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1	Urinary incontinence in bitches under primary veterinary care in England: prevalence
2	and risk factors

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25	
26	Structured Summary
27	Objectives
28	Urinary incontinence is reportedly common in bitches. This study aimed to estimate
29	prevalence and demographic risk factors in bitches under primary veterinary care in England.
30	Methods
31	The study population included all bitches within the VetCompass database from September 1 st ,
32	2009 to July 7th, 2013. Electronic patient records were searched for urinary incontinence cases
33	and additional demographic and clinical information was extracted.
34	Results
35	Of 100,397 bitches attending 119 clinics in England, an estimated 3,108 were diagnosed with
36	urinary incontinence. The prevalence of urinary incontinence was 3.14% (95% CI 2.97-3.33).
37	Medical therapy was prescribed to 45.6% cases. Predisposed breeds included the Irish Setter
38	(OR: 8.09, 95% CI 3.15-20.80, <i>P</i> < 0.001) and Dobermann (OR: 7.98, 95% CI 4.38-14.54, <i>P</i>
39	< 0.001). Bitches weighing at or above the mean adult bodyweight for their breed had 1.31
40	times the odds (95% CI 1.12-1.54, $P < 0.001$). Increasing adult bodyweight was associated
41	with increasing risk. Bitches aged 9 to < 12 years showed 3.86 (95% CI 2.86-5.20, $P < 0.001$)
42	times the odds, neutered bitches had 2.23 (95% CI 1.52-3.25, $P < 0.001$) times the odds and
43	insured bitches had 1.59 (95% CI 1.34-1.88, $P < 0.001$) times the odds.

44 Clinical I	mpact
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Urinary incontinence affects just over 3% of bitches overall but affects over 15% of bitches in high risk breeds including the Irish Setter, Dobermann, Bearded Collie, Rough Collie and Dalmatian. These results provide an evidence base for clinicians to enhance clinical recommendations on neutering and weight control, especially in high-risk breeds.

49

50 Key Words:

51 VetCompass, epidemiology, urethra, bladder, dog

52 Abbreviations

53 CI; confidence intervals, EPR; electronic patient record, OR; odds ratio, PMS: practice 54 management system, UI; urinary incontinence, USMI; urethral sphincter mechanism 55 incompetence,

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58 Introduction

59 Urinary incontinence (UI) is defined as involuntary leaking of urine from the bladder during 60 the storage phase of micturition and can result from anatomical or functional abnormalities 61 (Coit and others 2008, Schaer 2010). UI most commonly results from urethral sphincter 62 mechanism incompetence (USMI) in the adult bitch and from ectopic ureters in the juvenile 63 bitch (Gregory 1994, Holt 1985, Thrusfield and others 1998). A complete diagnostic workup is required to investigate bitches with UI to discriminate between congenital and acquired 64 65 disease, functional versus mechanical problems and to identify anatomical abnormalities 66 (Sam and Craig 2000). For bitches with acquired UI, a presumptive diagnosis of USMI is

67 often made based on patient history, absence of abnormalities on clinical examination and 68 response to medical treatment, including oestrogen or alpha adrenergic receptor agonist 69 medication individually or in combination, with improvement or complete response 70 supporting the diagnosis (Gregory 1994, Sam and Craig 2000). UI is often a distressing 71 disorder for both owners and their pets, and may negatively impact the interaction between 72 them (de Bleser and others 2011). Effective management is important to canine welfare to avoid sequelae such as ascending urinary tract infection, urinary scalding of the skin and 73 74 euthanasia of affected dogs (Schaer 2010).

75 Reliable and up-to-date data on the prevalence of UI that are generalisable to the dog 76 population in England are limited. Prevalence values for UI from 2% and 16% have been 77 reported in neutered bitches, varying across the study designs and denominator populations 78 investigated (Forsee and others 2013, Okkens and others 1997, Thrusfield and others 1998). 79 However, many of these reports have focused on the prevalence specifically of USMI and are 80 either dated, lacking in reliable counts and precision, or cannot estimate the true prevalence 81 of the condition because they did not include all animals in the underlying population (Holt 82 1985, Thrusfield and others 1998). Extrapolation of data between groups of dogs from 83 different continents may also be unreliable (Forsee and others 2013).

84 Risk factors reported for UI in bitches include breed, age, bodyweight, obesity, neutering 85 status, time of neutering, hormonal factors and tail docking (Arnold 1997, de Bleser and 86 others 2011, Forsee and others 2013, Gregory 1994, Holt and Thrusfield 1993, Power and others 1998, Spain and others 2004a, Thrusfield and others 1998). In the UK, Dobermann and 87 88 Old English Sheepdog are reported as predisposed breeds, with Rottweiler, Weimaraner, 89 Springer Spaniel and Irish Setter also considered at risk (Holt and Thrusfield 1993). In other 90 European countries, Boxers (Arnold 1997) and Bouvier des Flanders (Okkens and others 91 1997) have been reported at higher risk. The risk of UI is reported to rise with increasing age

(de Bleser and others 2011, Stöcklin-Gautschi and others 2001, Thrusfield and others 1998)
and increasing weight (Angioletti and others 2004, de Bleser and others 2011, Forsee and
others 2013, Okkens and others 1997, Stöcklin-Gautschi and others 2001). Obesity has not
been definitively confirmed as a cause of USMI (Angioletti and others 2004), but it may
worsen the degree of incontinence whereas bodyweight loss has been reported to improve
clinical signs of incontinence (Holt 2012).

