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Incidence and causes of pregnancy loss after day 70 of gestation in Thoroughbreds

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Summary

Background: Pregnancy loss after day 70 of gestation manifests as abortion, stillbirth or perinatal death. While previous studies have reported the diagnoses of laboratory submissions, none have quantified the incidence and causes of abortions, stillbirths and perinatal mortality at a population level.

Objectives: To report the incidence and causes of pregnancy loss after day 70 of gestation in a cohort of Thoroughbreds.

Study design: Retrospective cohort study.

Methods: Outcomes of day 70 pregnancies were collected from eight Thoroughbred farms over the 2013-2017 breeding seasons. Stud, veterinary and laboratory records were supplemented with publicly available data. Cause of loss was categorised using custom criteria.

Results: Data were collected on 3,586 pregnancies from 1,802 mares. The incidence risk of a pregnancy failing to produce a live foal at 24 hours post parturition was 7.3% (95% confidence interval (CI) 6.5-8.2, equating to 7.3 cases per 100 day-70 pregnancies). The incidence of pregnancy loss between day 70 and 300 of gestation, day 301 to 315 and stillbirth/perinatal death was 4.0% (95% CI 3.4-4.7), 0.3% (95% CI 0.2-0.6) and 1.4% (95% CI 1.1-1.9), respectively. Of the pregnancy losses where tissue was available, 61.1% were submitted for *post mortem* examination. The incidence risk of loss due to umbilical cord-related pathologies was 1.5% (95% CI 1.1-1.9), 0.4% (95% CI 0.2-0.6) for non-infectious placental disease and 0.3% (95% CI 0.2-0.6) for both infectious placentitis and Equine Herpesvirus infection. No primary diagnosis was made in 11.2% of the cases which underwent full *post mortem* examination.

Main limitations: It was not possible to differentiate between intra-partum stillbirth and early post-partum death.

Conclusion: Pregnancy loss after day 70 of gestation is a significant source of loss in the Thoroughbred with umbilical cord-related pathologies being the most commonly diagnosed cause. Reporting the incidence of pregnancy loss at a population level with clear case definitions will allow for accurate global comparisons.

Introduction

Equine pregnancies can fail throughout gestation with different, distinct, pathologies at play. The incidence of reported pregnancy loss has been quantified using data from Weatherbys' Return of Mares [1; 2] or cohort studies [3; 4], with losses after 42 days of gestation ranging from 7.4%-8.9% of confirmed pregnancies. Direct comparison between reproductive efficiency studies however is difficult due to the variation in case definitions, with the end point often being an ambiguous descriptor such as "term" or "foaling" [4-6]. Due to there being a number of different pathologies that can result in pregnancy loss in late gestation and the early neonatal period, it is important to define whether a loss is an abortion, stillbirth or perinatal death and then define the proportion of cases attributed to each. Quantifying the

losses using clear case definitions would enable accurate identification to where management strategies should be targeted and allow for temporal and geographic comparisons.

The causes of abortion can be grouped broadly into infectious and non-infectious in origin. The infectious causes reported in the UK consist primarily of cases of ascending bacterial placentitis and Equine Herpesvirus (EHV) (serotypes 1 and 4) however the majority of UK abortion case diagnoses fall into the non-infectious category [1; 2; 7; 8]. This finding is in contrast to international studies where infectious causes account for the majority of diagnosed cases; 49% in Italy, 47.4% in France, 29.6% in the USA and 26.8% in Germany [9-12]. The most commonly diagnosed cause of pregnancy loss in the UK is umbilical cord torsion (UCT) with vascular compromise, accounting for 38.8-46.2% of cases submitted to a diagnostic laboratory [2; 7]. Additionally, in recent years there have been a number of novel causes of abortion described outside the UK including placentitis due to *Chlamydia psittaci* infection*,* Equine Amnionitis and Fetal Loss following *Orcrogaster linifer* ingestion and Mare Reproductive Loss Syndrome caused by *Maracosoma americanum* [13-18]. Whilst neither *Orcrogaster linifer* nor *Maracosoma americanum* are found in the UK, the European oak processionary moth (OPM) (*Thaumetopoea processionea)* is present. To date, the larvae forms of the OPM have not been linked to abortion in the horse however the setae are known to cause a number of other clinical signs including labial angiooedema, conjunctivitis, ptyalism and respiratory distress. [19-21].

