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16 **Antibiotic use in first opinion equine practice in the UK. Serial point prevalence surveys in**
17 **17 practices.**

18
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24 **Summary**

25 **Background:** Monitoring antibiotic use (AMU) is a key component of antimicrobial
26 stewardship. Published data on AMU in first opinion equine practice is limited.

27 **Objectives:** To document AMU in first opinion equine practices.

28 **Study Design:** Repeated point prevalence surveys.

29 **Methods:** AMU was recorded one day every month for 12 consecutive months in 17 equine
30 practices.

31 **Results:** 252 horses were prescribed antibiotics across 2273 consultations (excluding routine
32 appointments) (11.1%; 95% CI 9.8 – 12.4%). Median number of consultations per practice
33 was 121 (IQR 112 – 159; range 27 - 303). Across 17 practices, the proportion of horses
34 receiving antibiotics varied by practice from 0% to 26.4%. Commonest indications for AMU
35 included: cellulitis (66; 26.8%), wounds (46; 18.7%), surgical prophylaxis (36; 14.6%),
36 respiratory infection (27; 11.0%) and skin infection (20; 8.1%). Commonest antibiotics
37 prescribed were potentiated sulphonamides (109; 43.6%), oxytetracycline (58; 23.2%),
38 procaine penicillin (40; 16.0%), and doxycycline (36; 14.4%). 45.0% of oxytetracycline use
39 was for surgical prophylaxis. 44.8% of procaine penicillin use was for cellulitis. 28.6% of

40 'other antimicrobial' use was for pyrexia of unknown origin. Use of antibiotics differed
41 significantly depending on the underlying diagnosis ($p < 0.001$). Median antibiotic dose rates
42 were: potentiated sulphonamides 30 mg/kg (IQR 27 – 75; range 10 – 75; $n = 96$); procaine
43 penicillin 19 mg/kg (IQR 15 – 23; range 7 – 30; $n = 35$); oxytetracycline 6 mg/kg (IQR 5 – 6;
44 range 4 – 30; $n = 55$); doxycycline 10 mg/kg (IQR 10 – 20; range 7 – 30; $n = 34$).

45 **Main Limitations:** Weight of horses were often estimated. Duration of antibiotic courses
46 was not recorded.

47 **Conclusions:** Antibiotics were prescribed in 11% of non-routine consultations. Commonest
48 indication for AMU was cellulitis. Potentiated sulphonamides, oxytetracycline and procaine
49 penicillin were the commonest prescribed drugs. Critically important antibiotic use was
50 infrequent. Dose rates varied but median values were generally appropriate.

51

52

53 **Introduction**

54

55 Antimicrobial (antibiotic) resistance (AMR) is a major health hazard that has been identified
56 by the World Health Organisation (WHO) as one of the top ten global health threats (World
57 Health Organisation 2015). Disease caused by resistant bacteria results in increased
58 severity, prolonged hospitalisation, and increased mortality risk, raising the social and
59 economic costs of the disease (World Health Organisation 2021). In simplistic terms, AMR
60 means that in the future the available antimicrobial agents might not be effective in the
61 treatment of many life-threatening bacterial infections in both humans and domestic
62 animals. The development of AMR is part of normal bacterial evolution (Lloyd and Page
63 2018), however, antimicrobial use (AMU) in humans and animals promotes the
64 development and spread of AMR (Tang *et al* 2017). The close association between animals,
65 including horses, and people provides opportunities for the transfer of resistance
66 determinants between these species (Parkhill 2022). There have been several recent
67 published studies that highlight the development and importance of AMR in horses (Chalder
68 *et al* 2020; Mercer and Davis 2019; Fonseca *et al* 2020; Isgren *et al* 2021; Marshall and
69 Marsella 2023). ~~Any AMU can lead to AMR, but the risk of AMR can change depending on~~
70 ~~the dose, duration and agent used. In view of increasing resistance to antimicrobial agents,~~
71 ~~including antibiotics, and a lack of novel agents, there has been increasing pressure for the~~

