 5.73	<0.001	
	West Highland White terrier*	2689	18	2.74	1.61 to 4.65	<0.001	
	Bulldog	929	5	2.2	0.88 to 5.50	0.091	
	Border collie*	2689	13	1.98	1.08 to 3.61	0.027	
	Cavalier King Charles spaniel*	2312	11	1.95	1.02 to 3.71	0.043	
	Border terrier	1280	6	1.92	0.83 to 4.45	0.13	
	Bichon	1530	7	1.87	0.85 to 4.11	0.118	
	Greyhound	1042	4	1.57	0.57 to 4.33	0.383	
	German shepherd dog	3534	15	1.74	0.98 to 3.07	0.057	
	Golden retriever	1927	5	1.06	0.43 to 2.65	0.898	
	Rottweiler	1327	4	1.23	0.45 to 3.40	0.685	
	Cocker spaniel	3915	12	1.25	0.67 to 2.34	0.476	
	Yorkshire terrier	3533	11	1.27	0.67 to 2.43	0.462	
	Jack Russell terrier	6773	17	1.03	0.60 to 1.76	0.923	
	Staffordshire Bull terrier	8333	19	0.93	0.56 to 1.57	0.793	
	Labrador retriever	9175	21	0.94	0.57 to 1.54	0.797	
Kennel Club Breed Groups	Not KC-recognised			Base			0.016
	Pastoral	7705	37	1.99	1.34 to 2.95	0.001	
	Working	5913	30	2.1	1.38 to 3.21	0.001	
	Gundog	19,871	64	1.34	0.96 to 1.86	0.087	
	Hound	4619	21	1.89	1.16 to 3.06	0.01	
	Terrier	14,966	56	1.55	1.10 to 2.19	0.012	
	Utility	8909	22	1.02	0.64 to 1.65	0.921	
	Toy	13,141	38	1.2	0.81 to 1.77	0.359	
Adult bodyweight (kg)	<10.0	17,927	67	Base			0.65
	10.0 to 19.9	18,558	88	1.27	0.92 to 1.74	0.143	
	20.0 to 20.9	14,431	57	1.06	0.74 to 1.51	0.759	
	30.0 to 30.9	12,101	49	1.08	0.75 to 1.57	0.67	
	≥ 40.0	6935	30	1.16	0.75 to 1.78	0.507	
Breed relative bodyweight	Lower	30,548	115	Base			0.153
	Equal/higher	39,404	176	1.19	0.94 to 1.50	0.155	
Age (years)	<3.0	45,395	24	Base			<0.001
	3.0 to <6.0	22,434	33	2.78	1.64 to 4.71	<0.001	
	6.0 to <9.0	17,237	43	4.72	2.86 to 7.78	<0.001	
	9.0 to <12.0	12,265	83	12.8	8.12 to 20.17	<0.001	
	≥ 12.0	9592	161	31.75	20.66 to 48.78	<0.001	
Neuter status	Entire	11,891	35	Base			<0.001
	Neutered	36,956	204	1.88	1.31 to 2.69	0.001	
Insurance	Non-insured	35,868	135	Base			<0.001
	Insured	26,049	153	1.56	1.24 to 1.97	<0.001	

Table 3: Breed-focused mixed-effects multivariable logistic regression results for risk factors associated with urinary incontinence diagnosis in male dogs attending primary-care veterinary practices in England. *P < 0.05.

Variable	Category	Number of non-cases	Number of cases	Odds ratio	95% confidence interval	Category P value	Variable P value
Breed	Crossbred	23,732	58	Base			<0.001
	Bull mastiff*	314	5	17.21	6.65 to 44.56	<0.001	
	Irish red setter*	142	5	12.79	4.83 to 33.84	<0.001	
	Fox terrier*	176	5	9.6	3.68 to 25.05	<0.001	
	Bulldog*	929	5	5.72	2.24 to 14.59	<0.001	
	Boxer*	1470	10	3.65	1.84 to 7.25	<0.001	
	English springer spaniel*	2186	18	3	1.75 to 5.16	<0.001	
	Rottweiler*	1327	4	2.36	0.85 to 6.58	0.101	
	Border terrier*	1280	6	2.16	0.92 to 5.06	0.076	
	German shepherd dog*	3534	15	2.07	1.16 to 3.69	0.014	
	Bichon	1530	7	1.98	0.89 to 4.40	0.092	
	Cavalier King Charles spaniel*	2312	11	1.98	1.03 to 3.81	0.041	
	West Highland White terrier	2689	18	1.66	0.97 to 2.84	0.064	
	Border collie	2689	13	1.46	0.80 to 2.69	0.22	
	Greyhound	1042	4	1.45	0.52 to 4.04	0.475	
	Cocker spaniel	3915	12	1.29	0.69 to 2.41	0.433	
	Staffordshire Bull terrier	8333	19	1.25	0.74 to 2.11	0.404	
	Yorkshire terrier	3533	11	0.98	0.51 to 1.88	0.959	
	Jack Russell terrier	6773	17	0.92	0.53 to 1.58	0.759	
	Labrador retriever	9175	21	0.88	0.53 to 1.46	0.614	
	Golden retriever	1927	5	0.66	0.26 to 1.65	0.373	
	Other breed-types	28,113	76	1.34	0.95 to 1.90	0.094	
Age (years)	<3.0	45,395	24	Base			<0.001
	3.0 to <6.0*	22,434	33	2.14	1.26 to 3.64	0.005	
	6.0 to < 9.0*	17,237	43	3.63	2.19 to 6.02	<0.001	
	9.0 to <12.0*	12,265	83	10.46	6.59 to 16.62	<0.001	
	≥ 12.0*	9592	161	32.53	20.95 to 50.51	<0.001	
Neuter status	Entire	11,891	35	Base			0.007
	Neutered	36,956	204	1.17	0.80 to 1.71	0.427	
Insurance	Non-insured	35,868	135	Base			<0.001
	Insured*	26,049	153	1.96	1.53 to 2.51	<0.001	

Table 4: Results for Kennel Club (KC) breed group and adult bodyweight as risk factors for urinary incontinence diagnosis in male dogs attending primary-care veterinary practices in England. These variables each individually replaced the breed variable in the original mixed-effects multivariable logistic regression modelling. * $P < 0.05$.

Variable	Category	Number of non-cases	Number of cases	Odds ratio	95% confidence interval	Category P value	Variable P value
Purebred status	Crossbred	23,732	58	Base			<0.001
	Purebred*	83,333	287	1.45	1.09 to 1.93	0.012	
KC breed group	Not KC-recognised	31, 941	77	Base			<0.001
	Utility	8909	22	1.2	0.74 to 1.93	0.462	
	Toy	13,141	38	1.39	0.93 to 2.05	0.105	
	Working*	5913	30	3.83	2.48 to 5.94	<0.001	
	Pastoral*	7705	37	1.76	1.18 to 2.62	0.005	
	Gundog	19,871	64	1.21	0.86 to 1.70	0.263	
	Hound*	4619	21	2.14	1.31 to 3.49	0.002	
	Terrier*	14,966	56	1.57	1.10 to 2.22	0.012	

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