98 Several studies have reported that neutering is associated with increased risk of UI in bitches 99 (de Bleser and others 2011, Forsee and others 2013, Spain and others 2004a, Stöcklin-100 Gautschi and others 2001, Thrusfield and others 1998) although a weak evidence base for 101 these conclusions was reported in a systematic review of the effect of neutering on UI 102 (Beauvais and others 2012). The evidence for an association between early neutering and UI 103 is controversial and appears to be weak; one study reported a reduced risk following 104 neutering before the first season (Stöcklin-Gautschi and others 2001) but evidence of 105 increased risk of UI in bitches neutered before 3 months of age seems stronger (Beauvais and 106 others 2012, Kustritz 2007, Spain and others 2004b).

107 The primary objectives of this study were to estimate the prevalence of UI in the general

108 population of bitches under primary veterinary care in England and to evaluate demographic

109 risk factors for diagnosis with UI, with a particular focus on breed effects. These results will

110 assist clinicians to identify individuals at risk in order to improve the diagnosis and

111 management of this condition and to support decision-making advice to owners of at-risk

112 individuals regarding neutering and weight management.

114 Materials and methods

115 The VetCompass Programme collates anonymised electronic patient record (EPR) data from 116 primary-care veterinary practices in the UK for epidemiological research (O'Neill and others 117 2014b). Collaborating practices were a convenience sample selected by their willingness to 118 participate and their recording of clinical data within an appropriately configured practice 119 management system (PMS). Practitioners could record summary diagnosis terms from an 120 embedded VeNom Code list during episodes of care (The VeNom Coding Group 2017). 121 Information collected relates mainly to the owned dog population and includes patient 122 demographic (species, breed, date of birth, sex, neuter status, insurance status and 123 bodyweight) and clinical information (free-form text clinical notes, summary diagnosis terms, 124 treatment and deceased status with relevant dates) data fields. EPR data are extracted from 125 PMSs using integrated clinical queries and uploaded to a secure VetCompass relational 126 database (O'Neill and others 2016a). 127 In this study, a cohort study design was used to estimate UI prevalence and to evaluate risk 128 factors for UI diagnosis (Pearce 2012). The sampling frame included all bitches with at least 129 one EPR (clinical note, VeNom summary term, bodyweight or treatment) uploaded to the 130 VetCompass database from September 1st, 2009 to July 7th, 2013 and that were deemed to be 131 under veterinary care during this period. The epidemiological unit for this study was the bitch 132 and each bitch was aimed to be included only once in the analysis by linking to its unique ID 133 code in the PMS. Sample size calculations estimated that a study population of 73,901 bitches 134 would be required to estimate the prevalence of a disease with an expected frequency of 2% 135 within 0.1% precision limits with a 95% confidence level, assuming a UK population of four million bitches (Asher and others 2011, Epi Info 7 CDC 2015)). Ethical approval of the 136 project was granted by the RVC Ethics and Welfare Committee (reference number 00/2014). 137

138 The inclusion criteria for a UI case required a final veterinary diagnosis of urinary 139 incontinence recorded in the EPR or prescription of a specific urinary incontinence therapy 140 (product containing phenylpropanolamine or estradiol). UI recorded as occurring secondary 141 to seizure activity was excluded. Case-finding involved initial screening of all EPRs for 142 candidate UI cases by searching the clinical free-text field (search terms included incont, 143 usmi, incompet, urethral sp, nocturia, wetting, wet the bed, dribbling urin, leaking urin), the 144 VeNom term field (*incont*) and the treatment field (*propal, incurin, enurace, urilin, proin*). 145 Findings from these searches were merged and the full clinical notes of a random subset were 146 manually reviewed for case inclusion by one author (AR). Randomisation used the RAND 147 function in Microsoft Excel (Microsoft Office Excel 2007, Microsoft Corp.). The count of 148 candidate cases that were manually reviewed was based on the power analysis described 149 earlier in the methods. Logistics constraints precluded manual review of all candidate cases. 150 Additional data were extracted on all confirmed UI cases to define each case as pre-existing 151 (first recorded prior to the study period) or incident (first recorded during the study period), 152 whether the animal died during the study period and, if so, the date and method of death 153 (euthanasia or unassisted) and whether UI was recorded as a contributory factor for the death. 154 For incident cases, the date of the first diagnosis and whether medication was prescribed to 155 control UI were also extracted. All bitches that were not identified as candidate UI cases 156 during the initial screening were included as non-cases in the risk factor analysis.

