Critically important antimicrobials are frequently used on equine racetracks

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OBJECTIVE
To characterize antimicrobial use on four racetracks in the eastern US during the peak racing 2017–2018 seasons.

PROCEDURES
Handwritten daily treatment sheets provided by attending veterinarians who listed treatments administered to horses stabled at the racetrack were obtained. Information contained in the treatment sheets included the date, name of the horse and its trainer, type of treatment, and a brief (usually 1-word) indication for treatment. The handwritten data listed on the racetrack treatment sheets were manually transcribed and analyzed.

RESULTS
A total of 2,684 antimicrobial prescriptions were recorded, representing 6.8% of all drug treatments. The most frequently prescribed antimicrobials were enrofloxacin, with 854 prescriptions (31.8% of antimicrobial treatments), followed by gentamicin (570 [21.2%] prescriptions), ceftiofur (388 [14.5%] prescriptions), and penicillin (220 [8.2%] prescriptions). The relative frequencies of antimicrobial class and indication for treatment varied significantly by racetrack and by prescribing veterinarian. Limitations associated with the data precluded ascertainment of the proportion of horses treated or exact indications for treatment.

CLINICAL RELEVANCE
Antimicrobials appeared to be prescribed relatively infrequently at racetracks relative to other drugs, but highly or critically important antimicrobials were most often used. The appropriateness of use of these drugs remains unknown.

Antimicrobial resistance threatens both animal and human health, and related strains of deadly antimicrobial-resistant pathogens such as extended-spectrum β-lactamase–producing Escherichia coli, methicillin-resistant Staphylococcus aureus, and multidrug-resistant Salmonella spp have been found in animals and people in close contact with each other.1–6 Because all antimicrobial use (AMU) results in selection pressure for antimicrobial resistance, there is an urgent need to better understand how antimicrobials are used in animal populations.7

While AMU is scrutinized in food animal production where there are restrictions on the use of certain antimicrobials, less attention has been paid to AMU in equine medicine, where no restrictions exist, and there is minimal literature on AMU in racehorses. A small number of studies8–12 have examined AMU in hospitalized horses or in equine ambulatory care, but no studies have investigated AMU in horses at the racetrack setting. Racetracks are environments where there is large-scale movement of horses from many different locations, and close contact between horses and people, including jockeys, trainers, owners, and spectators. These conditions are conducive to the potential spread of antimicrobial-resistant organisms. Understanding how antimicrobials are used in these settings is critical to evaluating the potential risk for the development and spread of antimicrobial resistance. The aim of this study was therefore to investigate and characterize AMU on 4 racetracks during peak racing seasons.

Materials and Methods
Data for this study were collected from 4 racetracks in the eastern US, 2 of which conducted Standardbred (harness) racing and 2 of which conducted Thoroughbred (flat) racing. Handwritten daily treatment sheets provided by attending veterinarians listing treatments administered to horses stabled at the racetrack in June, July, and August of 2017 and 2018 were obtained. Information contained in the treatment sheets included the date, name of the horse and its trainer, type of treatment, and a brief (usually 1-word) indication for treatment (ie, nature of ailment). The handwritten data listed on the racetrack treatment sheets were manually
transcribed into a data set by multiple members of the study team. Because there was no standardized method of listing drugs in the treatment sheets, all prescriptions were individually examined, and medications corresponding to an antimicrobial were identified based on the name of the active ingredient (eg, enrofloxacin) or brand (eg, Baytril), including all spelling variants (eg, enroflaxcin). A similar consolidation of variant spellings was performed for veterinarian and trainer names.

The large number of horses represented in the data set (n = 8,451) precluded manual consolidation of variant spellings of horse names. Therefore, the number of unique horse names in the database may have represented an overestimate of the true number of horses represented across all treatment sheets. There was no way of determining the number of horses that were eligible to receive a prescription (ie, the denominator), as no data were available on the total number of horses that were stabled on-site during the time period.

Indications for antimicrobial prescriptions were also individually examined and classified into the following broad categories:

1) Infectious (including key terms such as infection, swollen, cellulitis, fungus, and equine protozoal myeloencephalitis)
2) Trauma or injury (wound, injury, laceration, arthritis, and lame)
3) Sick (fever, dehydration, respiration, colic, and mucous)
4) Prophylactic (surgical, anesthesia, castrate, runs, training, prerace, and maintenance)
5) Unknown (illegible or blank entries or undiscernible reasons)

The distribution of antimicrobial types across track, month, year, ailment, and veterinarian was assessed, and the proportions of different antimicrobial classes across groups were compared using the χ² test. For each racetrack, the percentage of prescriptions that were antimicrobials was also calculated and compared by use of the χ² test. All analyses were performed with statistical software (R Studio).