It is evident through review of the literature that there is a need for a standardised approach when quantifying and diagnosing pregnancy losses. Prior studies on the case proportion of different diagnoses have been performed utilising material submitted for pathological examination at diagnostic laboratories, and may not reflect incidence at the population level. For instance, these studies do not take into account either those cases not submitted for diagnosis or the absolute number of losses in the population. Studies reporting incidence at a population level would allow for more accurate comparison of regional differences and in turn allow for exploration of risk factors; both for different reproductive loss phenotypes and the common primary diagnoses. This study aimed to report the incidence and causes of pregnancy loss after day 70 of gestation at a population level in a large cohort of Thoroughbreds. Additionally, the presentation of the loss and form of investigation will also be described.

Materials and Methods

Study population

This was a retrospective cohort study collecting data from five breeding seasons (2013-2017). A convenience sample of eight Thoroughbred stud farms was recruited, with data on all the mares cared for under their management made available. Stud records were supplemented with the veterinary practice records, diagnostic laboratory reports, Weatherbys' Return of Mares data (the Thoroughbred General Studbook records) and information extracted from the online Racing Post database (www.racingpost.co.uk). The inclusion criteria used were a Thoroughbred mare covered by a UK- or Ireland-based stallion, pregnant at day 70 of gestation. Day 70 of gestation was chosen in order to exclude losses diagnosed at the day 65 scans which were likely a result of pathologies established during the early pregnancy period [3].

Data collection

Mare data collected included year of birth, stud farm, year of cover, last service date and pregnancy outcome. When a pregnancy loss occurred the day the loss was diagnosed, the investigation carried out and results from the laboratory report were recorded. Data were coded for anonymity, with the codes maintained in a password-protected file. Data were entered into Microsoft Excel (version 2016[1]) and exported into SPSS (Version 26.0[2]) for descriptive analysis.

Foaling outcome was recorded as i) live foal at 24 hours post parturition, ii) pregnancy loss diagnosed up to day 300 of gestation, iii) pregnancy loss diagnosed between day 301 and 315 of gestation and iv) stillborn/perinatal death, defined as loss diagnosed between 316 days gestation and 24 hours post parturition. Exact time of death within the 24 hours post parturition was not available using the retrospective data. When a loss occurred it was categorised as: no abortus material available for examination (i.e. mares that were pregnant at day 70 and subsequently palpated not in foal), abortus material was available and only EHV PCR was performed, abortus material was available and a full *post mortem* examination by a pathologist was performed or abortus material was available but no known formal investigation took place.

The primary diagnosis from the pathologists' written *post mortem* report was categorised using custom criteria (Table S1), produced using peer-reviewed publications [1; 7; 14; 15]. One author (J.R.) categorised the diagnoses of all of the *post mortem* investigated pregnancy losses, and to validate the approach a second author (A.D.M.) blinded to the assigned categories graded a subset. These 35 categories were further grouped into umbilical cord-related pathologies, infectious placentitis (not including Equine Herpesvirus), Equine Herpesvirus infections, non-infectious placental disease, pathologies of fetal origin and no primary diagnosis.

Results

Descriptive statistics of the population

Data were collected on 3,586 pregnancies from 1,802 mares over five breeding seasons. Data were not available for the 2013 and 2014 seasons for one farm. Mares were covered by a total of 132 stallions located in the UK and Ireland. The median mare age was 8 years old (interquartile range [IQR] 6-11, range 3-23 years) and the median stallion age was 11 years old (IQR 7-14.8, range 3-25). Of the 3,586 pregnancies, 16.5% were from maiden mares, 66.1% foaling mares, 13.8% barren and 3.7% of mares were rested the previous season. The median number of mares per farm over the five years was 79 (interquartile range 55-107). Data were available for one breeding season for 813 mares, two years for 447 mares, three years for 334 mares, four years for 163 mares and five years for 45 mares.