A *breed* variable included any individual breeds with 10 or more UI cases, a grouped category of all remaining breeds and a general grouping of crossbred bitches. A *purebred* variable categorised all bitches with a recognisable breed name as 'purebred' and the remaining bitches 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 bitches were 163 classified as non-KC recognised (The Kennel Club 2017). Neuter described the recorded 164 status of the dog (neutered or entire) at the final EPR. Insurance described whether a dog was 165 recorded as insured at any point during the study period. Age described the age at the date of 166 first recorded diagnosis for incident UI cases so that the results reflect associations with the 167 age at 'becoming' a UI case. It was assumed that the dates for first diagnosis of UI cases 168 would be randomly spread throughout the study period and therefore Age described the age at 169 the mid-point between the dates of the first and final EPRs recorded during the study period 170 for the non-cases so that these ages would be as representative as possible of the expected 171 ages for these dogs if they had received a diagnosis of UI. Age (years) was categorised into 172 six groups (< 3.0, 3.0-5.9, 6.0-8.9, 9.0-11.9, \geq 12.0, not recorded). Adult bodyweight 173 described the maximum bodyweight recorded during the study period for bitches 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, 174 $30.0-39.9 \text{ kg} \ge 40.0 \text{ kg}$, not recorded). Mean adult bodyweight was calculated for each breed 175 176 in the study and used to generate a *breed relative bodyweight* variable that characterised 177 bitches as either below or equal/above the mean adult bodyweight for their breed. This variable allowed the effect of adult body weight within each breed to be assessed. 178 179 Following data checking and cleaning in Excel to assess the completeness, internal 180 data consistency and validity of the demographic and clinical data extracted from the 181 VetCompass database (Microsoft Office Excel 2013, Microsoft Corp.) (O'Neill and others 182 2016b), analyses were conducted using Stata Version 13 (Stata Corporation). No bitches were 183 removed from the analyses during the data cleaning process. The period prevalence with 95% 184 confidence intervals (CI) described the probability of having UI at any time during the study period and was based on complete examination of a subset of bitches that were diagnosed 185 186 with UI prior to the study period (pre-existing cases) as well as those diagnosed for the first 187 time during the study period (incident cases). The case count that would have been identified

188 if the entire set of candidate cases had been manually verified was calculated by weighting 189 the verified case numbers by the inverse of the proportion of candidate cases that was 190 manually verified (O'Neill and others 2016a). The overall period prevalence of UI was 191 estimated based on a denominator of all study bitches and the breed-specific period 192 prevalence of UI was estimated for each breed based on a denominator of all bitches of that 193 breed in the study. The CI estimates were derived from standard errors, based on 194 approximation to the normal distribution (Kirkwood and Sterne 2003). Descriptive statistics 195 characterised the breed, neuter status, insurance status, age and adult bodyweight for the 196 incident cases and non-case bitches. The medical management regimes were reported for 197 incident cases only because clinical records extending back to the original date of first 198 diagnosis of UI may not have been available for many pre-existing cases. Mortality results 199 were reported on all UI cases.

200 Binary logistic regression modelling was used to evaluate univariable associations between 201 risk factors (breed, purebred, KC breed group, adult bodyweight, breed relative bodyweight, 202 age, neuter and insurance) and incident cases of urinary incontinence. Inclusion of all cases 203 (pre-existent and incident) into risk factor analysis has the effect of evaluating risk factors for 204 'being' a case rather than for 'becoming' a case and therefore bias towards higher odds ratios 205 for factors associated with longer survival with UI. For example, long-lived breeds are more 206 likely to be included compared with short-lived breeds. The current study aimed to evaluate 207 risk factors for 'becoming' a case and therefore elected to include only incident cases that 208 were diagnosed with UI during the study period. Breed was a factor of primary interest for 209 the study. The *purebred*, KC breed group and adult bodyweight variables were correlated 210 with the *breed* variable and were therefore not simultaneously considered in multivariable 211 modelling. Instead, the results for these correlated variables were derived by individually replacing the *breed* variable from the final breed multivariable model. 212

213Risk factors with liberal associations in univariable modelling (P < 0.2) were taken forward214for multivariable evaluation. Model development used manual backwards stepwise215elimination. Clinic attended was evaluated as a random effect and pair-wise interaction216effects were evaluated for the final model (Dohoo and others 2009). The Hosmer-Lemeshow217test statistic and the area under the ROC curve were used to evaluate the quality of model fit218(non-random effect model) (Dohoo and others 2009, Hosmer and Lemeshow 2000).219Statistical significance was set at P < 0.05.

220

221 **Results**

The overall dataset comprised 100,397 bitches attending 119 clinics in England. Overall, 222 223 4,559 animals were identified as candidates for urinary incontinence. From 1,637 (35.9%) 224 candidates that were manually checked, 1,116 bitches met the case definition for UI that 225 comprised of 754 (67.56%) incident and 362 (32.44%) pre-existing cases. Data on all 1,116 226 UI cases were included in the demographic descriptive evaluation. Data on just the 754 227 incident UI cases were included in the medical management evaluation and the risk factor 228 analysis. An estimated 3,108 cases would have been identified if all candidate animals were 229 checked. After accounting for the sampling approach, the estimated prevalence for UI in 230 bitches overall was 3.14% (95% CI 2.97-3.33). Breeds with the highest prevalence included 231 the Irish Setter (32.3%, 95% CI 23.6-41.6), Dobermann (21.6%, 95% CI 17.4-26.6), Bearded 232 Collie (16.5%, 95% CI 11.6-22.8), Rough Collie (16.3%, 95% CI 12.1-20.9) and Dalmatian 233 (15.8%, 95% CI 12.2-19.7). The prevalence in crossbreds was 3.1% (95% CI 2.8-3.3) (Table 234 1).