72 ~~judicious use of antibiotics to ensure that their activity is preserved.~~ The term “antimicrobial
73 stewardship” (AMS) is used to describe the multiple approaches needed to sustain the
74 efficacy of antimicrobial drugs in the face of the increasing development and spread of AMR
75 in bacterial pathogens (Prescott 2020). Antimicrobial stewardship involves a dynamic and
76 multifaceted approach of continuous improvement based on reducing, improving,
77 monitoring and evaluating the use of antimicrobials so as to preserve their future efficacy
78 and to protect human and animal health (Weese *et al* 2013; Prescott 2020). The American
79 Veterinary Medical Association identified 5 core principles of AMS, including commitment to
80 stewardship, selection and use of antimicrobial drugs judiciously, and evaluation of
81 antimicrobial drug use in practices (American Veterinary Medical Association 2015).
82 Measurement of AMU is an essential step in improving prescribing practices. Antibiotic drug
83 use data are used to describe baseline practices, identify opportunities for improvement,
84 guide goal setting, and measure progress (Hsieh *et al* 2022). Several veterinary AMS
85 programmes with different interventions have now been shown to have a positive influence
86 on antimicrobial use in small animal practice (Singleton *et al* 2021).

87 There have been few published studies documenting AMU in horses. The Veterinary
88 Antimicrobial Resistance and Sales Surveillance (VARSS) report, which is published annually
89 by the Veterinary Medicines Directorate (VMD) in the UK, uses information provided by
90 veterinary pharmaceutical companies to report sales data for animals (UK-VARSS 2022).
91 However, these data do not include the use of antibiotic preparations licensed for use in a
92 different species (including humans) or extemporaneous preparations, which are commonly
93 used in horses (Bladon *et al* 2023). The VARSS report also provides no data on the
94 indications for AMU. Other previously published studies of AMU in horses include
95 practitioner survey data (Hughes *et al* 2013; Wilson *et al* 2022), evaluation of electronic
96 patient records (Ross *et al* 2016; Bollig *et al* 2021; Rule *et al* 2021; Allen *et al* 2022; Bladon *et al*
97 *et al* 2023) and analysis of practice antimicrobial sales data (Mair and Parkin 2022). In addition,
98 antibiotic use in the specific case of limb wounds in one UK referral hospital has been
99 documented (Ross *et al* 2016).

100 The objectives of this study were to record AMU in a group of first opinion ambulatory
101 equine practices in the UK. This was achieved by aggregating data from monthly single-day

102 point prevalence surveys over the course of 1 year. The study aimed to provide detailed and
103 accurate data about the most commonly used drugs, the indications and the dose rates of
104 prescribed antibiotics in equine general first opinion practices.

105 **Materials and Methods**

106 Systemic AMU was recorded on one day every month for 12 months (August 2021 to July
107 2022) in 17 first opinion equine practices, all part of the CVS Equine Group. Sixteen practices
108 were located in England and one in Wales. The day of the week selected for data collection
109 was rotated each month, avoiding data collection at weekends or on public holidays. The
110 day of data collection was determined prospectively, and clinicians were aware of the study
111 and the days selected. On each selected day, the number of non-routine consultations (i.e.
112 consultations for ill-health, and excluding routine consultations such as for vaccinations or
113 routine dental examinations) were recorded. For every horse prescribed an antibiotic on the
114 selected days (including repeat prescriptions), demographic data (age, breed, sex), weight
115 (estimated by the attending veterinarian), clinical diagnosis, details of antimicrobial
116 susceptibility testing (AST) if performed, and antimicrobial drugs prescribed (including name
117 of antimicrobial drug(s), dose and dose rate, route and frequency of administration) were
118 recorded.

119 Data were entered and organized in Microsoft Excel for Mac version 16.66.1 and analyses
120 were performed using Excel and Stata 17.0. Descriptive data were presented, and missing
121 data were excluded. Categorical data were presented showing the count and percentage.
122 Quantitative data were assessed for normality using the Shapiro-Wilk test and graphically.
123 Normally distributed data were summarised using the mean (standard deviation [SD]) and
124 non-normally distributed data using the median (interquartile range [IQR] and range).
125 Univariable categorical comparisons were made using chi-squared tests. Prevalence and
126 corresponding 95% confidence intervals (CI) derived from the standard errors were
127 reported.

