

Determinants of antimicrobial use practices among veterinary clinicians at The University of Tennessee Veterinary Medical Center

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Background. Antimicrobial drugs in veterinary medical practice are primarily prescribed for the purposes of maintaining or improving health and increasing productivity. However, their value is being eroded by antimicrobial resistance (AMR). Indiscriminate use of antimicrobial drugs is suggested as one of the modifiable factors contributing to the development of AMR. To reduce indiscriminate use and to improve antimicrobial use, veterinary practices are encouraged to adopt good stewardship practices. Therefore, the objectives of this study were: to identify factors influencing clinician decisions to begin using antimicrobials as well as the choice of antimicrobials used at The University of Tennessee Veterinary Medical Center (UTVMC); to evaluate the practices, perceptions, opinions and concerns of veterinary clinicians at UTVMC concerning antimicrobial use, antimicrobial stewardship, and AMR.

Methods. This study's protocol was approved by the University of Tennessee Knoxville IRB for the Protection of Human Subjects in Research. Survey software was used to send a questionnaire to 121 eligible participants, where all were UTVMC faculty with clinical appointments and house officers. Cumulative logit models were fitted to investigate associations between categorical explanatory variables and ordinal response variables.

Results. A response rate of 51.24% was achieved. Of the 62 respondents, 47 (75.81%) reported that bacteriological culture and antimicrobial susceptibility test results were extremely important in their antimicrobial prescription decision-making. Thirty-two (51.61%) respondents believed antimicrobials are being over-prescribed. The cephalosporin class was the most preferred antimicrobial class, while the lincosamide class was the least preferred. From the multivariable cumulative logit model, year of graduation from veterinary school ($P = 0.034$) and clinicians' primary patient load ($P = 0.009$) were significantly associated with clinicians' degree of concern about AMR.

Conclusions and clinical relevance. The findings suggest a need for more awareness about AMR among veterinary clinicians. Improvements in antimicrobial stewardship are needed, especially among veterinary clinicians who graduated after 1999. Educational practices that target modification of antimicrobial prescription practices of veterinary clinicians would likely improve a Good Stewardship Practice (GSP) mindset. GSP is important in prolonging the efficacy of currently available antimicrobial drugs.

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2 **of Tennessee Veterinary Medical Center**

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24 **Abstract**

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27 being eroded by antimicrobial resistance (AMR). Indiscriminate use of antimicrobial drugs is
28 suggested as one of the modifiable factors contributing to the development of AMR. To reduce
29 indiscriminate use and to improve antimicrobial use, veterinary practices are encouraged to adopt
30 good stewardship practices. Therefore, the objectives of this study were: to identify factors
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34 concerning antimicrobial use, antimicrobial stewardship, and AMR.

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38 appointments and house officers. Cumulative logit models were fitted to investigate associations
39 between categorical explanatory variables and ordinal response variables.

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42 in their antimicrobial prescription decision-making. Thirty-two (51.61%) respondents believed
43 antimicrobials are being over-prescribed. The cephalosporin class was the most preferred
44 antimicrobial class, while the lincosamide class was the least preferred. From the multivariable
45 cumulative logit model, year of graduation from veterinary school ($P = 0.034$) and clinicians'

46 primary patient load ($P = 0.009$) were significantly associated with clinicians' degree of concern
47 about AMR.

48 **Conclusions and clinical relevance.** The findings suggest a need for more awareness about
49 AMR among veterinary clinicians. Improvements in antimicrobial stewardship are needed,
50 especially among veterinary clinicians who graduated after 1999. Educational practices that
51 target modification of antimicrobial prescription practices of veterinary clinicians would likely
52 improve a Good Stewardship Practice (GSP) mindset. GSP is important in prolonging the
53 efficacy of currently available antimicrobial drugs.

54

55 **Introduction**

56 Antimicrobial drugs in veterinary medical practice are primarily prescribed for the
57 purposes of maintaining or improving health and increasing productivity (Marshall & Levy
58 2011). However, the emergence and spread of antimicrobial resistant microorganisms is eroding
59 the value of antimicrobial drugs (Dyar et al. 2016; Guardabassi & Prescott 2015). Although
60 antimicrobial resistance (AMR) is an ancient phenomenon (D'costa et al. 2011; Perry et al.
61 2016), indiscriminate use of antimicrobials has been suggested as one of the modifiable factors
62 contributing to the development of AMR. The increase in the prevalence of microorganisms
63 resistant to antimicrobials is now widely attributed to indiscriminate use, both in veterinary
64 medicine and in human medicine (De Briyne et al. 2013; Holmes et al. 2016).

65 Recent studies (Marshall & Levy 2011) have shown that indiscriminate use of
66 antimicrobials for both therapeutic and non-therapeutic use in animals leads to propagation and
67 shedding of substantial amounts of antimicrobial resistant microorganisms. It is now widely

68 known shedding of drug resistant microorganisms by animals leads to human infections through
69 direct contact or indirectly through colonization of humans by commensals, which may carry
70 transferable resistance genes across species through multiple pathways like food, water, airborne
71 particulate matter, and sludge and manure applications to food crop soils (Chung et al. 2017;
72 Marshall & Levy 2011; McEachran et al. 2015; Van Boeckel et al. 2015). Multi-drug resistant
73 infections exert a huge burden on veterinary medical care (Kuzi et al. 2016) and pose public
74 health risks (Walther et al. 2017; Weese et al. 2015). To reduce indiscriminate use and to
75 improve antimicrobial use, veterinary practices are encouraged (Prescott & Boerlin 2016; Weese
76 2006) to adopt good stewardship practices, such as effective infection control, bacteriologic
77 culture and antimicrobial susceptibility testing, and the use of individual practice guidelines for
78 antimicrobial stewardship.

79 Research conducted in a veterinary teaching hospital in the U.S. suggests clinicians are
80 frequently prescribing antimicrobials without proper documentation in medical records or
81 without indicating their use (Wayne et al. 2011). Veterinarians in another U.S. veterinary
82 teaching hospital believed antimicrobials were over-prescribed in veterinary practice. The
83 veterinarians in that hospital (Jacob et al. 2015) were concerned about AMR and supported the
84 idea of restricting the use of certain antimicrobial classes in companion animals. Prior to this
85 study, the factors that influenced University of Tennessee Veterinary Medical Center (UTVMC)
86 clinicians to start, delay, or discontinue the use of antimicrobials and/or to determine the class of
87 antimicrobials used were unknown. The perceptions, opinions, and concerns of UTVMC
88 veterinary clinicians in relation to antimicrobial use, antimicrobial stewardship, and AMR were
89 unknown and thus undocumented. Additionally, the association between the effort allocation to

90 veterinary clinical practice and the frequency of antimicrobial prescriptions for therapeutic
91 treatment of infectious diseases had not been explored.