235 Data completeness overall were: breed 99.9%, age 99.7%, adult bodyweight 65.6%, insurance

236 57.8% and neuter status 47.0%. Descriptive evaluation included 1,116 UI cases and 95,838

non-cases. The median (interquartile range [IQR], range) time between the first and final EPR

- across all study bitches was 0.6 years (0.0-2.1, 0.0-5.0). Of the UI cases with information
- 239 available, 871 (78.1 %) were purebred, 870 (95.92%) were neutered and 484 (53.3%) were
- insured. The median adult bodyweight was 22.6 kg (IQR: 13.6-30.9) and the median age at
- diagnosis was 10.6 years (IQR: 5.8-13.1) (Figure 1). The most common breeds diagnosed
- with UI were the Labrador Retriever (n = 92, 8.2%), Border Collie (59, 5.3%), German
- 243 Shepherd Dog (56, 5.0%), West Highland White Terrier (51, 4.6%) and Staffordshire Bull
- 244 Terrier (48, 4.3%), along with 244 (21.9%) crossbreds.
- Of the non-case bitches with information available, 73,877 (77.1%) were purebred, 35,037
- 246 (80.3%) were neutered and 21,091 (38.8%) were insured. The median adult bodyweight was
- 247 16.4 kg (IQR: 9.5-26.4) and the median age was 3.9 years (IQR: 1.3-8.0). The most common
- breeds among the non-case bitches were the Staffordshire Bull Terrier (8,074, 8.4%),
- Labrador Retriever (7,906, 8.3%), Jack Russell Terrier (6,432, 6.7%) and Cocker Spaniel
- 250 (3,516, 3.7%) along with 21,895 (22.9%) crossbreds.
- 251 Medical therapy directed specifically at managing UI was prescribed to 344/754 (45.6%) of
- the incident UI cases. During the study period, 407/1,116 (36.5%) of the studied UI caseload
- died. The median age at death was 13.7 (IQR 1.1-15.0, range 1.1-18.9) years and 366/387
- 254 (94.6%) deceased bitches with a recorded mechanism of death were euthanased. UI was
- recorded as either contributory or the main reason for death in 68/407 (16.7%) incontinent
- bitches that died.
- 257 Risk factor analysis included 754 incident UI cases and 95,838 non-cases. Univariable
- logistic regression modelling identified seven variables liberally associated (P < 0.20) with
- 259 urinary incontinence: (breed, KC breed group, adult bodyweight, breed relative bodyweight,
- 260 age, neuter and insurance) (Table 2). Following evaluation using multivariable logistic
- 261 regression, the final breed model comprised five risk factors: *breed, breed relative*

262 *bodyweight, age, neuter* and *insurance*. No biologically significant interactions were 263 identified. Modelling was improved by inclusion of the clinic attended as a random effect (P264 < 0.001, rho = 0.032, indicating that the clinic attended accounted for 3.2% of variation) so 265 the clinic random effect was retained in the final model. For the final non-clustered breed 266 model, the Hosmer-Lemeshow test indicated no evidence of poor model fit (P = 0.777) and 267 the area under ROC curve (0.848) indicated excellent UI discrimination (Hosmer and 268 Lemeshow 2000).

269 After accounting for the effects of the other variables evaluated, 10 breeds showed increased 270 odds of UI compared with crossbred bitches. Breeds with the highest odds included the Irish 271 Setter (OR: 8.09, 95% CI 3.15-20.80, P < 0.001), Dobermann (OR: 7.98, 95% CI 4.38-14.54, P < 0.001), Bull Mastiff (OR: 6.24, 95% CI 2.67-14.58, P < 0.001), Rough Collie (OR: 3.75, 272 95% CI 1.96-7.18, P < 0.001), Dalmatian (OR: 3.26, 95% CI 1.76-6.06, P < 0.001) and 273 274 Boxer (OR: 3.03, 95% CI 1.95-4.72, P < 0.001). The Jack Russell Terrier, Yorkshire Terrier 275 and Cocker Spaniel showed reduced odds. Bitches weighing at or above the mean adult 276 bodyweight for their breed had 1.31 times the odds (95% CI 1.12-1.54, P < 0.001) of UI 277 compared with bitches weighing below their breed mean. Increasing age was associated with 278 increasing risk of developing urinary incontinence; the odds of UI increased sequentially with 279 each category of increasing age. Bitches aged 9 to less than 12 years showed 3.86 (95% CI 280 2.86-5.20, P < 0.001) times the odds of UI compared with those aged less than 3 years. 281 Neutered bitches had 2.23 (95% CI 1.52-3.25, P < 0.001) times the odds and insured bitches 282 had 1.59 (95% CI 1.34-1.88, P < 0.001) times the odds of UI compared with entire and 283 uninsured bitches respectively (Table 3).