### Results

The 4 tracks varied in capacity, from 660 stalls at track D to 1,650 stalls at track B. The number of veterinarians, trainers, and horses operating out of each of these tracks also varied and did not always correlate to the track capacity (Table 1). An estimated 8,492 horses received at least 1 prescription (any drug) during the entire time period, and a total of 39,460 unique prescriptions were recorded, with each prescription entry representing a day of treatment, in which multiple types of drugs could have been dispensed, not a unique drug prescription.

A total of 16 different types of antimicrobials were prescribed (Table 2) and accounted for 2,684 prescriptions (6.8% of all prescriptions). The most frequently prescribed antimicrobial was enrofloxacin, with 854 dispensations (31.8% of antimicrobial prescriptions), followed by gentamicin (570 [21.2%]), ceftiofur (388 [14.5%]), and penicillin (220 [8.2%]; Figure 1). Prescribed ceftiofur consisted mostly of the long-acting free acid form (Excede; 376/388 [96.9%]). Both enrofloxacin and ceftiofur are classified as Highest-Priority Critically Important Antibiotics (HPCIA). Racetrack A had the most prescriptions overall with a total of 18,201, 7.0% of which were anti-

### Table 1—Capacity, staff, and antimicrobials prescribed on 4 racetracks in the eastern US from 2017 to 2018.

<table>
<thead>
<tr>
<th>Track</th>
<th>Type of track</th>
<th>No. of stalls at track</th>
<th>No. of veterinarians</th>
<th>No. of trainers</th>
<th>No. of horses receiving any prescriptions*</th>
<th>No. of horses prescribed antimicrobials*</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Standardbred</td>
<td>1,232</td>
<td>17</td>
<td>90</td>
<td>3,552</td>
<td>477</td>
</tr>
<tr>
<td>B</td>
<td>Thoroughbred</td>
<td>1,650</td>
<td>7</td>
<td>118</td>
<td>2,160</td>
<td>289</td>
</tr>
<tr>
<td>C</td>
<td>Thoroughbred</td>
<td>1,400</td>
<td>10</td>
<td>95</td>
<td>1,596</td>
<td>168</td>
</tr>
<tr>
<td>D</td>
<td>Standardbred</td>
<td>660</td>
<td>3</td>
<td>61</td>
<td>1,181</td>
<td>212</td>
</tr>
</tbody>
</table>

*Estimate based on the number of unique horse names listed in the treatment sheets from that track.

### Table 2—Antimicrobials prescribed to horses on 4 racetracks in the Eastern US during June to August of 2017 and 2018.

<table>
<thead>
<tr>
<th>Antimicrobial class</th>
<th>Active ingredients</th>
<th>No. (%) of prescriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminoglycosides</td>
<td>Amikacin</td>
<td>115 (4.6)</td>
</tr>
<tr>
<td></td>
<td>Gentamicin</td>
<td>570 (22.8)</td>
</tr>
<tr>
<td></td>
<td>Neomycin-thiostreton, neomycin-bacitracin-polymyxin</td>
<td>28 (1.1)</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Cefoxitin</td>
<td>11 (0.4)</td>
</tr>
<tr>
<td></td>
<td>Ceftiofur</td>
<td>388 (15.5)</td>
</tr>
<tr>
<td></td>
<td>Ceftiofur sodium (Naxcel)</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>Ceftiofur free acid (Excede)</td>
<td>376</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>Enrofloxacin</td>
<td>854 (34.1)</td>
</tr>
<tr>
<td>Penicillins</td>
<td>Procaine penicillin G</td>
<td>220 (8.8)</td>
</tr>
<tr>
<td>Phenicols</td>
<td>Chloramphenicol</td>
<td>4 (0.2)</td>
</tr>
<tr>
<td>Sulfonamides/combinations</td>
<td>Trimethoprim-sulfadiazine, sulfamethoxazole</td>
<td>52 (2.1)</td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>Doxycycline</td>
<td>73 (2.9)</td>
</tr>
<tr>
<td></td>
<td>Oxytetracycline</td>
<td>191 (7.6)</td>
</tr>
</tbody>
</table>
microbials. In racetracks B and C, 7.0% of prescriptions were also antimicrobials. Racetrack D dispensed the highest proportion of antimicrobials at 10.0% of 6,738 total prescriptions. The most frequently prescribed antimicrobial was enrofloxacin on tracks A and B and ceftiofur on tracks C and D (Figure 2). The number of antimicrobial prescriptions either increased or stayed the same from 2017 to 2018 ($P > 0.05$), with the exception of ceftiofur which decreased by more than half ($P < 0.001$). However, without knowing the number of horses that were eligible for treatment, it was unclear whether the proportion of horses prescribed antimicrobials changed.