92 The objectives of this study were to identify the factors that influence UTVMC clinicians
93 to begin using antimicrobials, to analyze the clinicians' preferential choices of antimicrobials,
94 and to evaluate the perceptions, opinions, and concerns of veterinary clinicians regarding
95 antimicrobial use, antimicrobial stewardship, and AMR. These findings will be beneficial in
96 improving antimicrobial stewardship and educational training on judicious use of antimicrobials.
97 Ultimately, these efforts could prolong the efficacy of current antimicrobials and reduce the
98 burden of AMR within veterinary medicine and public health.

99 **Materials and Methods**

100 **Study design and administration of survey**

101 This study's protocol was approved by the University of Tennessee Knoxville
102 Institutional Review Board for the Protection of Human Subjects in Research (UTK IRB-16-
103 02956-XP). The survey questionnaire was developed, and validated by four professionals with
104 expertise in survey research. Next, the survey questionnaire was pre-tested among 4 veterinary
105 clinicians at UTVMC. Comments from the pretest were addressed to improve questionnaire
106 clarity. The survey software (Qualtrics software, January–March 2017, Provo, UT) was set to
107 record responses in progress after each respondent began the survey, allowing respondents to
108 pause and return to the survey as time permitted. The anonymize function in the survey software
109 was optimized, so responses were not attached to any personal identifiers. Adjustments were
110 made to adapt the survey for computer, tablets, and cell phone responses. The updated survey
111 was tested to assess and adjust the functionality of the survey software settings.

112 The survey had 36 questions programmed to capture the respondent’s demographics and
113 their antimicrobial prescription practices, perceptions, opinions, and concerns about
114 antimicrobial use, antimicrobial stewardship, and AMR. Questions regarding demographic
115 information included the nature of their clinical position (faculty versus house officers), the
116 primary type of patients seen (small animal, food animal, equine, etc.), whether they had
117 specialty board certification, where their veterinary degree was obtained (U.S. versus non-U.S.),
118 their total number of years in clinical practice from time of graduation, and their year of
119 graduation from veterinary school. This demographic information was treated as explanatory
120 variables in the analysis. Frequency of antimicrobial prescription and the degree of concern
121 about antimicrobial resistant infections were the main outcomes of interest. Ordinal Likert scales
122 were mostly used to capture participant responses to questions relating to perceptions about
123 antimicrobial use practices.

124 The email addresses of 121 eligible participants, including all faculty with clinical
125 appointments, residents, and interns at UTVMC, were entered into the survey software. To
126 increase response rate, the eligible participants were notified about the study during departmental
127 meetings a week before the study’s start date. Another email reminder was delivered to all 121
128 potential respondents an hour before the survey invitations were sent.

129 The invitation to participate contained information about the rationale and objectives of
130 the study. Respondents were required to “accept” or “decline” giving their consent to participate,
131 and no incentive was provided for participation or completion. The survey was designed to be
132 completed in 20 minutes or less, set to accept only one response from each respondent, and
133 remained open for 6 weeks (January 27, 2017 through March 10, 2017). Weekly follow-up email

134 reminders were sent out to non-respondents, and a thank you message was sent to all respondents
135 at the end of the study.

136

137 **Statistical analysis**

138 Descriptive and inferential analyses was completed using commercial statistical software
139 (SAS, version 9.4, SAS Institute Inc, Cary, NC). Descriptive statistics (frequencies, proportions,
140 and median) were used to summarize the data. Side-by-side bar charts and stacked bar charts for
141 responses on the three-point scales and on the Likert scales were created using another
142 commercial software (Tableau software, version 8.2, Seattle, WA). Missing data was treated as
143 such. Antimicrobial drugs were ranked from most to least used and were grouped by name into
144 similar classes as described previously (Green et al. 2010; Jacob et al. 2015). The commonly
145 prescribed antimicrobial drugs were grouped into medically important antimicrobial classes as
146 grouped by the United States Food and Drug Administration (FDA 2015).

147 Spearman's rank correlation (PROC CORR) was used to evaluate for correlations
148 between two ranked variables: for example, the proportion of total professional activity
149 dedicated to clinical practice (effort allocation to clinical practice) and the frequency of
150 prescription of antimicrobials for therapeutic purposes. Cumulative logit models were fitted to
151 assess the association between various predictors and several outcomes. The probabilities
152 modeled were cumulated over the lower ordered values as previously described (Agresti 2006).
153 Number of years in clinical practice (clinical experience) was treated as quantitative by assigning
154 scores to its categories. For categorical explanatory variables, both univariable and multivariable
155 analyses (PROC LOGISTIC) were performed.

156 Based on the univariable analyses, potential predictors at a $P \leq 0.10$ were considered for
157 inclusion in the multivariable analyses. However, for two predictor variables (number of years in
158 clinical practice from the time of graduation from veterinary school and year of graduation from
159 veterinary school) measuring a similar characteristic, only one variable (year of graduation from
160 veterinary school) was used in the multivariable model building. The multivariable cumulative
161 logit model was fitted using manual backwards elimination with the ordinal response variable—
162 clinicians' degree of concern about AMR—as the outcome. At the multivariable step of model
163 building, statistical significance was assessed at $P = 0.05$.

164 A high-performance procedure (PROC HPLOGISTIC) was used to investigate the effects
165 of antimicrobial class on clinicians' frequency of prescription and to identify differences in
166 preference between classes of antimicrobials (based on comparisons between classes). During
167 the evaluation, the tetracyclines (eighth class) was set as the reference class. The probability of
168 disliking a class of antimicrobial was modelled.

169 The score test for the proportional odds assumption, deviance, and Pearson goodness-of-
170 fit statistics were used to assess the model fit. For the high-performance procedure (PROC
171 HPLOGISTIC), a plot of the empirical cumulative logit function was created to test whether the
172 proportional odds assumption held. This plot yielded approximately parallel empirical
173 cumulative logits giving visual evidence that the proportional odds model was appropriate. The
174 95% confidence intervals were utilized to test significant associations. Values of $P < 0.05$ were
175 considered significant.

176

177 **Results**

178 **Descriptive statistics**

179 Of the 121 invited participants, 62 (51.24%) responded to the survey. A few survey
180 questions were unanswered by some of the participants. The median time taken to complete the
181 survey was 9.82 minutes (range 4.2 – 10,271.47 minutes). The demographic information of the
182 participants is presented in **Table 1**. Among all the factors that influenced the choice of
183 antimicrobial drug(s) for clinical use at UTVMC, results from bacteriological culture and
184 antimicrobial susceptibility tests was the most important influencer. On the other hand, pressure
185 from clients/producers to the clinician to prescribe antimicrobials and fear of litigation by the
186 client/producer in the event of an undesirable clinical outcome were the least important
187 influencers. A detailed description of the factors influencing choice of antimicrobials for clinical
188 use is shown in **Figure 1**.