128

129 **Results**

130 Overall, 252 horses were prescribed antibiotics in 2273 non-routine consultations (11.1%;
131 95% CI 9.8 – 12.4%). The median number of consultations per practice was 121 (IQR 112 –
132 159; range 27 - 303). Across the 17 first opinion practices, the proportion of horses receiving

133 antibiotics varied by practice from 0.0% (practice 15) to 26.4% (practice 4) (Table 1). The
134 median practice prevalence of antibiotic prescriptions was 9.4% (95% CI 6.6 – 12.6%). The
135 seasonal prevalence of antimicrobial prescriptions across the year is shown in Table 2 and
136 Figure 1. There was no demonstrable pattern to antibiotic prescriptions over the study 12
137 months.

138 The most common breeds receiving antibiotics were: Thoroughbreds / crosses (75; 31.3%);
139 warmblood crosses (40; 16.7%); cobs / crosses (38; 15.8%); sport horses / crosses (30;
140 12.5%); and ponies / crosses (27; 11.3%). The horses prescribed antibiotics included 84
141 females (34.6%), 131 geldings (53.9%) and 28 entire males (11.5%). The median age was 10
142 years (IQR 5 – 16; range 0.7 – 32). The median estimated weight was 500kg (IQR 450 – 550;
143 range 37 – 650kg).

144 The most frequent diagnostic categories for horses prescribed antibiotics were cellulitis (66;
145 26.8%), wounds (46; 18.7%), surgical prophylaxis (36; 14.6%), respiratory disease (27;
146 11.0%), and skin disease (20; 8.1%) (Figure 2). Skin wounds and wounds potentially involving
147 bone and/or synovial cavities accounted for 23.2% of antibiotic prescriptions. The most
148 commonly prescribed antibiotics were potentiated sulphonamides (trimethoprim /
149 sulphadiazine) (109; 43.6%), oxytetracycline (58; 23.2%), procaine penicillin (40; 16.0%), and
150 doxycycline (36; 14.4%). Metronidazole, ceftiofur, enrofloxacin and gentamicin each
151 accounted for less than 1% of antibiotic prescriptions (Figure 3). A single dose of an
152 antibiotic followed by dosing with a different second antibiotic was administered in 39 cases
153 (15.7%). The route of administration of the antibiotics in the 252 horses were *per os* (141;
154 56.6%), intravenous (63; 25.3%), and intramuscular (45; 18.1%).

155
156 The distribution of the different antimicrobial drugs used to treat different conditions is
157 shown in Figure 4. Surgical prophylaxis accounted for 45.0% of oxytetracycline use. Cellulitis
158 accounted for 44.8% of procaine penicillin use. Pyrexia of unknown origin accounted for
159 28.6% of 'other antimicrobials' (excluding trimethoprim / sulphadiazine, oxytetracycline,
160 procaine penicillin and doxycycline) use. The use of each antibiotic differed significantly
161 depending on the underlying diagnosis ($p < 0.001$). Antibiotic susceptibility testing results
162 were obtained prior to antimicrobial prescription in only 4 cases (2%).

163 The median antibiotic dose rates are shown In Table 3.

164 - A second antimicrobial was prescribed in 51 cases, and 36% of the cases where a
165 second antimicrobial was used were cellulitis cases (Figure 5).

