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Original Research

Descriptive Study of Medication Usage and Occurrence of Disease and Injury During Gestation in Thoroughbred Broodmares

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ABSTRACT

The study aimed to (1) describe the use of reproductive therapeutics; (2) estimate the incidence of disease and injury; and (3) describe non-reproductive medications administered during pregnancy in Thoroughbred broodmares. A prospective birth cohort was established on seven farms across the UK and Ireland. Details of dams' signalment, breeding history, reproductive management during the breeding season(s) and veterinary-attended episodes of illness or injury and medication usage during gestation were retrieved retrospectively for 275 pregnancies in 235 mares over two breeding seasons. Results are reported at pregnancy-level of mares with data available. Preoestrus medications, ovulatory agents and post-covering treatments were administered to 55% (n = 85/155, 95% Confidence interval (CI) 47–62), 64% (n = 101/157, 95% CI 57–71) and 73% (n = 109/150, 95% CI 65–79) of mares respectively. Antibiotics were utilized in 69% (n = 75/109, 95% CI 60–77) of post-covering treatments. Of mares with no visible fluid on post-covering ultrasound, 37% (n = 24/65, 95% CI 26–49) still received treatment. Thirty-four percent (n = 70/203, 95% CI 28–41) of mares suffered at least one veterinary-attended episode of disease or injury, with conditions affecting the musculoskeletal system (23%, n = 46/203, 95%CI 17–29) and placentitis (5%, n = 10/203, 95% CI 3–9) most prevalent. Forty-seven percent (n = 95/203, 95% CI 40–54) of mares received at least one non-reproductive medication during gestation, antibiotics (25%, n = 51/203, 95% CI 20–31) and non-steroidal anti-inflammatory drugs (23%, n = 47/203, 95% CI 18–29) being most frequently prescribed. Post-covering treatments often included antibiotics and were sometimes given in the absence of fluid, highlighting a need to further understand therapeutic rationale. Disease occurrence and medication usage during gestation were frequent and warrant additional investigation.

1. Introduction

Over the last decade, there has been a trend for increasing use of reproductive therapeutics in Thoroughbred broodmares [1–4], despite per-cycle pregnancy rates, incidence of pregnancy loss, live foal rates, and the prevalence of conditions such as postcovering endometritis remaining largely unchanged [1,2,5]. Antibiotic preparations appear to be commonly included in such treatment regimens [2,3], raising concerns over whether current practices align with industry guidelines for antimicrobial stewardship [3,6].

There is currently a lack of information on the use of non-reproductive medications in Thoroughbred broodmares during the gestation period. Moreover, little is known about the incidence of many important diseases occurring during pregnancy including placentitis, which has been associated with pregnancy loss [7], intrauterine foetal growth retardation, prematurity, and congenital sepsis [8]. The ability of the mature phenotype to be altered by adaptive responses of the foetus in response to exposures during in-utero growth and development is well established [9]. To date in equines, predominantly via experimental intervention studies, exposures such as nutritional status of the pregnant mare and intrauterine growth restriction of the foetus have been demonstrated to be associated with postnatal body conformation, developmental orthopaedic disease (DOD), immune response and energy homeostatic mechanisms of the foal [10–12]. Furthering understanding of medication usage and benchmarking the frequency of conditions

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occurring during pregnancy in Thoroughbreds is therefore important, not only to fill knowledge gaps, but also to help inform future research priorities by providing detailed gestational exposures that could be investigated when considering the developmental origins of offspring health and disease. Such work would also importantly be in keeping with a recent industry welfare strategy which called for improved transparency of breeding practices in Thoroughbreds [13].

The objectives of this study were therefore to (1) describe the use of reproductive therapeutics; oestrus induction (preoestrus) agents, ovulatory agents and postcovering treatments; (2) estimate the incidence of disease and injury during gestation; and (3) describe medication usage (excluding postcovering treatments) during gestation, in Thoroughbred broodmares on farms in the UK and Ireland.

2. Materials and Methods

Ethical approval was granted by the Royal Veterinary College's Clinical Research Ethical Review Board (URN: 2018 1843).