189 Regarding the sources UTVMC clinicians rely on to determine their choice of
190 antimicrobial for clinical use, peer-reviewed scientific literature, peer support by
191 clinicians/pharmacist within the hospital, peers within and outside of the hospital, and
192 textbooks/drug handbooks were the most important sources of information on antimicrobial
193 drugs. In contrast, pharmaceutical company representatives, veterinary information network
194 (VIN), and online resources were the least important sources of information for the majority of
195 clinicians. A detailed description of the sources of antimicrobial information the clinicians use to
196 make their choices on antimicrobials for clinical use is shown in **Figure 2**.

197 Frequency of prescriptions differed among the surveyed clinicians. Twenty respondents
198 (32.26%) reported prescribing antimicrobials for therapeutic purposes more than 5 times a week,
199 while 35 of 62 (56.45%) respondents reported prescribing antimicrobials for prophylactic
200 purposes (**Figure 3**). Of the 35 respondents who reported prescribing antimicrobials for

201 prophylactic purposes, 23 (65.71%) reported using antimicrobials for pre-operative surgical
202 prophylaxis, 29 (85.29%) reported prescribing antimicrobials for post-operative surgical
203 prophylaxis, and 29 (82.86%) reported using antimicrobials for peri-operative surgical
204 prophylaxis (**Figure 4**).

205 Clinicians' opinions on antimicrobial use at UTVMC differed. Although 1 respondent
206 (1.61%) thought antimicrobials at UTVMC are prescribed based only on confirmed infections,
207 21 (33.87%) thought antimicrobials are sometimes prescribed based on no documented evidence
208 of infection, 38 (61.29%) thought that antimicrobials are sometimes prescribed for suspected (but
209 not confirmed) infections, and 2 (3.23%) reported not being sure. One clinician (1.61%) believed
210 that antimicrobials are under-prescribed at UTVMC. Twenty-nine (46.77%) and 32 (51.61%)
211 respondents thought antimicrobials are optimally prescribed and over-prescribed at UTVMC,
212 respectively. In response to whether veterinarians raised on farms prescribed antimicrobials more
213 often than those not raised on farms, 10 (16.13%) respondents agreed, 35 (56.45%) neither
214 disagreed nor agreed, and 17 (27.42%) disagreed.

215 Overall, 2 (3.23%) respondents believed UTVMC had an antimicrobial stewardship
216 program; 51 (82.26%) respondents were not sure, while 9 (14.52%) thought UTVMC did not
217 have an antimicrobial stewardship program. Within the faculty cohort (n = 44), 8 (13.11%)
218 respondents believed there was no antimicrobial stewardship program at UTVMC, 34 (55.74%)
219 were not sure, and 2 (3.28%) thought that an antimicrobial stewardship program currently exists.
220 However, within the 17 house officers, 1(1.64%) respondent thought no antimicrobial
221 stewardship program existed, and 16 (26.23%) respondents were not sure. The respondent who
222 did not disclose the nature of their clinical position was also not sure of the existence of
223 antimicrobial stewardship program at UTVMC. Of the 9 respondents who reported no

224 antimicrobial stewardship program currently existing, 2 (22.22%) did not think UTVMC should
225 develop and implement an antimicrobial stewardship program, while 7 (77.78%) thought the
226 opposite.

227 Regarding the respondents' familiarity with Veterinarian Client Patient Relationship
228 (VCPR), 3 (4.84%) were not familiar at all, 9 (14.52%) were moderately familiar, 17 (27.42%)
229 were very familiar, 33 (53.23%) were extremely familiar. A comparison of the level of
230 familiarity with the VCPR between faculty with clinical appointment and house officers is
231 shown in **Figure 5**. Overall, 10 (16.13%) reported that they never utilize VCPR in their
232 antimicrobial prescription practice, 3 (4.84%) rarely used VCPR, 4 (6.45%) sometimes utilized
233 VCPR, 10 (16.13%) often utilized VCPR, and 35 respondents (56.45%) always utilized VCPR
234 in their antimicrobial prescription practice. A comparison of the use of VCPR in antimicrobial
235 prescription practice of respondents based on the nature of clinical position is shown in **Figure 6**.

236 For responses to the question about the extent to which their veterinary medical training
237 alone adequately equipped them with knowledge on rational use of antimicrobials, one clinician
238 (1.61%) responded "not at all," 3 (4.84%) responded "a little," 22 (35.48%) responded
239 "somewhat," 28 (45.16%) responded "quite a bit," and 8 (12.9%) responded "very much." One
240 clinician (1.61%) responded that present-day veterinary medical students do not receive any
241 adequate training on rational use of antimicrobials, 9 (14.75%) responded "a little," 28 (45.90%)
242 responded "somewhat," 21 (34.43%) responded "quite a bit," and 2 (3.28%) responded "very
243 much."

244 Seventeen (27.42%) clinicians have never read the United States Food and Drug
245 Administration (FDA) / American Veterinary Medical Association (AVMA) guidelines for
246 judicious use of antimicrobials, 19 (30.65%) rarely read the guidelines, 20 (32.26%) sometimes

247 do, and 6 (9.68%) very often read the guidelines. In rating other veterinarians' concerns about
248 AMR, 18 clinicians (29.03%) thought other veterinarians were slightly concerned about AMR,
249 36 (58.06%) believed that others were moderately concerned, 5 (8.06%) reported that others
250 were quite concerned, and 3 (4.84%) thought others were very concerned. With respect to their
251 clients' concern about AMR, 27 clinicians (43.55%) thought their clients were not concerned, 25
252 (40.32%) believed they were slightly concerned, 8 (12.9%) thought the clients were moderately
253 concerned, and 2 (3.23%) believed they were quite concerned.

254 Twelve respondents (19.35%) strongly disagreed with the statement "antimicrobial
255 classes commonly used in human medicine should not be used in veterinary medicine because
256 their use in veterinary medicine selects for AMR in microbes affecting humans." Thirty-two
257 (51.61%) disagreed with this statement, 11 (17.74%) neither disagreed nor agreed, and 7
258 (11.29%) agreed with this statement.