166

167 **Discussion**

168 Our study successfully used a repeated point prevalence survey method to record antibiotic
169 use in first opinion equine practice. The most prescribed antibiotics were potentiated
170 sulphonamides oxytetracycline, procaine penicillin and doxycycline. To the authors'
171 knowledge, this is the largest study to record accurate AMU data in first opinion equine
172 practice using serial point prevalence surveys. Similar methodology could be readily applied
173 to future studies of antibiotic use in all species. Another benefit of the repeated point
174 prevalence approach is the relatively limited imposition on staff around data collection
175 compared to longer collection timeframes. Bollig and colleagues (2022) reported a point
176 prevalence study, and collected antibiotic prescription data from electronic patient records
177 from dogs, cats and horses in veterinary practices in Minnesota and Dakota, USA, but this
178 was limited to one day per quarter for one year, and included only 3 exclusively equine
179 practices and 3 mixed small animal /equine practices. We are not aware of other published
180 studies using a point prevalence methodology in equine practice. Surveillance of AMU is
181 essential for benchmarking performance and identifying opportunities for improvement
182 (Allen *et al* 2022). This study has provided novel data on AMU in first opinion equine
183 veterinary practices in the UK that can be used to inform AMS programmes and set
184 priorities for surveillance. The optimum way of reporting antibiotic usage remains unclear,
185 but the point prevalence survey methodology used in this study provided valuable patient-
186 level surveillance data, including the indications, choice, dosing and routes of AMU. The
187 main limitation of point prevalence surveys is inherent to the method used, namely the
188 interpretation of single point data. However, this methodology has been widely used in
189 human healthcare, for example to identify priorities for quality improvement strategies to
190 reduce hospital acquired infections (Davey *et al* 2010).

191 Antibiotics were prescribed in 11.1% of non-routine consultations in this study. This
192 compares with 8.5 % of 39,483 total visits in a retrospective, observational study using
193 electronic patient records in an ambulatory equine practice of a university veterinary

194 practice in the mid-Atlantic United States (Rule et al 2021); however, the latter study
195 included both routine and non-routine consultations, with “healthy visits” accounting for
196 41.7% of all visits. Antimicrobial prescriptions were recorded in 30.2 % of emergency visits
197 and 7.9 % of non-emergency visits in that study. The study of Bollig *et al* (2022) from the
198 USA recorded only 202 equine consultations (including routine consultations and
199 hospitalised patients), of which 33 (16.3%) were prescribed antibiotics (9 of which were
200 topical preparations); of 183 outpatient consultations, only 14 (7.7%) were prescribed
201 antibiotics.

202 Allen *et al* (2022) used electronic patient records of horses in 39 UK veterinary practices to
203 record the use of antibiotics licensed for systemic use during 2018. Antimicrobials were
204 prescribed to 12 538 (19.5%) equids in that study, which was higher than in our study.
205 However, it is difficult to compare different studies that use different methodologies, and
206 like our results, the proportion of equids receiving systemic antimicrobials in the study of
207 Allen *et al* (2022) varied considerably in different practices from 3.0% to 33.5%. However,
208 the study included 6 equine hospitals, and equids attended by an equine veterinary hospital
209 had 1.9 times the odds of systemic AMU compared with those attended by a veterinary
210 practice without hospital status. Differences between practices likely reflect differences in
211 underlying case demographics, caseload, provision of and adherence to practice guidelines
212 and individual clinician habits (Allen *et al* 2022). The results of our study, as well as others,
213 suggest that antibiotics are prescribed less frequently in horses in first opinion practice than
214 in small animals. For example, the frequency of antimicrobial use in first opinion small
215 animal consultations in the UK was reported to be 25 % in dogs and 21 % in cats in one
216 study (Buckland *et al* 2016).

217 The most prescribed antibiotics in our study were potentiated sulphonamides (43.6%),
218 oxytetracycline (23.2%), procaine penicillin (16.0%), and doxycycline (14.4%). Potentiated
219 sulphonamides have been identified as the most commonly prescribed antimicrobial drugs
220 in other studies documenting antimicrobial use in horses in the UK (Hughes *et al* 2013; Allen
221 *et al* 2022; Mair and Parkin 2022; Wilson *et al* 2022; Bladon *et al* 2023). For example, in the
222 study of Bladon *et al* (2023), potentiated sulphonamides represented 79% of all used
223 antibiotics by weight, and in the study of Allen *et al* (2022) potentiated sulphonamides were