The distribution of indications for treatment varied by track and drug type. The category that appeared with the overall highest frequency was infectious (1,024 [42.6%] entries), followed by unknown (800 [33.3%] entries), trauma or injury (521 [21.7%] entries), and prophylactic (59 [2.5%] entries). The leading indication for tracks A, B, and C was infectious, while unknown indications predominated for track D. For all antimicrobials except ceftiofur, infectious causes were the most common indications for treatment. For ceftiofur, traumatic causes were the leading indications for use.

To determine whether horses generally received single or multiple types and doses of antimicrobials, the number of antimicrobial prescriptions associated with unique horse names was examined. Most horses (2,430 [90.6%]) received only a single type of antimicrobial, and most horses received only 1 prescription during their time at the track (Figure 3), with instances decreasing as the number of repeat prescriptions increased, although some horses received more than 20 prescriptions.

The relative frequencies of antimicrobial class and indication for treatment varied significantly by the prescribing veterinarian. The proportion of prescriptions that were antimicrobials varied from 0.4% to 38% across veterinarians (Figure 4). While it was impossible to know how similar the caseload seen by each veterinarian was, the distribution of indications for all prescriptions did significantly differ across veterinarians ($P < 0.001$).
Discussion

This was the first large-scale study investigating patterns of AMU at equine racetracks, with one of the main findings being that the most commonly used antimicrobials are those that fall into the category of HPCIAs. A large number of horses pass through racetracks, and substantial comingling of horses and people occurs at racetrack facilities. Racetracks thus represent an opportune environment for the selection of antimicrobial resistance and the spread of antimicrobial-resistant bacteria among horses and between horses and people. Understanding the extent to which antimicrobials are used in the racetrack setting is important for understanding the potential selection pressures that exist.

Antimicrobials represented 7% of prescriptions on racetracks, thus constituting a minority of prescriptions. In comparison, NSAIDs represented 31.5% of prescriptions, and other types of prescriptions included steroids, sedatives, diuretics, bronchodilators, antiparasitics, vitamins, nutritional and joint supplements, antifibrinolytic agents (eg, aminocaproic acid), gastroenteric drugs (eg, omeprazole or sucralfate), and reproductive-associated drugs (eg, estradiol or altrenogest; data not shown).

Enrofloxacin was the most frequently prescribed antimicrobial overall, and the 4 most frequently administered antimicrobials were all considered to be either highly important (penicillin), critically important (aminoglycosides), or of the highest priority (fluoroquinolones orthird-generation cephalosporins) by the World Health Organization.14 The British Equine Veterinary Association considers fluoroquinolones and third- or fourth-generation cephalosporins to be protected drugs that should only be used in equine medicine when an infection has been confirmed through culture and susceptibility,15 and the European Medicines Agency places these drugs in category B (restrict), recommending their use in animals be restricted.16 The critical importance of these drugs should thus preclude their use for empiric or prophylactic therapy.

Enrofloxacin may have been the most commonly prescribed drug because of its ease of administration and broad-spectrum nature. It is efficacious when given as a single dose therapy, which is likely preferable for young, potentially fractious racehorses, and its spectrum of action is sufficiently broad to be active against a wide range of gram-positive and gram-negative bacteria such as Staphylococcus sp, Proteus sp, Klebsiella sp, Pasteurella sp, and E coli.17 Other reasons for its frequent use could be its simplicity of use relative to alternative drugs. For example, procaine penicillin is listed as a controlled therapeutic substance by the Racing Medication and Testing Consortium because of the blocking effects of procaine, with a withdrawal time of 48 hours, mandatory withdrawal prior to entry, mandatory reporting of treatments, and surveillance requirement on race day. Additionally, this drug is injected IM twice a day, which often results in soreness or swelling at the injection site. For this reason, alternatives such as enrofloxacin may have been preferred.

The use of enrofloxacin in horses remains highly controversial, and there are no FDA-approved enrofloxacin products for horses. In humans, fluoroquinolone use is restricted in children due to increased risk of musculoskeletal damage.18 There is also growing evidence that fluoroquinolone treatment causes tendinopathy in adults, which can result in tendon damage up to 6 months after administration.19 Risk of tendon damage is increased with concurrent use of corticosteroids.20 For this reason, the European Medicines Agency recently banned or restricted the use of individual fluoroquinolone antimicrobials21 and the FDA has issued warnings regarding their use in humans.22 In vitro research has shown that enrofloxacin negatively affects equine tenocyte proliferation23 and has toxic effects on equine chondrocytes.24 Individual horses receiving enrofloxacin at high doses have developed tendinitis or desmitis.25 Given that most racehorses are juvenile athletes, the frequent use of enrofloxacin, which may affect tendon and cartilage health, is concerning. The current recommendation is to only use enrofloxacin based on culture and susceptibility, and when no other antimicrobials are appropriate.17 Given that most horses received only a single prescription of antimicrobial, it appears that enrofloxacin was either used as a first-line treatment or prophylactically.