Additionally, *KC breed group* and *adult bodyweight* were significant risk factors when used to replace the breed variable in the final breed model. There was no evidence for an association between purebred status and UI (P = 0.938). Of the KC breed groups, Working 288 0.001) group bitches showed higher odds of UI compared with bitches that were not of KC

recognised breeds. Toy breeds had reduced odds of UI (OR 0.69, 95% CI 0.50-0.95,

290 P=0.025). Increasing adult bodyweight was associated with increasing odds of UI. Bitches

weighing over 30kg had 2.94 times the odds (95% CI 2.27-3.80, P < 0.001) of UI compared

292 with bitches weighing under 10 kg (Table 4).

293

294 **Discussion**

295 This study investigated UI in bitches attending 119 primary-care practices in England by 296 analysing a database containing the clinical records of 100,397 bitches. Access to such large 297 counts of bitches supports the reporting of an estimated prevalence of 3.14% for UI diagnosed 298 in this population and this result is likely to be more accurate and generalisable than earlier 299 smaller studies and those focusing on either at-risk dogs or referral populations (Bartlett and 300 others 2010, O'Neill and others 2014a). Irish Setter, Dobermann, Bull Mastiff, Rough Collie, 301 Dalmatian and Boxer breeds had the highest odds of UI, with approximately one third of all Irish Setters being diagnosed with the condition. Jack Russell Terriers and Yorkshire Terriers 302 303 had reduced odds. The risk of UI increased with age and weight. Neutered bitches and insured 304 animals were also associated with increased risk of UI.

Direct comparisons between the results of the current study with previous reports are complicated by the differing aims and study populations of the previously available studies. Many earlier investigations aimed to specifically investigate the USMI subset of UI cases rather than the more general UI caseload covered by the current study (Gregory 1994, Holt 1985). These earlier studies often also focused entirely on a particular risk group (e.g. neutered bitches) rather than the total bitch population and often did not include a control group which

^{287 (}OR 3.07, 95% CI 2.29-4.11, P < 0.001) and Pastoral (OR 1.87, 95% CI 1.47-2.39, P <

311 may bias the reported demographic, prevalence, incidence and risk factor findings (Arnold 312 1997, de Bleser and others 2011, Forsee and others 2013, Thrusfield and others 1998). 313 However, despite these constraints, many of the breeds identified at higher odds in the current 314 study are consistent with results from previous studies, including the Irish Setter, Dobermann, 315 Weimaraner and Springer Spaniel (Holt and Thrusfield 1993) and Boxer (Arnold 1997). Boxers 316 were the most commonly diagnosed breed in a UK urinary incontinence study (four of 18 cases 317 overall) (Thrusfield and others 1998) and we found an increased odds of over 3 times the 318 crossbred controls for this breed nearly 2 decades later. However, by contrast, the Old English 319 Sheepdog has also previously reported at increased risk (Holt and Thrusfield 1993) but was not 320 identified with increased odds of UI in the current study. This may result from true changing 321 risk for these breeds over time, a changing breed demographic over time or insufficient breed 322 counts in the current study for adequate statistical power.

323 The current study identified that bitches of adult bodyweight over 10 kg have approximately 324 twice the odds of UI, concurring with several previous reports (Angioletti and others 2004, de 325 Bleser and others 2011, Okkens and others 1997, Stöcklin-Gautschi and others 2001). Bitches 326 weighing over 15 kg were previously reported with 7 times the odds of UI, although this study 327 included only neutered females (Forsee and others 2013). Bitches in the UK from heavier 328 breeds were reported with increased risk of UI (Thrusfield and others 1998). Of the ten breeds 329 identified in our study with increased odds of UI in the multivariable analysis, only the English 330 Springer Spaniel did not represent a large or giant breed. Bodyweight and breed are highly 331 related factors whereby individual breed standards often include reference to bodysize 332 characteristics (The Kennel Club 2017). Consequently, statistical modelling methods can 333 struggle to dissect and clarify which of these correlated breed or bodyweight variables 334 represents the major association (Dohoo and others 2009). However, the finding of the current 335 study that bitches *within* individual breeds weighing at or above the breed average have 1.3

times the odds of UI compared with bitches below the breed average may assist in addressing this question somewhat and supports the conclusion that bodyweight in addition to breed is a substantial risk factor for UI.