224 given to 50.2% of the equids receiving antibiotics. The frequent choice of potentiated
225 sulphonamides in equine practice is likely, at least partially, to be due to its broad spectrum,
226 ease of administration and relatively low cost. In the study by Allen *et al* (2022), Category B
227 antimicrobials (based on the European Medicines Agency classification (European Medicines
228 Agency 2019)) were prescribed to 1.9% of veterinary-attended equids, with third generation
229 cephalosporins and quinolones the most frequently prescribed antimicrobial classes in this
230 group. These results are similar to our study, where antimicrobials classified under the
231 European Medicines Agency as Category B (enrofloxacin and ceftiofur) were each used in
232 less than 1% of prescriptions. Since this study was performed, cefazolin (a first generation
233 cephalosporin) has become available in the UK, as a “special” product, which may be used in
234 the place of ceftiofur in some cases in the future. Other drugs considered to be important
235 for human healthcare include aminoglycosides and aminopenicillins, but none of these
236 drugs were used in the present study. Bacteriological culture and AST was performed in only
237 one horse prior to prescription of one of these drugs. This contravenes guidelines and
238 recommendations, produced by the World Organisation for Animal Health (OIE), World
239 Health Organisation and British Equine Veterinary Association, which suggest that highest-
240 priority critically important antimicrobials should only be used with supporting culture and
241 sensitivity testing (BEVA 2019). However, it is acknowledged that it is not always possible to
242 obtain samples for culture and sensitivity in cases of PUO and cellulitis.

243 In the study of Rule *et al* (2021) from the USA, aminoglycosides were the most frequently
244 prescribed antimicrobials (20.3 %), followed by potentiated sulphonamides (20.2 %) and
245 tetracyclines (18.3 %). However, that study included topical (e.g. ocular) and local (e.g. intra-
246 synovial, intra-uterine, etc) administration of antimicrobials, with the commonest
247 indications for AMU being ocular conditions; these results cannot, therefore, be directly
248 compared with our study of systemic antimicrobial use only. In the study of Bollig *et al*
249 (2022), also in the USA, the most commonly prescribed antibiotic in horses was ceftiofur, a
250 third-generation cephalosporin that is considered a highest priority critically important
251 antimicrobial. Ceftiofur’s broad spectrum activity and safety profile make it a versatile
252 agent for the treatment of horses, including the treatment of respiratory infections, skin
253 infections, abscesses, urinary tract diseases and sepsis (Hardefeltd *et al* 2021; Ryan *et al*
254 2023). Ceftiofur crystalline free acid, that is available in the USA, provides a long-acting

255 intramuscular option; however, this formulation is not available in the UK. As stated
256 previously, the recent introduction of cefalozin in the UK under the “specials” import
257 scheme might alter the perceived need to use ceftiofur in cases supported by bacteriological
258 culture and AST.

259 The most common specific indications for systemic AMU in our study were cellulitis (26.8%),
260 wounds (18.7%), surgical prophylaxis (14.6%), respiratory infection (11.0%), and skin
261 infection (8.1%). These results are somewhat different to the results of the study of Allen *et al*
262 *al* (2022) where integumentary disorders (40.5% of antimicrobial courses), surgical
263 prophylaxis (29.0%) and musculoskeletal conditions (22.8%) were the commonest reasons
264 for AMU. However, this latter study included local use of antimicrobials licensed for
265 systemic use, which likely explains some of the differences in the results, for example the
266 higher frequency of AMU for musculoskeletal conditions reported by Allen *et al* (2022);
267 antimicrobial drugs are commonly employed locally in the uterus, eyes, joints, tendon
268 sheaths, etc, in equine practice, often unassociated with systemic use, and these uses were
269 not recorded in the present study. Our results were also different from those of Bollig *et al*
270 (2022), where ocular, respiratory, skin, and orthopaedic diseases were the commonest
271 indications for antibiotic use, but this included topical and local as well as systemic
272 treatments, and included hospitalised horses.