2.1. Data Collection and Processing

A prospective Thoroughbred birth cohort was established where foals were enrolled from seven farms across the UK and Ireland in 2019 and 2020 and followed until leaving the farm to enter pretraining or until they left the study. The foals' dams were identified, and their stud and veterinary records retrieved. Where available, data were collected on mares' signalment, breeding history, reproductive management during the breeding season(s) of interest including details of any oestrus-induction agents or ovulatory agents administered, service date, covering stallion and details of any post-covering treatments (defined as intra-uterine or parenteral therapies administered within 48 hours of covering following ultrasonographic examination of the reproductive tract). In addition, dates and details of any other medications administered and any episodes of illness or injury that required veterinary intervention during gestation were retrieved. All data were entered into a purpose-designed form within a custom Access database (Microsoft Access 2016, Microsoft Corporation).

Data on mare age, number of previous live foals, status at the start of the breeding season and covering stallion were verified using Weatherbys' return of mares records [14–16] and the Racing Post website [17]. Status at the start of the breeding season was categorized into: foaling (mare produced a live foal from the previous breeding season), maiden (mare had never produced a live foal) and no live foal (mare had failed to produce a live foal in the previous season but had previously produced one or more live foals). Gestation length was calculated as foaling date minus last service date. Medications were separated into: reproductive therapeutics, (oestrus induction agents, ovulatory agents, and post-covering treatments); medications administered at the time of manual twin reduction (where this occurred); and other medications which were prescribed during gestation to pregnant mares. All medications were initially described by active ingredient, then active ingredients were grouped by category, for example antibiotic or non-steroidal anti-inflammatory drug (NSAID); data on route of administration were also recorded. The Veterinary Formulary [18] was used to verify information. Data were examined alongside veterinary records, to identify repeat prescriptions which were made for an ongoing course of treatment with the same medication. Episodes of mare illness and injury during gestation were categorised, using diagnoses and clinical descriptions recorded in veterinary records. To aid this process, case definitions were created based on the literature [19–23] (Supplementary Table 1). All veterinary and medication data were categorized independently by two veterinary-qualified reviewers (RM, JCA-S); in case of disagreement a third reviewer (KV) was available so a final consensus decision could be made.

2.2. Data Analyses

Analyses were carried out using Stata (Release 16, StataCorp LP, and College Station, TX). To describe mare and pregnancy-level features, histograms were plotted of continuous data and visually inspected for normality. Mean and standard deviation (SD) were reported for normally distributed data and median and inter-quartile range (IQR) were reported for non-normally distributed data. Frequencies, proportions and 95% confidence intervals (CI) were calculated for all categorical variables. Analysis accounting for any non-independence of observations was considered beyond the scope of this descriptive study.

Due to the nature of the study design (birth cohort) data were collected at the pregnancy-level, meaning that only reproductive therapeutics administered around coverings that resulted in the birth of a live foal are described in this work. These data, along with data describing episodes of illness or injury and the prescription of medications during gestation, were collected retrospectively. As such, it was not possible from available records to be certain whether repeated administrations of the same reproductive therapeutic, episodes of the same condition or prescriptions of the same medication occurring may have been related, for example a second episode or prescription of a previously described medication/condition may have been a continuation or recurrence of a previous one. For this reason, it was elected to only include the first use of a category of medication/first episode of a particular condition in a mare in the calculation of proportions and 95% CI at the pregnancy level. However, at the pregnancy-level mares may have received more than one category of medication or suffered first episodes of more than one category of disease. Results for episodes of disease and injury occurring during gestation were also calculated as proportions and 95% CI of the total number of reported episodes of illness and injury. Gestational age at the time of event or was calculated as the date of the event/administration of medication minus the last service date.

3. Results

3.1. Description of Data

Data were available for 275 pregnancies, carried by 235 mares on seven stud farms over two breeding seasons (with n = 40 mares from two of the farms providing data in both seasons). Pregnancies resulted in 138 colts and 137 fillies (n = 197 born in 2019 and n = 78 born in 2020). Six farms were based in the UK and one in Ireland. The average number of mares per farm over the two breeding seasons was 34 (SD 22, range 10-104).