259 For the statement "antimicrobial drug use in veterinary practice may lead to AMR in
260 pathogens affecting humans," 1 (1.61%) strongly disagreed, 8 (12.9%) disagreed, 17 (27.42%)
261 neither disagreed nor agreed, 24 (38.71%) agreed, and 12 (19.35%) strongly agreed. One
262 respondent (1.61%) was not concerned about antimicrobial resistant infections. Two (3.23%)
263 were slightly concerned; 27(43.55%) were moderately concerned. Nineteen respondents
264 (30.65%) were quite concerned, and 13 (20.97%) were very concerned about antimicrobial-
265 resistant infections.

266

267 **Univariable analyses**

268 There was a weak positive correlation ($r = 0.20211$, $P = 0.1152$) between proportion of
269 total professional activity dedicated to clinical practice (effort allocation to clinical practice) and

270 frequency of prescription of antimicrobials for therapeutic treatment of infectious diseases.
271 Likewise, there was a very weak positive correlation ($r = 0.1654$, $P = 0.1989$) between period of
272 graduation from veterinary school and frequency of prescription of antimicrobials for therapeutic
273 treatment of infectious diseases.

274 At this hospital, cephalosporin class was the most preferred antimicrobial class followed
275 by penicillins, while the lincosamides class was least preferred. The tetracycline class was more
276 preferred when compared to the aminoglycosides class. Similarly, the fluoroquinolones,
277 lincosamides, macrolides, and sulfas classes were less favorable than the tetracycline class ($P <$
278 0.05). The preferential ordering of the medically important antimicrobial classes based on the
279 frequency of prescriptions was as follows: cephalosporins > penicillins > tetracyclines >
280 fluoroquinolones > sulfas > aminoglycosides > macrolides > lincosamides (**Table 2**).

281 There was a significant association between the number of years in clinical practice
282 (clinical experience) and the degree of concern about antimicrobial resistant infections. The odds
283 of being at a low end of the degree of concern scale decreased as number of years in clinical
284 practice (clinical experience) increased. The estimated odds of the degree of concern about
285 antimicrobial resistant infections being below any given level (instead of above it) multiplied by
286 0.95 (OR = 0.95 ; 95% CI, 0.91 to 0.99 ; $P = 0.018$). Number of years in clinical practice and year
287 of graduation from veterinary school were highly correlated ($r = 0.915$, $P < 0.001$). Of the two,
288 the year of graduation was included in the multivariable model building because of ease in
289 interpretation.

290 Results from the univariable analyses for associations between various categorical
291 predictors and clinicians' degree of concern about antimicrobial resistant infections is presented
292 in **Table 3**. No significant association ($P = 0.307$) was found between gender and the degree of

293 concern for antimicrobial resistant infections. For male clinicians, the estimated odds that the
294 response was below any particular level of concern (instead of above it) were 1.01 times the
295 estimated odds for female clinicians. A significant association ($P = 0.043$) was found between
296 the nature of clinical position and the degree of concern about AMR. For house officers, the
297 estimated odds that the response was below any particular level of concern were 3.19 times the
298 estimated odds for faculty with clinical appointments. House officers were more likely to be less
299 concerned when compared to faculty with clinical appointments.

300 Year of graduation from veterinary school was significantly associated ($P = 0.040$) with
301 the degree of concern about antimicrobial resistant infections. For clinicians who graduated from
302 2000–2009, the estimated odds that the response was below any particular level of concern were
303 2.83 times the estimated odds for those who graduated from 1970–1999. For clinicians who
304 graduated from 2010–2016, the estimated odds that the response was below any particular level
305 of concern were 4.55 times the estimated odds for those who graduated from 1970–1999.
306 Clinicians who graduated after 1999 tended to be less concerned about AMR when compared to
307 those who graduated from 1970–1999.

308 Where veterinary degree was obtained was not significantly associated ($P = 0.343$) with
309 the degree of concern about antimicrobial resistant infections. However, for participants who
310 obtained their veterinary degree from a US veterinary school, the estimated odds that the
311 response was below any particular level of concern were 1.788 times the estimated odds for
312 those who obtained their veterinary degree from outside the US. Specialty board certification
313 was not significantly associated ($P = 0.054$) with the degree of concern about antimicrobial
314 resistant infections. For participants without specialty board certification, the estimated odds that

315 the response was below any particular level of concern were 2.84 times the estimated odds for
316 those with board certification.

317 Primary patient load was not significantly associated ($P = 0.067$) with the degree of
318 concern about antimicrobial resistant infections. For participants whose primary patient load
319 involved other animal species (equine, food animal, mixed animal, exotics, all large-equine, and
320 food animal), the estimated odds that the response was below any particular level of concern
321 were 2.47 times the estimated odds for small animal clinicians. Participants whose primary
322 patient load involved other animal species were more likely to be less concerned about
323 antimicrobial resistant infections when compared to small animal clinicians.

324

325 **Multivariable analyses**

326 From the univariable models, four predictors—the nature of clinical position ($P = 0.043$),
327 year of graduation from veterinary school ($P = 0.040$), specialty board certification ($P = 0.054$),
328 and primary patient load ($P = 0.067$)—were included in the multivariable model using a liberal
329 value of $P \leq 0.10$ as the cut-off point. In the multivariable cumulative logit model, only two
330 predictors, year of graduation from veterinary school ($P = 0.034$) and clinicians' primary patient
331 load ($P = 0.009$) were found to be significantly associated with clinicians' degree of concern
332 about antimicrobial resistant infections. For clinicians who obtained their veterinary degree from
333 2010 to 2016, the estimated odds that the response was below any particular level of concern
334 about AMR (instead of above it) were 5.09 times the estimated odds for clinicians who graduated
335 between 1970 to 1999 (OR for 2010–2016 vs 1970–1999, 5.09; 95% CI, 1.46 to 17.72; $P =$
336 0.011). In other words, controlling for primary patient load, clinicians who graduated from 2010

337 to 2016 tended to be less concerned about AMR when compared to those who graduated from
338 1970 to 1999.

339 Although not significantly different, the estimated odds that the response was below any
340 particular level of concern about AMR (instead of above it) for clinicians who obtained their
341 veterinary degree from 2000–2009 were 2.77 times the estimated odds for clinicians who
342 graduated from 1970–1999 (OR for 2000–2009 vs 1970–1999, 2.77; 95% CI, 0.88 to 8.68; $P =$
343 0.080). Similarly (although not significantly different), the estimated odds that the response was
344 below any particular level of concern about AMR (instead of above it) for clinicians who
345 obtained their veterinary degree from 2010–2016 were 1.84 times the estimated odds for
346 clinicians who graduated from 2000–2009 (OR for 2010–2016 vs 2000–2009, 1.84; 95% CI,
347 0.57 to 5.95; $P = 0.311$).