339 The current study identified that the odds of developing UI rise progressively and substantially 340 with age. UI cases with congenital and anatomical aetiology tend to present at younger ages 341 (Holt and Moore 1995). The current study included UI cases from all causes and the 342 association with increased age shown here suggests that the majority of UI in bitches is 343 acquired and likely to be USMI. Very similar odds ratios to the current study for the age 344 categories were also reported in a specific USMI study of UK neutered bitches (de Bleser and 345 others 2011). It is worth noting that it is possible that some bitches in the current with congenital 346 or anatomic causes (e.g. ectopic ureters) may not have been diagnosed until later in life which 347 might limit this conclusion (McLoughlin and Chew 2000). Other causes of UI that should also be considered include neoplasia, detrusor over-activity, pelvic bladder and neurological disease 348 349 (Crawford and Adams 2002, Noël and others 2010, Norris and others 1992, Olby and others 350 2003).

351 Neutered bitches had increased odds of UI in our study, independently of relative bodyweight 352 and age. This finding agrees with a number of other studies that report neutering as a risk factor 353 for UI in bitches (de Bleser and others 2011, Forsee and others 2013, Spain and others 2004a, 354 Stöcklin-Gautschi and others 2001, Thrusfield and others 1998). However, a systematic review 355 of the effect of neutering on UI concluded that the evidence base for such assertions was weak 356 (Beauvais and others 2012). Neutering of bitches is reported to increase the ratio of collagen 357 to muscle in the urethra, is associated with obesity which can worsen the signs of UI even if it 358 is not truly a cause, and also leads to lower blood oestrogen levels which may reduce urethral 359 smooth and striated muscle tone (Coit and others 2008, de Bleser and others 2011). In the 360 current study, neutered bitches had 2.2 times the odds of UI on multivariable analysis compared 361 with entire animals which would appear to support an association between neutering and 362 urinary incontinence. However, data were not available on the age at neutering or the time from 363 neutering to the onset of UI and therefore this limits the study to reporting just associations for 364 neutering rather than assigning casualty (Pandis 2011). Associations between neutering and UI 365 are likely to be very complex, with many and varied interactions related to the timing of 366 neutering (both absolute in terms of age and relative in terms of puberty), method of neutering, and other factors including breed, age, bodyweight and obesity that would require prospective 367 368 focused cohort study designs for fuller elucidation (Coit and others 2008, Dohoo and others 369 2009). Unfortunately, body condition score and obesity data were not available for the current 370 study.

371 This report identifies some important welfare implications for bitches diagnosed with UI. Of 372 the 407 affected bitches with UI that died during the study period, their UI condition 373 contributed either partly or wholly to 16.7% of the deaths. Many of these patients are likely to 374 have suffered morbidity as a result of UI sequelae including urinary scalding and urinary tract 375 infection (Schaer 2010, Scott and others 2002). UI can also have a negative impact on the owner-pet relationship resulting from house soiling, emotional stress and malodour (de Bleser 376 377 and others 2011). The current study also shows that 45.6% of incident cases received specific 378 medical management for UI which may impose financial and potentially emotional strain on 379 owners.

The study had some limitations. Not all of the candidate cases identified in the original search strategy were manually reviewed in detail and therefore the prevalence estimates were calculated based on the subset that were examined. However, the subset of candidate animals reviewed should reflect the study population overall as a result of their randomised selection and the sizeable number of cases (n = 1,116) manually identified. As previously reported, these data were not recorded primarily for research purposes and thus were limited by some missing and incomplete data as well as also relying on the clinical acumen and record-keeping of the
clinicians (Mattin and others 2015, O'Neill and others 2016a, Shoop and others 2015). The
study included all cases diagnosed with UI and did not attempt to categorise into congenital,
anatomic or acquired subsets.

390 Conclusion

This is the largest study describing the prevalence and risk factors for UI in dogs published to date. UI is shown to be commonly diagnosed in primary-care practice in England, affecting just over 3% of bitches overall but recorded in over 15% of bitches in a number of high risk breeds including the Irish Setter, Dobermann, Bearded Collie, Rough Collie and Dalmatian. The prevalence and risk factors identified can assist clinicians by improving the evidence base supporting clinical recommendations on neutering and weight control, especially in the highrisk breeds identified here.

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399 Conflict of Interest

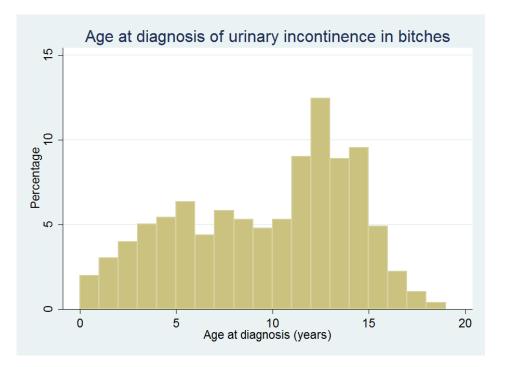
400 One author (DON) is supported at the RVC by a Kennel Club Charitable Trust award. The401 other authors have no conflicts of interest to declare.

402 Acknowledgments

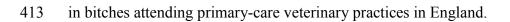
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VetCompass.

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410 Figures



412 Figure 1. Age at diagnosis of urinary incontinence in 754 incident cases of urinary incontinence



421 Tables

- 422 Table 1: Estimated prevalence and 95% confidence interval (CI) of urinary incontinence in
- 423 bitches of commonly diagnosed dog breeds attending primary-care veterinary practices in
- 424 England.