273 Only 4 prescriptions in our study followed bacterial culture and AST. The ability to perform
274 diagnostics in the field is often limited by cost, logistics, facilities and other factors.
275 Therefore, a definitive diagnosis is not always made, and empirical treatment is commonly
276 pursued. Veterinarians have previously identified cost of culture and sensitivity testing and
277 lack of rapid diagnostic tests as barriers to appropriate AMU (Rule *et al* 2021). The finding
278 that bacteriological culture was not commonly used to support antimicrobial selection in
279 our study agrees with the results of other published studies (Hughes *et al* 2013; Welsh *et al*
280 2017; Rule *et al* 2021).

281 This study documented dose rates for the antimicrobials which has not been accomplished
282 in other published studies of antimicrobial use in horses in first opinion equine practice.
283 Bladon *et al* 2023 recorded antibiotic usage in 14 equine veterinary practices (both hospital
284 and ambulatory practices) using one specific practice management software over a ten-year

285 period (2012-2021). No distinction between systemic administration and local
286 administration of the antibiotics was possible in this study. The study of Bladon *et al* (2023)
287 study used an average weight to calculate dose rates, but this will have led to inaccuracies in
288 the results since weights of animals are not consistently recorded in the electronic patient
289 records. Estimating the weight of each horse prescribed an antibiotic in the current study
290 allowed more accurate dose rates calculations for the antibiotics to be recorded. The
291 median dose rate recorded for the trimethoprim / sulphadiazine (39 mg/kg) and doxycycline
292 (10 mg/kg) matched the recommended dose rates listed in the BEVA Protect-ME toolkit
293 (BEVA 2019). However, the median dose rates for oxytetracycline (6 mg/kg) and procaine
294 penicillin (19 mg/kg) were lower than current recommendations (6.6 mg/kg and 22 mg/kg
295 respectively) (Hardefeldt *et al* 2021). Wide variations in dose rates in individual patients
296 were also identified, which highlights an issue that requires further work and improvement.
297 Inappropriate dose rates of antimicrobials are a known factor that contributes to the
298 development of AMR (Lloyd and Page 2018).

299 There were several limitations of this study. The point prevalence surveys required manual
300 input of data from the veterinary practices. Ultimately, automated data input from
301 electronic patient records should permit easier collection of AMU in equine practices, but
302 this requires accurate recording of clinical and demographic data, which is currently limited
303 in most practice management system records. The further development of equine
304 veterinary disease surveillance initiatives such as EVSNET
305 (<https://www.liverpool.ac.uk/evsnet/>) and Equine VetCompass
306 ([https://www.rvc.ac.uk/vetcompass/research-projects-and-](https://www.rvc.ac.uk/vetcompass/research-projects-and-opportunities/projects/vetcompass-equine)
307 [opportunities/projects/vetcompass-equine](https://www.rvc.ac.uk/vetcompass/research-projects-and-opportunities/projects/vetcompass-equine)) should ultimately provide increased
308 opportunities to record and monitor AMU at the individual practice level.

309 The collaborating veterinary practices in our study represented a convenience sample of UK
310 equine practices (all practices were part of the CVS Equine Group) which may have
311 introduced some selection bias, due to availability of different drug preparations within the
312 corporate group; however, this was considered to be negligible. In addition, the duration of
313 antimicrobial therapy was not recorded in this study; this is likely to be another important
314 factor that may contribute to the development of AMR. The primary goal of the study was

315 to understand antibiotic prescribing rates and common indications in first opinion equine
316 veterinary practices. Given the study design, clinical outcomes could not be determined
317 from this data set. Additionally, while indications for prescriptions of antibiotics were
318 recorded, diagnosis was not recorded for animals that did not receive a prescription of
319 antibiotics. This precluded us from reporting on the rates of antibiotic prescribing for
320 specific conditions; this should be a goal of future studies. Finally, the results of this study
321 cannot be extrapolated to all equine first opinion practices in view of the highly variable
322 populations of horses in different practices.

323 Despite the limitations of this study, our results are useful in establishing baseline rates that
324 can subsequently be used to assess the success of antimicrobial stewardship initiatives.
325 Documenting antimicrobial use is a fundamental step towards gauging appropriateness of
326 use and developing stewardship policies. Analysis of AMU data also allows for comparison
327 of antimicrobial prescribing patterns between practices, which can be used to assess
328 stewardship strategies.

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