348 For participants whose primary patient load involved other animal species (equine, food
349 animal, mixed animal, exotics, all large—equine, and food animal), the estimated odds that the
350 response was below any particular level of concern about AMR (instead of above it) were 3.98
351 times the estimated odds for small animal clinicians (OR for others vs small animal, 3.98; 95%
352 CI, 1.42 to 11.16; $P = 0.009$). In other words, controlling for year of graduation from veterinary
353 school, clinicians whose primary patient load involved other animal species tended to be less
354 concerned about antimicrobial resistant infections when compared to small animal clinicians.
355

356 **Discussion**

357 This study was designed to identify the factors influencing clinicians to begin an
358 antimicrobial regimen, the process of choosing the antimicrobials used at UTVMC, and evaluate

359 the perceptions, opinions, and concerns of veterinary clinicians at UTVMC about antimicrobial
360 use, antimicrobial stewardship, and AMR. In this study, we identified several factors that
361 influence clinician decisions to prescribe antimicrobial agents. Our results have shown the
362 relationships between demographic characteristics of veterinary clinicians and the clinicians'
363 degree of concern about AMR at a veterinary teaching hospital in the United States.
364 Additionally, we have shown the preferential ordering of medically important classes of
365 antimicrobial drugs based on UTVMC veterinary clinicians' self-reported frequency of
366 prescription.

367 For this survey, we achieved a response rate of 51.24%. This response rate was high
368 when compared to other surveys among veterinarians in the US and elsewhere (Chipangura et al.
369 2017; Fowler et al. 2016; Grayzel et al. 2015; Jacob et al. 2015; Postma et al. 2016). The high
370 response rate achieved in this study may have resulted from the efforts employed to increase the
371 response rate, including attending departmental and weekly clinical rounds meetings before the
372 survey was sent and sending out weekly email reminders to participants. A previous study
373 (Postma et al. 2016) suggested that communicating the importance of the survey along with
374 sending reminders to respondents through diverse media could improve response rates.

375 In the present study, 47 respondents (75.81%) reported results from bacteriological
376 culture and susceptibility tests to be an extremely important factor in deciding the choice of
377 antimicrobial to use. This is consistent with the findings of other studies, (De Briyne et al. 2013;
378 Jacob et al. 2015) where veterinarians rated bacteriologic culture and antimicrobial susceptibility
379 among the most important factors in clinical decision making. We believe this is a very
380 important finding given that use of bacteriological culture and antimicrobial susceptibility test
381 results, along with other Good Stewardship Practices (GSP), is very important in the practice of

382 evidence-based antimicrobial therapy (Guardabassi & Prescott 2015; Prescott & Boerlin 2016;
383 Rubin 2013). Pressure from clients/producers to the clinician to prescribe antimicrobials was
384 scored “not at all important” by 45.16% of the respondents and “slightly important” by 40.32%
385 of the respondents. Likewise, fear of litigation by the client/producer was not an important
386 factor. These findings suggest that power distance, (Hulscher et al. 2010) the hierarchical
387 distance between the veterinary clinician and client/producer in the UTVMC clinical setting, is
388 narrow, and uncertainty avoidance may not be a very influential factor in prescription decision
389 making in the UTVMC clinical setting. Culture and societal norms are known to influence
390 antimicrobial prescribing practices (Cheng & Worth 2015) with cultural measures of uncertainty
391 avoidance and wide power distance between the clinician and client/producer influencing
392 prescription practices. Clinicians with high uncertainty avoidance would be more likely to
393 prescribe antimicrobials in the event of undesirable clinical outcomes.

394 The sources of antimicrobial information that clinicians utilize in determining their
395 choice of antimicrobial for clinical use at UTVMC are similar to those identified in other studies
396 in the US and elsewhere (De Briyne et al. 2013; Hardefeldt et al. 2017; Hughes et al. 2012; Jacob
397 et al. 2015; Knights et al. 2012; Postma et al. 2016). Peer-reviewed literature was ranked as
398 “extremely important” by 35 of 62 (56.45%) respondents, while pharmaceutical company
399 representatives were ranked “not at all important” by 34 of 62 (54.84%) respondents. A previous
400 study (Hughes et al. 2012) reported that 70% of their respondents ranked pharmaceutical
401 companies as an important source of information on antimicrobial drugs.

402 In routine surgical practice, antimicrobial drugs may appropriately be used pre-
403 operatively, peri-operatively, or post-operatively for prophylaxis against surgical site infections,
404 often based on the judgement of the surgeon. Appropriate use of antimicrobials for surgical

405 prophylaxis is especially important when surgeries are performed either in suboptimal
406 conditions, such as in farm animal practice, (Dumas et al. 2016) or when the surgical procedure
407 is classified as contaminated (Boothe & Boothe 2015). In the present study, 35 of 62 (56.45%)
408 reported that they prescribe antimicrobials for prophylactic purposes. Of the 35 respondents who
409 reported prescribing antimicrobials for prophylactic purposes, 23 (65.71%) reported that they use
410 antimicrobials for pre-operative surgical prophylaxis, 29 (82.86%) reported that they use
411 antimicrobials for peri-operative surgical prophylaxis, and 29 (85.29%) reported that they
412 prescribe antimicrobials for post-operative surgical prophylaxis. These results show that at this
413 hospital, antimicrobials are used for surgical prophylaxis by a large segment of clinicians. In
414 addition, only a few respondents (14.75%) reported that they prescribe antimicrobials for
415 metaphylaxis, while the majority reported that they never prescribe antimicrobials for
416 metaphylaxis. This suggests that prescription of antimicrobials for metaphylaxis at this hospital
417 is occasional and perhaps only in exceptional situations.

418 In this study, 21 respondents (33.87%) thought that antimicrobials are sometimes
419 prescribed based on no documented evidence of infection, while 38 (61.29%) thought that
420 antimicrobials are sometimes prescribed for suspected (but not confirmed) infections. A recent
421 retrospective study (Wayne et al. 2011) from a veterinary school showed similar findings: 38%
422 of antimicrobial prescription did not have documented evidence of infection, while 45% of
423 antimicrobial prescriptions at that hospital were for suspected infections. In our study, 32
424 respondents (51.61%) believed that antimicrobials are over-prescribed. Clinicians in another US
425 teaching hospital (Jacob et al. 2015) also held a similar view that antimicrobials were
426 overprescribed.