We also found that the proportion of prescriptions that were antimicrobials and the distribution of types of antimicrobial varied by track and by prescribing veterinarian. This is consistent with other studies12,26 which found that veterinarians, even
those with presumably similar caseloads, had widely varying antimicrobial prescribing patterns. While infectious causes were the most common indication for antimicrobial treatment on 3 of the 4 racetracks, a wide variety of infectious conditions affecting different organ systems exist, and the terms that were assigned to this category were often vague (eg, infection or infected). Therefore, it is difficult to know whether differences in prescribing patterns by veterinarians were due to different caseloads or different prescribing habits and choices.

Only 2 other studies have documented antimicrobial prescriptions for racing horses. In 1 small study, Pearson asked trainers from a racetrack in Canada to list the types of medications administered to their horses over the previous 10 days. The author found that antimicrobials were the fifth most commonly administered medication, after furosemide, anti-inflammatoryatories, bronchodilators, and herbal medicines, and that antimicrobials were administered to approximately 7% of the horses that were stabled at the track in the previous 10-day period. This is similar to our study in that antimicrobial treatments represented a small proportion of all prescriptions. However, in contrast to our study, treatments were derived by trainer self-reporting and the period of interest was only 10 days.

In another small study of hospital treatment records of poorly performing racehorses subsequently diagnosed with nonseptic inflammatory airway disease, it was found that 38 of 55 (69%) of these racehorses received antimicrobials, most commonly trimethoprim-sulfadiazine. While these findings are not entirely comparable to our results because they represent prescriptions for hospitalized racehorses and not horses stabled at the track, it is of interest to note that a high proportion of horses with airway disease received antimicrobials. In contrast, only 13.1% and 11.8% of horses with a sick or infectious categorization at the racetracks in our study received antimicrobials.

One of the ultimate goals of studying AMU on the racetrack is to determine the risk of antimicrobial resistance in the racetrack setting and the extent to which this risk could contribute to the global manifestation of antimicrobial resistance. While the number of horses in the US (slightly under 2 million) is relatively small compared to other companion animals and food animals, they do receive large volumes of antimicrobials due to their size and there is substantial intermingling of horses at racetracks, where resistant determinants could be spread from horse to horse or from horses to people. Thus, the contribution of horses to the global spread of antimicrobial resistance is likely not negligible. In fact, 2 studies have documented the presence of higher rates of antimicrobial resistance in racing horses: one study found that racing horses were significantly more likely to harbor methicillin-resistant *Staphylococcus* than breeding or riding horses, while another study found that 21% of *E coli* isolates from racehorses were resistant to at least 1 antimicrobial. However, no information on AMU within these populations was available; thus, the extent to which AMU drives the development and spread of antimicrobial resistance within the racetrack setting is unknown. Future research in this area is critically needed.

Several limitations apply to the present study, primarily due to the nature of the data set. First, it was impossible to determine the absolute number of horses that passed through the racetracks and were therefore eligible to receive a prescription. Even identifying the total number of stalls and the typical occupancy of these stalls is insufficient, as there is a great deal of turnover among the occupants, with horses arriving for race days and stabled horses shipped to other facilities to race. Thus, we were able to derive a numerator for the number of horses treated, but no denominator; therefore, the proportion of horses stabled at the racetrack during that time period that received an antimicrobial prescription remains unknown. Second, units of dispensation were not always clear. We assumed that an entry for a drug represented a single dose, but it is possible, for example, that an entire bottle of a drug may have been dispensed on that day for that prescription. Finally, very limited information was available on the nature of the conditions for which the horses were being treated. Entries were often vague, illegible, or missing. Indications for treatment and therefore the appropriateness of AMU were impossible to ascertain.

Despite the shortcomings of the data set, a remarkable takeaway from the study reported here is that HPClAs are very frequently used in the equine racetrack setting, perhaps even overused. The use of these drugs selects for antimicrobial resistance genes, including those on mobile genetic elements bearing multiple resistance determinants that are easily transferred horizontally between bacteria (especially *Enterobacteriaceae*). For example, plasmid-borne determinants of fluoroquinolone resistance are frequently associated with extended-spectrum β-lactamases. Future studies are warranted to more thoroughly investigate indications for treatment and to correlate AMU with antimicrobial resistance. Demonstration of a strong link between use of these drugs and antimicrobial resistance in these settings may provide sufficient evidence for legislation or new consensus statements around the use of these antimicrobials.

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### References