Incidence and causes of pregnancy loss

The outcomes of the day 70 pregnancies are presented in Table 1. An outcome was available for 3,516 pregnancies, with the remaining 70 pregnancies (2.0%) being lost to follow up. The incidence of day 70 pregnancies which failed to produce a live foal at 24 hours post parturition was 7.3% (n=257, 95% confidence interval [CI] 6.5-8.2), ranging from 5.9% to 8.1% between 2013 and 2017. This equates to 7.3 cases per 100 day-70 pregnancies. Of the pregnancies which failed to produce a live foal 141 were diagnosed between day 70 and 300 of gestation, 12 between day 301 and 315 and 50 after day 315 representing a population incidence risk of 4.0% (95%CI 3.4-4.7), 0.3% (95% CI 0.2-0.6) and 1.4% (95%CI 1.1-1.9), respectively. In terms of cases per 100 pregnancies, this equates to four cases of loss diagnosed between day 70 and 300 of gestation, 0.3 cases diagnosed between day 301 and 315 and 1.4 cases diagnosed after day 315. Pregnancy loss resulting from mare death during gestation accounted for 21 of the losses, an incidence risk of 0.6% (95% CI 0.4-0.9), or 0.6 cases of mare death per 100 day 70 pregnancies. A further 33 (incidence risk 0.9% [95% CI 0.6-1.3]) pregnancies were known to have failed to produce a live foal but the gestation age at the time of loss or any further information was not available. Of the mares which suffered pregnancies losses, 13 suffered a loss in two seasons and two mares suffered losses in three seasons. Of the mares that suffered multiple pregnancy losses, only four of the losses were submitted for *post mortem* examination in successive years, with no repeat categorised causes of loss observed within a mare. Pregnancy losses were observed on all the farms, with two farms having one year each where they did not observe any pregnancy losses. The yearly farm incidences of loss between day 70 and 300 of gestation ranged from 0.0% (one-sided 97.5% CI 0.0-5.3) to 16.0% (95% CI 4.5-36.1), 0.0%

(one-sided 97.5% CI 0.0-1.9) to 2.6% (95% CI 0.1-13.5) for losses between day 301 and 315 and 0.0% (one-sided 97.5% CI 0.0-1.9) to 11.1% (95% CI 4.2-22.6) for losses after day 315. This equates to between zero and 16, 2.6 and 11.1 cases per 100 day 70 pregnant mares respectively. The live foal incidence of day 70 pregnancies at 24 hours post parturition was 92.7% (n=3,259, 95% CI 91.8-93.5), or 92.7 foals per 100 day 70 pregnancies.

Of the 153 pregnancy losses diagnosed prior to day 315 of gestation, 67.1% (n=98) were submitted to a diagnostic laboratory for investigation (full *post mortem* examination or EHV PCR only), 28% (n=48) were not available for submission due to no abortus material being found and 4.8% (n=7) of the cases had no known diagnostic investigation. When a stillbirth/perinatal death was observed, 70% (n=35) of cases were submitted for diagnostic investigation, 20% (n=10) were not submitted for investigation and in 5% (n=5) no fetal or placental tissue was found.