Median mare age at covering for the 275 pregnancies was 7 years (IQR 5–10, range 3–22). At covering 18% of mares (n = 48/272, 95% CI 14–23) were reported to be maidens, 18% (n = 49/272, 95% CI 14–23) were reported to have failed to produce a live foal from covering in the previous breeding season and 64% (n = 175/272, 95% CI 58–70) were reported to have produced a live foal as a result of a covering in the previous breeding season. Seventy-two percent of pregnancies (n = 197/275, 95% CI 66–77) were conceived in 2018 and 28% (n = 78/275, 95% CI 23–34) in 2019. Thirteen percent of pregnancies were the result of coverings in February (n = 35/273, 95% CI 9–17), 29% in March (n = 79/273, 95% CI 24–35), 38% in April (n = 105/273, 95% CI 33–44), 18% in May (n = 49/273, 95% CI 14–23) and 2% in June (n = 5/273, 95% CI 1–4). Coverings were performed by one of 89 different stallions;

the maximum number of coverings per stallion was 33, the minimum 1 and median 2 (IQR 1–4). Mean gestation length was 344 days (SD 11, range 314–381, n = 273).

3.2. Use of Reproductive Therapeutics

Table 1 displays a summary of reproductive therapeutics administered to the various subsets of mares for whom data were available, stratified by mare age (quartile) and status at covering.

3.2.1. Pre-oestrus Medications

Data on pre-oestrus medication usage prior to the covering which resulted in a live foal were available for n = 155 pregnancies, of which 55% (n = 85/155, 95% CI 47–62) received at least one pre-oestrus medication and 45% (n = 70/155, 95% CI 37–53) did not. Of pregnancies in which pre-oestrus medication was administered 54% received prostaglandin F2 alpha (n = 46/85 95% CI 43–64), 12% domperidone (n = 10/85 95% CI 6–20), 9% sulpiride (n = 8/85 95% CI 5–17), and 8% altrenogest (n = 7/85 95% CI 4–16). Other reported medications included dexamethasone (n = 2), various intrauterine preparations (n = 4) and a goserelin implant (n = 1). Of pregnancies in which pre-oestrus medications were administered, 26% (n = 23/85, 95% CI 19–37) received multiple medications.

3.2.2. Ovulatory Agents

Data on ovulatory agent usage prior to the covering resulting in a live foal were available for n = 157 pregnancies, of which 64% (n = 101/157, 95% CI 57–71) received an ovulatory agent and 36% (56/157, 95% CI 29–43) did not. Of those receiving agents 57% (n = 58/101, 95% CI 48–66) were described as deslorelin implants, 34% (n = 34/101, 95% CI 25–43) deslorelin injection and 9% (n = 9/101, 95% CI 5-16) human chorionic gonadotrophin (hCG).

3.2.3. Post-covering Treatments

Data on whether a post-covering treatment was administered following the covering which resulted in the birth of a live foal were available for n = 150 of pregnancies, of which 73% (n = 109/150, 95% CI 65–79) received at least one post-covering treatment, the remaining 27% (n = 41/150, 95% CI 21–35) were reported to have received no treatment. Of pregnancies receiving post covering treatments 69% (n = 75/109, 95% CI 60–77) received oxytocin, 69% (n = 75/109, 95% CI 60–77) received an intrauterine antibiotic preparation and 62% (n = 67/109, 95% CI 52–70) received intrauterine saline. Intrauterine antibiotic preparations were described as aminoglycosides in combination with penicillins (n = 66), penicillins only (n = 7) or cephalosporins (n = 2). Other post-covering treatments included intrauterine saline, hydrogen peroxide, plasma, iodine or dimethyl sulfoxide and parenteral dexamethasone or flunixin. Of pregnancies receiving post-covering therapies, 77% (n = 84/109, 95% CI 68–84) received a combination (for example intrauterine antibiotic and saline and parenteral oxytocin) of therapeutics.