Breed	Prevalence	95% CI
Irish Red Setter	32.3	23.6-41.6
Dobermann	21.6	17.4-26.6
Bearded Collie	16.5	11.6-22.8
Rough Collie	16.3	12.1-20.9
Dalmatian	15.8	12.2-19.7
Weimaraner	10.7	7.7-14.4
Bull Mastiff	10.4	7.0-14.7
Miniature Poodle	9.5	6.5-13.6
Boxer	7.3	5.9-8.8
English Springer Spaniel	6.8	5.6-8.1
Border Collie	6.6	5.6-7.6
Greyhound	6.4	5.1-8.1
West Highland White Terrier	6.0	5.1-7.1
German Shepherd Dog	4.8	4.1-5.6
Golden Retriever	4.4	3.4-5.5
Rottweiler	3.8	2.8-5.0
Labrador Retriever	3.2	2.8-3.6
Crossbreed	3.1	2.8-3.3
Cocker Spaniel	2.0	1.6-2.6
Cavalier King Charles Spaniel	1.8	1.3-2.5
Yorkshire Terrier	1.7	1.3-2.2
Staffordshire Bull Terrier	1.6	1.4-2.0
Jack Russell Terrier	1.5	1.2-1.8

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430Table 2: Univariable logistic regression results for risk factors associated with incidence of431urinary incontinence in 96,592 bitches attending primary-care veterinary practices in England.432 $^{\dagger}P < 0.05$.

Variable	Category	Non-case	Case	Odds ratio	95% CI	Category <i>P</i> -value	Variable <i>P</i> -value
Purebred status	Crossbred	21,895	179	Base			0.569
	Purebred	73,877	575	0.95	0.80-1.13	0.567	
Common breeds	Crossbreed	21,895	179	Base			< 0.001
	Irish Red Setter [†]	99	5	6.18	2.49-15.35	< 0.001	
	Dobermann [†]	297	13	5.35	3.01-9.51	< 0.001	
	Rough Collie [†]	274	11	4.91	2.64-9.13	< 0.001	
	Dalmatian [†]	366	12	4.01	2.22-7.26	< 0.001	
	Bearded Collie [†]	175	5	3.49	1.42-8.60	0.006	
	Weimaraner [†]	350	9	3.15	1.60-6.19	0.001	
	Bull Mastiff [†]	259	6	2.83	1.24-6.45	0.013	
	Boxer [†]	1,272	24	2.31	1.50-3.55	< 0.001	
	Greyhound [†]	1,059	19	2.19	1.36-3.54	0.001	
	West Highland White Terrier [†]	2,306	35	1.86	1.29-2.67	0.001	
	English Spaniel Springer [†]	1,684	24	1.74	1.14-2.68	0.011	
	Border Collie [†]	2,434	34	1.71	1.18-2.47	0.004	
	German Shepherd Dog	3,204	35	1.34	0.93-1.92	0.119	
	Miniature Poodle	282	3	1.30	0.41-4.10	0.653	
	Golden Retriever	1,618	17	1.29	0.78-2.12	0.325	
	Labrador Retriever	7,906	64	0.99	0.74-1.32	0.946	
	Rottweiler	1,171	9	0.94	0.48-1.84	0.857	
	Cavalier King Charles Spaniel	1,991	11	0.68	0.37-1.24	0.208	
	Other breed-types [†]	25,930	143	0.67	0.54-0.84	< 0.001	
	Cocker Spaniel [†]	3,516	17	0.59	0.36-0.97	0.039	
	Staffordshire Bull Terrier [†]	8,074	39	0.59	0.42-0.84	0.003	
	Yorkshire Terrier [†]	3,244	14	0.53	0.31-0.91	0.022	
	Jack Russell Terrier [†]	6,432	26	0.49	0.33-0.75	0.001	
Kennel Club Breed Groups	Not KC-recognised	29,499	211	Base			< 0.001
	Pastoral [†]	6,931	101	2.03	1.60-2.59	< 0.001	
	Working [†]	5,007	64	1.79	1.35-2.37	< 0.001	

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	$Gundog^{\dagger}$	16,943	156	1.29	1.05-1.58	0.017	
	Hound	4,296	37	1.20	0.85-1.71	0.299	
	Terrier	13,597	95	0.98	0.77-1.25	0.850	
	Utility	7,876	44	0.78	0.56-1.08	0.137	
	Toy [†]	11,623	46	0.55	0.40-0.76	< 0.001	
Adult							
bodyweight (kg)	< 10.0	20,184	118	Base			< 0.001
	10.0-19.9 [†]	16,598	175	1.80	1.43-2.28	< 0.001	
	20.0-20.9*	14,564	206	2.42	1.93-3.04	< 0.001	
	30.0-30.9*	7,822	149	3.26	2.56-4.15	< 0.001	
	\geq 40.0 [†]	2,686	50	3.18	2.28-4.44	< 0.001	
Breed relative bodyweight	Lower	41,905	404	Base			< 0.001
	Equal/Higher [†]	19,949	294	1.53	1.31-1.78	< 0.001	
Age (years)	< 3.0	40,489	68	Base			< 0.001
	3.0 - < 6.0 [†]	20,578	127	3.67	2.74-4.94	< 0.001	
	6.0 - < 9.0 [†]	14,850	117	4.69	3.48-6.33	< 0.001	
	9.0 - < 12.0 [†]	10,864	144	8.02	6.01-10.72	< 0.001	
	$\geq 12.0^{\dagger}$	8,988	298	19.74	15.15- 25.72	< 0.001	
Neuter status	Entire	8,618	30	Base			< 0.001
	Neutered [†]	35,037	594	4.87	3.37-7.03	< 0.001	
Insurance	Non-insured	33,322	309	Base			< 0.001
	Insured [†]	21,091	330	1.69	1.44-1.97	< 0.001	