Table 2 presents the grouped categories attributed to the losses which underwent *post mortem* investigation and the population incidence risk. Umbilical cord-related (UC) pathologies accounted for the highest proportion of grouped diagnoses at 44.8% (n=52) and had an incidence risk of 1.5% (95% CI 1.1-1.9) between day 70 of gestation and 24 hours post parturition, equating to 1.5 cases per 100 day 70 pregnancies. Umbilical cord-related pathologies included 23 cases of UCT, 28 cases of suspected UCT and one case of "other" pathologies involving the UC. Non-infectious placental disease accounted for 11.2% (n=13) of the cases, with a population incidence risk of 0.4% (95% CI 0.2-0.6), or 0.4 cases per 100 day 70 pregnancies. The non-infectious placental diseases comprised of cases with morphological changes including; placental oedema, villous atrophy and chorioallantoic mineralisation and ischaemic necrosis not associated with UC pathologies. Infectious placentitis was diagnosed in 10.3% (n=12) of cases, with a population incidence risk of 0.3% (95% CI 0.2-0.6), equating to 0.3 cases per 100 day 70 pregnancies. There were two cases of ascending bacterial placentitis, five cases of suspected haematogenous (non-ascending) bacterial placentitis, one case of ascending fungal placentitis and in four cases neither the pathogen nor the distribution of lesions was identified in the written report. Pathology of fetal origin accounted for 5.2% of *post mortem* examined cases (n=6) with a population incidence risk of 0.2% (95% CI 0.1-0.4), or 0.2 cases per 100 day 70 pregnancies. Fetal origin cases included carpal contracture, fetal oversize, neonatal sepsis (with no comment on placental disease), scoliosis and facial deformities. No primary diagnosis was assigned in 11.2% (n=13) of the *post mortem* investigations due to insufficient material submitted (e.g. fetus but no fetal membranes or vice versa), excessive autolysis or insufficient pathological findings. The overall incidence risk for Equine Herpesvirus-related loss was 0.3% (n=11, 95%

CI 0.2-0.6), or 0.3 cases per 100 day 70 pregnancies, but showed yearly variation ranging from 0.0% to 0.9% in 2015 (zero to 0.9 cases per 100 day 70 pregnancies).

Discussion

This is the first study to date detailing the incidence risk of different causes of mid and late term pregnancy loss. The findings provide a valuable benchmark for comparison, both globally and temporally within Thoroughbred populations. The most commonly diagnosed cause of pregnancy loss after day 70 of gestation was UC-related pathologies, accounting for 1.5% of all day 70 pregnancies, and 44.8% of those submitted for full *post mortem* examination. This equates to 1.5 UC-related losses per 100 pregnant mares. Infectious placentitis, commonly reported in other geographic regions [10; 11], was only a small contributor to abortion in this cohort with an incidence risk of 0.3%, or 0.3 losses per 100 pregnant mares. Encouragingly, in this population, there were no cases identified of the novel causes of abortion that have been described outside the UK in recent years [13-17; 22], nor any cases exhibiting lesions suggestive of *Leptospira* spp. infection.

The incidence of a pregnancy failing to produce a live foal between day 70 of gestation and 24 hours post parturition was 7.3%, which included 0.6% due to mare death. The outcome of the pregnancy was unknown in 70 cases (2.0%), which included mares that did not remain residing on the stud for the duration of their pregnancy, most likely due to either being sold and/or exported. The incidence of mare deaths was lower than previously reported for the 2002 breeding season [4]. Allen *et al.*'s study of reproductive efficiency in UK Thoroughbreds over the 2002 breeding season reported 8.9% of day 15 pregnancies failed between day 42 of gestation and foaling (including stillbirths) [4], not directly comparable to our study as it additionally included losses between 42 and 70 days. Work done by Rose *et al.* over the 2013 and 2014 breeding seasons found that 1.6% of the pregnancies in their population were lost between 42 and 65 days of gestation [3]. Whilst comparison between the findings of these reproductive efficiency studies is complicated due to the differing time periods and definitions used, there is no evidence to show or suggest improvement or deterioration in pregnancy loss figures over the last 15 years.

Comparison between the incidence of pregnancy loss in this study and those of previous work should take into account the study population. Although the average mare ages were similar compared to previous studies [4; 5], the proportion of barren mares in this study population was lower [4; 5]. While the pregnancy is the unit of interest, mare status can have a significant impact on pregnancy loss [4; 5]. The

inclusion criteria of this study may have led to a "healthy worker effect", biasing the population to those that can conceive and maintain the pregnancy past day 70 of gestation. No significant yearly variation was observed in the incidence risk of pregnancy loss, as indicated by overlapping confidence intervals, however there has been an increase, from 5.9% in 2013 to 7.5% in 2017. While some yearly variation is expected it would be prudent to monitor this and if this continues explore the causes behind these changes. Whilst additional data collection from other diagnostic laboratories and veterinary practices could help define the 0.9% of day 70 pregnancies that failed to produce a live foal but where no further information was available, the percentage of missing outcomes was considerably lower than in previous reports [4; 23; 24].