Data describing the presence or absence of fluid on post-covering ultrasonographic examination were available for n = 129 pregnancies, of which 50% (n = 64/129, 95% CI 41–58) were reported to have intrauterine fluid visible on ultrasound examination within the 48 hours following covering (further descriptions of any fluid were not available). All pregnancies (100%, n = 64/64, 95% CI 94–100) reported as having uterine fluid and 37% (n = 24/65, 95% CI 26–49) of those reported with no uterine fluid on post-covering examination received at least one post-covering treatment.

3.2.4. Medications Administered at Manual Twin Reduction

Data confirming whether or not a twin reduction had been performed were available for n = 188 pregnancies. Manual

Table 1
Summary of reproductive therapeutics administered before or after 275 coverings (resulting in the birth of a live foal) of 235 mares on seven stud farms over two breeding seasons (n = 197 in 2018 and n = 78 in 2019). Data reported as number and proportion with 95% confidence interval (CI) of pregnancies for which data were available (N) and stratified by quartile of mare age (years) and mare status at the time of covering.

Reproductive Therapeutic	All Pregnancies			Mare Age at Covering (Quartile) - % Receiving (95% CI)				Mare Status at Covering -% Receiving (95% CI)		
	n	%	95% CI	2–5 y	6–7 years	8–10 years	>10 years	NLF	Foaling	Maiden
Pre-oestrus medication (N = 155[a])				40.0 (27.0–54.5)	46.1 (31.6–61.4)	43.6 (29.3–59.0)	53.1 (36.4–69.1)	38.1 (20.7–59.1)	48.1 (39.1–57.4)	37.5 (21.2–57.3)
PG F2a	46	29.7	23.0–37.3							
Domperidone	10	6.4	3.5–11.5							
Sulpiride	8	5.2	2.6–9.8							
Altrenogest	7	4.5	2.2–9.0							
Others[b]	7	4.5	2.2–9.0							
Ovulatory agent (N = 157)				68.9 (54.3–80.5)	57.5 (42.2–71.5)	76.3 (60.8–87.0)	52.9 (36.7–68.5)	70.8 (50.8–85.1)	60.5 (51.2–69.2)	75.0 (55.1–88.0)
Deslorelin implant	58	36.9	29.7–44.7							
Deslorelin injection	34	21.7	15.9–28.7							
hCG	9	5.7	3.0–10.5							
Post-covering treatment (N = 150[a])				60.5 (45.6–73.6)	78.4 (62.8–88.6)	70.3 (54.2–82.5)	84.8 (69.1–93.3)	91.6 (74.2–97.7)	75.0 (65.7–82.4)	46.1 (28.5–64.5)
Oxytocin	75	50.0	42.1–57.9							
IU antibiotic	75	50.0	42.1–57.9							
IU saline	67	44.7	36.9–52.7							
Others[c]	18	12.0	7.7–18.2							

Abbreviations: CI, Confidence interval; NLF, No live foal in previous breeding season; IU, Intrauterine; PG, Prostaglandin.
[a] Mares may have received more than one pre-oestrus medication or post-covering treatment.
[b] Others, various intra-uterine; preparations (n = 4), dexamethasone (n = 2), goserelin implant (n = 1).
[c] Others = non-specified IU treatment (n = 3), IU hydrogen peroxide (n = 5), IU plasma (n = 1), IU iodine (n = 1) or IU dimethyl sulfoxide (n = 1) and parenteral dexamethasone (n = 5), flunixin (n = 1) or buserelin (n = 1).

Table 2
Summary of recorded events of disease or injury requiring veterinary intervention during gestation (last service date to foaling date) for 203 pregnancies in 174 mares from seven stud farms over two breeding seasons. Proportions and 95% confidence intervals (CI) given of the total number of reported episodes (n = 90) and of total number of pregnancies (n = 203). Gestational age at time of first veterinary intervention calculated from last service date.