437	Table 3: Breed-focused mixed-effects multivariable logistic regression results for risk factors
438	associated with urinary incontinence diagnosis in bitches attending primary-care veterinary

practices in England. * CI confidence interval. $^{\dagger}P < 0.05$.

Variable	Category	Odds ratio 95% CI*		Category <i>P</i> -value	Variable <i>P</i> -value
Common breeds	Crossbreed	Base			< 0.001
	Irish Red Setter [†]	8.09	3.15-20.80	< 0.001	

	Dobermann [†]	7.98	4.38-14.54	< 0.001	
	Bull Mastiff [†]	6.24	2.67-14.58	< 0.001	
	Rough Collie [†]	3.75	1.96-7.18	< 0.001	
_	Dalmatian [†]	3.26	1.76-6.06	< 0.001	
	Boxer [†]	3.03	1.95-4.72	< 0.001	
	Weimaraner [†]	2.65	1.32-5.32	0.006	
	Bearded Collie	2.22	0.87-5.67	0.096	
_	Greyhound [†]	2.05	1.26-3.35	0.004	
	English Spaniel Springer [†]	1.65	1.07-2.57	0.025	
	Rottweiler	1.63	0.82-3.23	0.160	
	German Shepherd Dog [†]	1.62	1.12-2.35	0.011	
	West Highland White Terrier	1.23	0.85-1.78	0.280	
	Border Collie	1.22	0.84-1.78	0.302	
	Labrador Retriever	0.90	0.67-1.20	0.474	
	Miniature Poodle	0.88	0.27-2.82	0.825	
	Golden Retriever	0.83	0.50-1.37	0.462	
	Staffordshire Bull Terrier	0.83	0.58-1.18	0.292	
	Cavalier King Charles Spaniel	0.64	0.34-1.18	0.152	
	Cocker Spaniel [†]	0.57	0.34-0.94	0.029	
	Yorkshire Terrier [†]	0.47	0.27-0.81	0.007	
	Jack Russell Terrier [†]	0.43	0.28-0.65	< 0.001	
Breed relative bodyweight	Lower	Base			< 0.001
	Equal/Higher [†]	1.31	1.12-1.54	< 0.001	
Age (years)	< 3.0	Base			< 0.001
	$3.0 - < 6.0^{\dagger}$	1.88	1.39-2.55	< 0.001	
	$6.0 - < 9.0^{\dagger}$	2.20	1.62-2.99	< 0.001	
	9.0 - < 12.0 [†]	3.86	2.86-5.20	< 0.001	
	$\geq 12.0^{\dagger}$	12.65	9.61-16.65	< 0.001	
Neuter status	Entire	Base			< 0.001
	Neutered [†]	2.23	1.52-3.25	< 0.001	
Insurance	Non-insured	Base			< 0.001
	Insured [†]	1.59	1.34-1.88	< 0.001	

Table 4: Results for Kennel Club (KC) breed group and adult bodyweight as risk factors for urinary incontinence diagnosis in bitches attending primary-care veterinary practices in England. These variables each individually replaced the breed variable in the original mixedeffects multivariable logistic regression modelling. *CI confidence interval. [†]P < 0.05.

Variable	Category	Odds	95% CI	Category P-	Variable P-
variable	Category	ratio	9570 CI	value	value
KC Breed	Not KC-	Base			< 0.001
Group	Recognised	Dase			< 0.001
	Utility	0.95	0.68-1.32	0.749	
	Toy [†]	0.69	0.50-0.95	0.025	
	Working [†]	3.07	2.29-4.11	< 0.001	
	Pastoral [†]	1.87	1.47-2.39	< 0.001	
	Gundog	1.17	0.94-1.45	0.157	
	Hound	1.33	0.93-1.91	0.113	
	Terrier	1.04	0.81-1.34	0.739	
Adult					
bodyweight	< 10.0	Base			< 0.001
(kg)					
	10.0-19.9 [†]	1.61	1.27-2.05	< 0.001	
	20.0-20.9 [†]	2.24	1.77-2.83	< 0.001	
	30.0-30.9 [†]	2.94	2.27-3.80	< 0.001	
	\geq 40.0 [†]	3.65	2.56-5.22	< 0.001	

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