427 In the present study, only 2 (3.23%) respondents reported that UTVMC has an
428 antimicrobial stewardship program, 51 (82.26%) of respondents reported they are “not sure”
429 whether UTVMC has an antimicrobial stewardship program, and 9 (14.52%) reported that
430 UTVMC did not have an antimicrobial stewardship program. In reality, there was no
431 antimicrobial stewardship program being implemented at this hospital at the time the present
432 survey was conducted. Clinicians were trusted and expected to make sound judgement on
433 judicious use of antimicrobials based on their veterinary training. These findings suggested a
434 need to develop and implement an antimicrobial stewardship program at this hospital.
435 Additionally, the disparities in these opinions might be due to variations in knowledge and
436 awareness among respondents about what constitutes an antimicrobial stewardship program,
437 suggesting a need for more training and awareness on antimicrobial stewardship and GSP.
438 Antimicrobial stewardship programs involve multifaceted approaches that aim to sustain the
439 efficacy of antimicrobial drugs, while minimizing the emergence of AMR (Prescott & Boerlin
440 2016). Some of the respondents in this survey reported that they were not at all familiar with
441 VCPR. It might be possible that respondents who reported that they were not at all familiar with
442 VCPR had clinical duties that did not directly involve antimicrobial prescription. Some
443 respondents stated that their clinical duties did not directly involve prescription of antimicrobials.
444 Other respondents reported that they never utilize VCPR in their antimicrobial prescribing
445 practice. This might be because utilization of VCPR in a tertiary care veterinary teaching
446 hospital like UTVMC may be impractical in certain clinical situations because some patients
447 from referring veterinarians may be admitted for emergency veterinary care and not be involved
448 in VCPR.

449 To promote judicious use of antimicrobials, some regulatory bodies and veterinary
450 professional organizations have developed guidelines for judicious antimicrobials by veterinary
451 clinicians. A previous study suggested that compliance with antimicrobial use guidelines may
452 have led to a reduction in overall antimicrobial use at a veterinary teaching hospital (Weese
453 2006). However, in the present study, seventeen (27.42%) clinicians never read FDA/AVMA
454 guidelines for judicious use of antimicrobials, 19 (30.65%) rarely read the guidelines, 20
455 (32.26%) sometimes read, and 6 (9.68%) very often read the FDA/AVMA guidelines. These
456 findings suggest a generally low uptake of antimicrobial use guidelines among the respondents
457 of this survey. It is possible that there is little awareness among the respondents about the
458 existing guidelines for judicious use of antimicrobials. A previous survey (Grayzel et al. 2015)
459 found that 218 of 247 (88%) respondents were unaware of the available guidelines for judicious
460 use of antimicrobials. There is need for more awareness about and compliance with the available
461 antimicrobial use guidelines among veterinary clinicians.

462 A previous study (Gjelstad et al. 2011) suggested that antimicrobial prescribing may be a
463 time-saving strategy for some busy physicians. At the design of this present study, we had
464 hypothesized that busy veterinary clinicians with less effort allocation to clinical practice and
465 more effort allocation to other non-clinical duties would perhaps play safe by prescribing broad-
466 spectrum antimicrobials as a timesaving strategy in the face of diagnostic uncertainties.
467 However, our findings showed that effort allocation to clinical practice was not significantly
468 correlated with frequency of prescription of antimicrobials for therapeutic treatment of infectious
469 diseases at UTVMC.

470 Our study provides evidence of the preference ordering of medically important
471 antimicrobial classes at UTVMC. At this hospital, cephalosporins were the most preferred class

472 followed by the penicillins. Recent studies of veterinary antimicrobial prescribing practices in
473 the US also showed similar findings, with β -lactams being the most commonly prescribed drug
474 class (Baker et al. 2012; Fowler et al. 2016). Our findings suggest the need for antimicrobial
475 stewardship strategies, such as de-escalation and antimicrobial cycling, to minimize likely
476 buildup of AMR to the most preferred classes at this hospital.

477 In this study, experience of the veterinary clinician, measured as number of years in
478 clinical practice, had a significant effect ($P < 0.05$) on the degree of concern about antimicrobial
479 resistant infections, suggesting that clinicians with more clinical experience tended to be more
480 concerned about antimicrobial resistant infections. We consider this a novel finding. Arguably,
481 this study demonstrates for the first time that the experience of the veterinary clinician, measured
482 as number of years in clinical practice, is significantly associated with clinician's degree of
483 concern about antimicrobial resistant infections.

484 In the multivariable cumulative logit model, we have shown that year of graduation from
485 veterinary school ($P = 0.034$) and clinicians' primary patient load ($P = 0.009$) were significantly
486 associated with clinicians' degree of concern about AMR. Moreover, for clinicians who obtained
487 their veterinary degree from 2010-2016, the estimated odds that the response was below any
488 particular level of concern about AMR (instead of above it) were 5.09 times the estimated odds
489 for clinicians who graduated from 1970-1999. Clinicians who graduated after 1999 generally
490 tended to be less concerned about AMR than those who graduated from 1970-1999. There are
491 two possible explanations for this finding. First, it could be that clinicians who graduated from
492 1970-1999 are more experienced and have received greater exposure and awareness about the
493 risks associated with antimicrobial resistant infections when compared to those who graduated
494 after 1999. Second, it is possible that this finding reflects an inadequate emphasis on the

495 judicious use of antimicrobial drugs in the teaching of veterinary pharmacology and therapeutics
496 in veterinary schools over the recent years. The opinion of other researchers is that the teaching
497 of AMR and antimicrobial pharmacology in most veterinary schools is inadequate. In the present
498 study, one clinician (1.61%) responded that present day veterinary medical students do not at all
499 receive adequate training on rational use of antimicrobials, 9 (14.75%) responded “a little,” 28
500 (45.90%) responded “somewhat,” 21 (34.43%) responded “quite a bit,” and 2 (3.28%) responded
501 “very much.” Similarly, clinicians whose primary patient load involved other animal species
502 tended to be less concerned about antimicrobial resistant infections when compared to small
503 animal clinicians. This finding may reflect perhaps greater access by small animal clinicians to
504 continued professional development related to rational antimicrobial use. The differences in
505 clinicians’ degree of concern about AMR by year of graduation from veterinary school and by
506 clinicians’ primary patient load needs to be further investigated in other veterinary teaching
507 hospitals. It would be interesting to evaluate the associations between year of graduation from
508 veterinary school, primary patient load, and clinicians’ degree of concern about AMR in other
509 tertiary veterinary teaching hospitals as well as in primary care veterinary hospitals. Educational
510 interventions, such as an increased educational emphasis about antimicrobial stewardship
511 approaches for veterinary students and continuing professional development for practicing
512 veterinarians aimed at promoting prudent antimicrobial use by veterinary clinicians at all levels
513 of clinical experience, may be helpful in modifying prescription behaviors and practices of
514 clinicians. Good education of antimicrobial prescribers has been suggested as a potent approach
515 to reduction of non-judicious antimicrobial use through improved understanding and acceptance
516 of antimicrobial stewardship (Guardabassi & Prescott 2015).