Condition	Episodes (n = 90)			Pregnancies (n = 203)			Gestational Age (d)	
	n	%	95% CI	n	%	95% CI	Median	IQR
Musculoskeletal disease/injury	54	60.0	50.0–89.5	46	22.7	17.4–28.9	179	140–215
Trauma	22	24.4	16.7–34.2	20	9.8	6.5–14.7	170	115–268
Cellulitis/mud fever	16	17.8	11.2–26.9	15	7.4	4.5–11.8	230	109–293
Foot pain/abscess/laminitis	15	16.7	10.4–25.7	13	6.4	3.8–10.6	119	72–196
Pelvic fracture	1	1.1	0.2–6.0	1	0.5	0.1–2.7	295	N/A
Placentitis	10	11.1	6.1–19.3	10	4.9	2.7–8.8	297	213–325
Mastitis	9	10.0	5.3–17.9	9	4.4	2.3–8.2	141	116–176
Colic	9	10.0	5.3–17.9	9	4.4	2.3–8.2	125	37–336
Conjunctivitis/eye ulcer	5	5.6	2.4–12.5	5	2.5	1.0–5.6	62	61–76
Other[a]	3	3.3	1.1–9.3	3	1.5	0.5–4.3		

CI, confidence interval; IQR, Inter-quartile range; Other[a], choke (n = 1), sinusitis (n = 1), atrial fibrillation (n = 1).

twin reductions were reported to have been performed in 16% (n = 30/188, 95% CI 11–22) of these pregnancies. Median gestational age at twin reduction was 16 days (IQR 15–16, range 13–24). Data on medications given at the time of reduction were available for 24/30 reductions, all of which included flunixin (n = 24/24, 95% CI 86–100). The most commonly reported usages were flunixin in combination with hyoscine (37%, n = 9/24, 95% CI 21–57), flunixin alone (29%, n = 7/24, 95% CI 15–49), and flunixin in combination with sedation (21%, n = 5/24, 95% CI 9–41).

3.3. Disease and Injury During Gestation

Data describing whether mares had required veterinary intervention for a disease or injury during the gestation period were available for n = 203 pregnancies. Overall, veterinary intervention was required for disease or injury in the mare at least once in 34% (n = 70/203, 95% CI 28–41) of pregnancies. A total of 90 recorded events required veterinary intervention (median 1 event/pregnancy, range 1–4) equating to an overall risk in the cohort of pregnancies of 44% (n = 90/203, 95% CI 38–51). Median gestational age at first veterinary intervention was 193 days (IQR 119–295, range 4–344). A summary of the most common events of disease or injury requiring veterinary intervention during gestation is given in Table 2.

3.4. Medications Administered During Gestation

Excluding post-covering treatments and/or medication administered at the time of manual twin reduction, at least one medication was administered to the mare between the date of last cover and date of foaling in 47% (n = 95/203, 95% CI 40–54) of pregnancies. A summary of the most frequently administered medications during gestation is given in Table 3.

Trimethoprim/sulphonamides were the most common category of antibiotic (administered at least once during 13% of pregnancies, n = 26/203, 95% CI 9–18) followed by tetracyclines (7%, n = 15/203, 95% CI 4–12), penicillins (6%, n = 12/203, 95% CI 3–10) and aminoglycosides (5%, n = 11/203, 95% CI 3–9). Other reported antibiotic categories were cephalosporins (administered during n = 2 pregnancies) and fluoroquinolones (n = 1). Phenylbutazone was the most commonly administered NSAID (administered at least once during 15% of pregnancies, n = 30/203, 95% CI 10–15), followed by flunixin (8%, n = 17/203, 95% CI 6–13) then aspirin (1%, n = 2/203, 95% CI 0.3–3).

Overall, of the 95 mares to which at least one medication (excluding post-covering treatments and/or those administered at manual twin reduction) was administered during gestation, 66% (n = 63/95, 95% CI 56–75) were also reported to have suffered at least one veterinary-attended episode of illness or injury at which the reason for prescription of medication(s) was recorded. Antibiotics were most frequently prescribed for the treatment of cellulitis/mud fever (n = 14), trauma to the musculoskeletal system (n = 13), placentitis (n = 10), and mastitis (n = 9). Non-steroidal anti-inflammatory agents were most frequently prescribed for musculoskeletal disease or injury (n = 36) and colic (n = 8). Altrenogest was prescribed for the treatment of placentitis (n = 8) or mastitis (*n*=1) and hyocine was prescribed for the treatment of colic. Medications reported have been administered to mares during gestation that were not reported to have received veterinary treatment for illness or injury were; altrenogest (administered during n = 21 pregnancies), antibiotics (n = 13), sedatives (n = 9), and NSAIDs (n = 3).