517 The main limitation of our study is the relatively few respondents (n = 62). It is also
518 possible there was a flaw in survey design that could have affected how the respondents
519 interpreted the survey questions. Similarly, fewer house officers (n = 17) responded to the survey
520 when compared to faculty with clinical appointments (n = 44), despite a response rate of 51.24%.
521 The response rate could not be increased beyond 51.24%. However, there was greater variation
522 in respondents in terms of gender, number of years in clinical practice, and specialty board
523 certification. Response bias (social desirability bias) and non-response bias, could have impacted
524 the validity of this study. It is possible that the survey answers of the respondents could have
525 differed from the answers of non-respondents. Non-responder analysis was not possible because
526 it would breach the confidentiality and anonymity of the responses. Despite the above
527 limitations, the results of this study provide useful information that is vital for improvements in
528 antimicrobial stewardship.

529

530 **Conclusions**

531 For many clinicians at this hospital, bacteriological culture and susceptibility tests were
532 an extremely important factor influencing the choice of antimicrobial agents, while peer-
533 reviewed literature and peers (other veterinarians) were very important sources of antimicrobial
534 information. This study revealed that at the time when this study was conducted, cephalosporin
535 class was the most preferred class of antimicrobials, while the lincosamide class was the least
536 preferred at this hospital. Furthermore, clinicians' degree of concern about AMR differed by year
537 of graduation from veterinary school and clinicians' primary patient load, with clinicians who
538 graduated after 1999 generally tending to be less concerned about AMR than those who

539 graduated from 1970-1999. Clinicians whose primary patient load involved other animal species
540 tended to be less concerned about antimicrobial resistant infections when compared to small
541 animal clinicians. There is need for more awareness about AMR and about guidelines for
542 judicious use of antimicrobials among veterinary clinicians. Improvements in antimicrobial
543 stewardship are needed, especially among clinicians who graduated after 1999. The findings of
544 this study should be helpful in improving antimicrobial stewardship and educational practices on
545 judicious use of antimicrobials in veterinary teaching hospitals. This, in the long run could lead
546 to a modification of prescription practices of veterinary clinicians, thus contributing to the
547 reduction of the AMR burden in veterinary medicine and public health.

548

549 **Acknowledgements**

550 The authors thank Ms. Cary Springer, Drs. Nancy Howell, J. Mark Fly, and Agricola
551 Odoi for technical assistance. No third-party funding was received in connection with this study
552 or the writing or publication of this manuscript.

553

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Figure 1

Factors that influence antimicrobial use at The University of Tennessee Veterinary Medical center

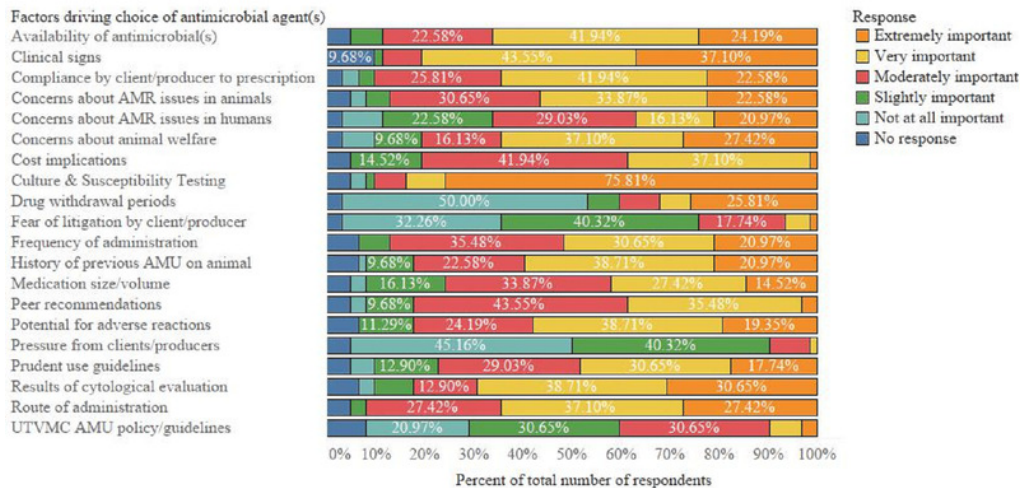


Figure 2

Distribution of sources of antimicrobial information that clinicians utilize in determining their choice of antimicrobial for clinical use at UTVMC

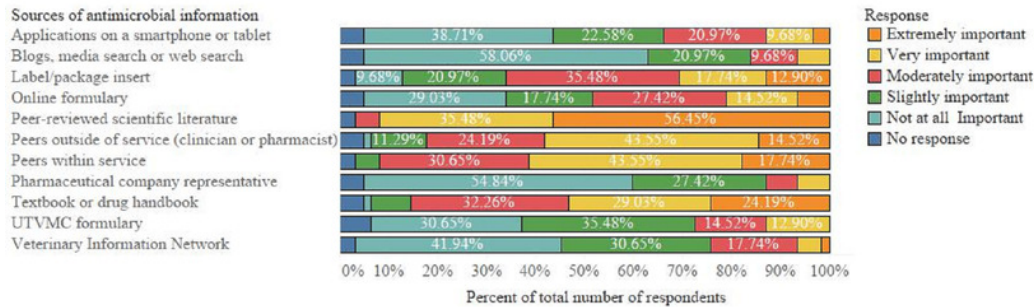


Figure 3

Self-reported antimicrobial prescription practices of veterinary clinicians at UTVMC, 2017

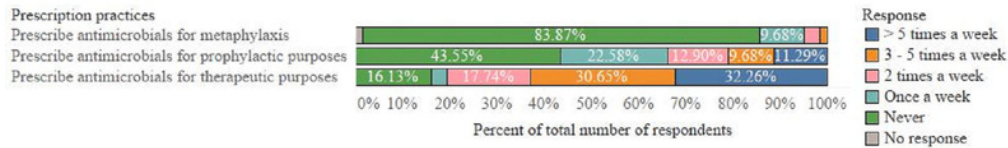


Figure 4

Self-reported antimicrobial prescription practices for surgical prophylaxis by veterinary clinicians at UTVMC, 2017

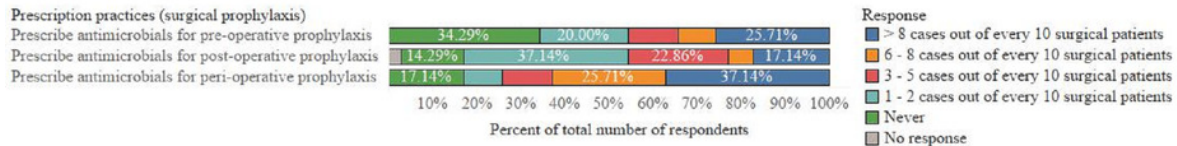


Figure 5

Clinicians' self-reported level of familiarity with VCPR at UTVMC, 2017.