Table 3
Summary of medications (excluding post-covering therapeutics and/or those administered at the time of manual twin reduction) reported to have been administered at least once during gestation (last service date to foaling date) for 203 pregnancies in 174 mares on seven farms over two breeding seasons. Proportions and 95% confidence intervals (CI) given of the total number of pregnancies (n = 203).

	Pregnancies (n = 203)		
Medication	n	%	95% CI
Antibiotic	51	25.1	19.6–31.5
NSAID	47	23.1	17.8–29.4
Altrenogest	30	14.8	10.5–20.3
Sedative	14	6.9	4.1–11.2
Hyocine	7	3.4	1.7–6.9
Other[a]	10	4.9	2.7–8.8

NSAID, non-steroidal anti-inflammatory drug; CI, confidence interval, Other[a], silver sulfadiazine (n = 4), omeprazole (n = 2), paraffin oil (n = 1), local anaesthetic (n = 1), prednisolone (n = 1), triamcinolone (n = 1).

4. Discussion

This study utilized data from a birth cohort study to describe the use of reproductive therapeutics and the incidence of disease, injury and medication usage during pregnancy in Thoroughbred broodmares. Findings have updated knowledge by providing up-to-date estimates of the use of reproductive therapeutics in Thoroughbred broodmares. Post-covering treatments were administered to the majority of mares and frequently included antibiotic preparations. Novel estimates were produced which demonstrated a high incidence of disease and medication usage during pregnancy in Thoroughbreds, with over two thirds of mares requiring veteri-

nary intervention at least once for disease or injury during gestation and almost half of mares receiving at least one (excluding post-covering therapeutics and/or those administered at the time of twin manual reduction) medication during gestation.

A study by Rose et al. published in 2018 [2], concluded that the use of reproductive therapeutics in Thoroughbred broodmares appeared to have increased considerably over the last decade [1,2,4]. The present study on the whole supports this, with proportions of mares receiving pre-oestrus medications and post-covering treatments being higher (55% cf. 39% and 73% cf. 62% respectively) than those reported in that study. Interestingly however, the proportion receiving ovulatory agents was significantly lower (64% cf. 92%) in the present study, despite the distributions of mare age, parity and status being similar between the two studies. The study conducted by Rose et al. consisted of a convenience sample of farms based only in the Newmarket area, whereas in the present work, although also using a convenience sample, farms were spread across the UK and Ireland and serviced by a number of different (n = 6) veterinary practices.

Volumes of uterine fluid >2 cm post-covering has been associated with reduced conception rates in broodmares [24,25]. Despite such evidence, in the present study, a notable proportion (37%) of mares reported to have no visible fluid still received at least one post-covering treatment. A finding which raises important questions about therapeutic rationale in these individuals. It was also of interest to note that proportions of mares receiving post-covering treatments did not appear different between mare age categories, suggesting perhaps that older multiparous mares which may be more prone to developing post-covering endometritis, the condition for which post-covering therapy is most commonly utilized [26], did not appear to be being specifically targeted in the present study population. Over two thirds (69%) of all post covering-treatments in the present study included at least one antibiotic, raising yet further questions about therapeutic rationale, when available evidence suggests that the prevalence of bacterial post-covering endometritis in Thoroughbred broodmares is low [2,5,27]. Decision making around the use of post-covering therapeutics in mares is recognized to be challenging, as the short window of time within which treatments can be safely administered often does not allow for data such as culture and sensitivity results to be utilized [3]. In Thoroughbreds there may also be added pressures on decision making due to the desire for mares to conceive as early as possible within a short breeding season, as early-foals have realized better sales prices [28,29] and racing [28,30] performance outcomes when compared to those born later in the season. The continued increase in the use of post-covering therapies as demonstrated by this work, particularly in the absence of fluid, highlights the need for further evaluation of current rationale, particularly where best practice might suggest a more judicial use of antimicrobials and question the need for some treatments [6,31]. Investigation of the influence of current strategies on conception rates, assessments of methods of identifying cases warranting antimicrobial therapy and cost-benefit analyses would all be of benefit to the industry in order to support both therapeutic decision making and antimicrobial stewardship.