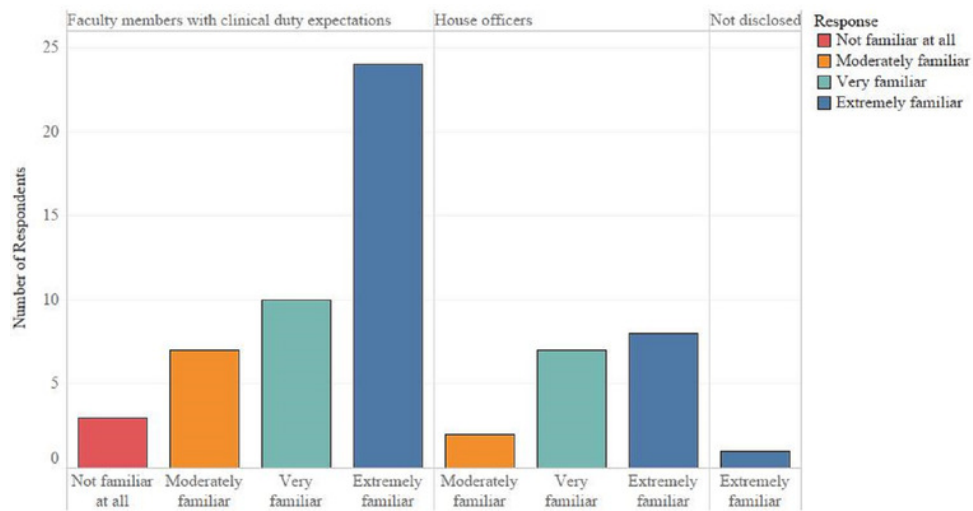


Figure 6

Self-reported use of VCPR in antimicrobial prescription practice by veterinary clinicians at UTVMC, 2017.

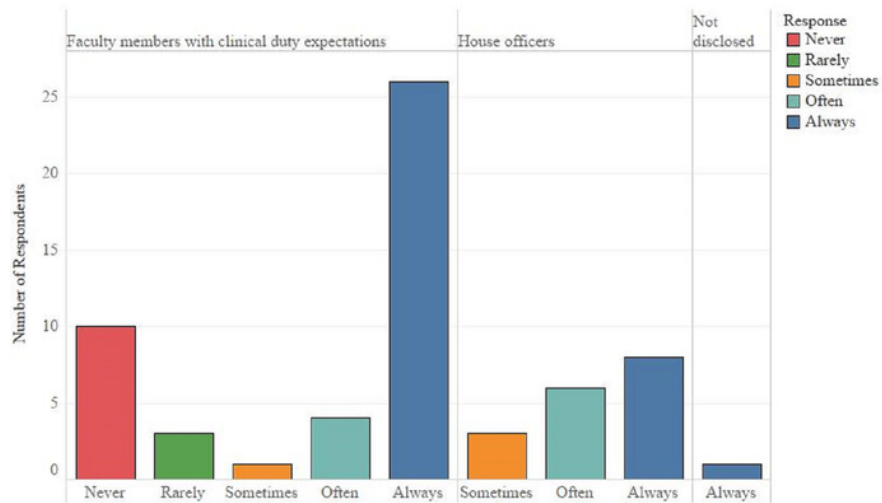


Table 1 (on next page)

Demographics of participants on an online survey to identify determinants of antimicrobial use practices among veterinary clinicians at UTVMC, 2017

1

Variable	Number (%) of respondents
Gender	
Female	37 (59.68)
Male	21 (33.87)
Preferred not to report gender	4 (6.45)
Nature Clinical Position	
Faculty member with clinical duty expectations	44 (71)
House officers	17 (27.4)
Not reported	1 (1.6)
Year of graduation from veterinary school	
1970 - 1999	21 (33.87)
2000 - 2009	22 (35.48)
2010 - 2016	19 (30.65)
College where veterinary degree was obtained	
U.S veterinary school	51 (82.26)
Non-U.S veterinary school	11 (17.74)
Primary patient load	
Small animal	37 (59.68)
Equine	8 (12.9)
Food animal	7 (11.29)
Mixed animal	4 (6.45)
Exotic	5 (8.06)
All large: equine and food animal	1 (1.61)
Specialty board certification	
Obtained specialty board certification	43 (69.4)
No specialty board certification	19 (30.64)

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Table 2 (on next page)

Results showing the preference ordering (from most preferred to least preferred) of medically important antimicrobial classes based on clinicians' self-reported frequency of prescription at UTVMC.

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Antimicrobial class	Parameter estimate	Standard error	Odds ratio (95% CI)	<i>P</i> value
Cephalosporins (most preferred class)	-0.4027	0.3410	0.67 (0.34 – 1.30)	0.238
Penicillins	-0.2669	0.3524	0.77 (0.38 – 1.53)	0.449
Tetracyclines (reference class)	—	—	—	—
Fluoroquinolones	0.5596	0.3374	1.75 (0.90 – 3.39)	0.097
Sulfas	1.0817	0.3422	2.95 (1.51 – 5.77)	0.002
Aminoglycosides	2.1030	0.3513	8.19 (4.11 – 16.31)	<0.001
Macrolides	1.6893	0.3442	5.42 (2.76 – 10.63)	<0.001
Lincosamides (least preferred class)	2.8381	0.3585	17.08 (8.46 – 34.49)	<0.001

2

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Table 3 (on next page)

Univariable analyses for associations between various demographic predictors and clinicians' degree of concern about antimicrobial resistant infections at UTVMC, 2017

1

2

Variable	Category	OR (95% CI)	P Value
Gender	Male vs Female	1.01 (0.37 – 2.74)	0.307
Nature of clinical position	House officers vs Faculty with clinical appointment	3.19 (1.04 – 9.79)	0.043
Year of graduation from veterinary school	2000 – 2009 vs 1970 – 1999	2.83 (0.91 – 8.77)	0.071
	2010 – 2016 vs 1970 – 1999	4.55 (1.35 – 15.38)	0.015
	2010 – 2016 vs 2000 – 2009	1.61 (0.49 – 5.25)	0.431
Where Veterinary Degree was obtained	US vs Non-US	1.79 (0.54 – 5.94)	0.343
Specialty board certification	No vs Yes	2.84 (0.98 – 8.19)	0.054
Primary patient load	Others* vs Small animal	2.47 (0.94 – 6.52)	0.067
*Others was a cluster that was formed out of 5 categories: equine, food animal, mixed animal, exotics, all large (equine and food animal).			

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