Just over a third of mares (34%) in the current study experienced at least one veterinary-attended episode of disease or injury during gestation, with conditions affecting the musculoskeletal system (both infectious, non-infectious and traumatic in origin) being the most commonly reported reason for mares requiring veterinary intervention. Musculoskeletal disease and injury have frequently been reported as the most common cause of mortality and morbidity in other Thoroughbred populations [32–34], however estimates during gestation have not previously been reported.

This study is also, to the authors' knowledge, the first of its type to provide estimates of the incidence of placentitis (5%) and mastitis (4%) requiring veterinary intervention during gestation in Thoroughbred broodmares. It should be considered that due to the nature of the present study where only pregnancies resulting in the birth of a live foal were included, conditions such as placentitis, which is thought to be responsible for around 0.3% of abortions in UK Thoroughbreds [7], may therefore be underestimated. It was interesting to note in the present study that the majority of pregnancies reported to have received medication with no history of veterinary intervention were given altrenogest. Altrenogest is commonly prescribed off-licence to prevent pregnancy failure in the treatment of conditions such as placentitis [35,36]. Therefore, it could be speculated that mares receiving altrenogest with no record of disease or injury, may have had either a previous history or perhaps even findings suggestive of sub-clinical placentitis at routine examination. Findings from this study therefore support the need for further work to evaluate both the incidence of placentitis and the use of altrenogest during gestation in Thoroughbred broodmares.

The current study also provides novel benchmarking of non-reproductive medication usage in pregnant Thoroughbreds, with almost half (47%) of all mares being administered at least one medication during gestation, excluding those administered post-covering and/or following twin reduction. Antibiotics and NSAIDs were most frequently administered, each prescribed at least once in around a quarter of all pregnancies. Despite medications such as phenylbutazone, an NSAID, being commonly used in pregnant mares without reports of catastrophic side effects in terms of loss of the pregnancy, no definitive safety studies have been carried out [37] and foetotoxic effects have been reported in experimental animal models [38]. Given the high levels of medication usage reported in this study, findings support the need for work to further understanding of medication usage during gestation in Thoroughbreds, particularly evaluation of associations with offspring health outcomes.

The main limitations of this work were the retrospective nature of the data, which were not recorded for the purpose of the study and therefore often incomplete, and resultant relatively small sample sizes for some estimate calculations. The self-selection of farms as those willing to participate in the study may affect the generalizability of findings, as participants may not be representative of the source population. The use veterinary records to identify episodes of disease or injury in mares during gestation are likely to underestimate true rates of some diseases in this population, where it is likely that some cases may be managed on farm without veterinary intervention. Some estimates are also likely to be underestimated by the decision to calculate proportions using only the first reported episode of each condition, due to lack of certainty whether repeated episodes of the same condition were continuations or genuine recurrences.

5. Conclusions

There is a continuing trend for the use of reproductive therapeutics, particularly post-covering treatments containing antimicrobials in the majority of Thoroughbred broodmares, including in the absence of intrauterine fluid, highlighting important knowledge gaps around decision making and cost-benefits of current strategies. Occurrence of disease and medication usage during gestation are high, warranting additional investigation, particularly in the context of associations with offspring health outcomes.

Ethics statement

Ethical approval was granted by the Royal Veterinary College's Clinical Research Ethical Review Board (URN: 2018 1843).

Authors' declarations of competing interests

None

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CRediT authorship contribution statement

Rebecca Mouncey: Conceptualization, Methodology, Software, Formal analysis, Investigation, Data curation, Writing – original draft, Visualization. **Juan Carlos Arango-Sabogal:** Formal analysis, Writing – review & editing. **Amanda de Mestre:** Conceptualization, Writing – review & editing, Funding acquisition. **Kristien Verheyen:** Conceptualization, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jevs.2022.104104.

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