The findings of this study provide an important benchmark; however, it is important to recognise the animals in this study were all Thoroughbreds residing at intensively managed medium to large stud farms in the UK or Ireland. The mares and pregnancies in this study were closely managed throughout conception, gestation and parturition. Therefore, extrapolating these data to less intensively managed horses should be done with care. We are not aware of any studies reporting the incidence of causes of abortion in other breeds, although some information can be gleaned from laboratory-based studies reporting on mixed populations [25]. There have been case reports of umbilical cord torsion in breeds other than the Thoroughbred [26, 27], and differences in the length of the amniotic portion of the umbilical cord identified between breeds [28]. Whether this leads to breed pre-disposition for UCT is not known therefore care must be taken in applying the findings of this study to other breeds

The gestational age used to differentiate between miscarriage and stillbirth in human medicine is pregnancy loss "before fetal viability is achieved" [29]. Unlike in humans, equine fetal viability *ex utero* is reached comparatively much later in gestation, due to not only the development of the fetus itself, but also the availability of medical interventions and the economic considerations. Previous studies have presented equine abortion, or the "pre-viable period", as pregnancy loss prior to day 300 in gestation [30, 31]. In addition to reporting the losses up to day 300 in gestation, this study quantified those occurring between day 301 and 315. This grouping was chosen as a distinct phenotype from those lost after day 315 following consultation with several large hospital units who manage neonatal Thoroughbreds. Day 315 was selected due to the perceived increased risks in this population of failure to survive to discharge or, if so, reach athletic potential compared to those born after day 315. These considerations therefore may influence management decisions on a live yet compromised foal. The incidence of pregnancy loss up to day 315 of gestation was three-fold higher when compared with stillbirth/perinatal death, indicating fetal demise *in utero* is much more common than complications around the time of parturition consistent with

published work [4]. It was difficult to accurately discern retrospectively from the veterinary and pathology reports, those foals that died prior to parturition, or those that died during or soon after parturition, therefore stillbirth and perinatal death were combined for the purpose of this study.

Of the pregnancy losses occurring between day 70 and 315 of gestation, no fetal or placental material was found for 31.4% compared to 10% of the stillbirths/perinatal deaths. The losses were diagnosed on routine reproductive examinations, commonly occurring at the start of October in the UK due to the reproductive practices and stallion contracts. Little has been reported about the physiology of these "silent" pregnancy losses occurring between day 70 of gestation and the October checks, and while it is often hypothesised that they are reabsorbed further work needs to be carried out. Encouragingly, 93.3% of these losses where tissue was available were submitted for EHV screening although this submission rate reduced to 77.8% for the stillbirths and perinatal deaths. The Horseracing Betting Levy Board Code of Practice recommends that all abortions, stillbirths and foal deaths within 14 days of birth that could be EHV related, should be submitted to a diagnostic laboratory for testing [32]. This lower submission rate for stillbirths and perinatal deaths may be a reflection of a clear clinical diagnosis such as a dystocia or congenital defect, however EHV screening should always be encouraged for disease surveillance. To the authors' knowledge, this is the first study to report the proportion of pregnancy losses submitted for diagnostic examination, providing valuable insight into how representative laboratory studies are of the population. Of the pregnancy losses where material was available for examination, only 61.1% of these underwent a full *post mortem* examination. The reasons for this are likely multifactorial and may include considerations such as finances, state of preservation of the material, clinical presentation and perceived benefit of a specific diagnosis.

Umbilical cord-related pathologies were the most frequently diagnosed cause of pregnancy loss, accounting for 44.8% of the *post mortem* examined losses and an incidence of nearly 4-fold higher than the next most common cause, non-infectious placental disease, accounting for 11.2% of *post mortems*. Umbilical cord-related pathologies encompass torsion of the umbilical cord (UCT) which leads to occlusion of the blood supply to the fetus, excessively long umbilical cords associated with cervical pole ischaemic necrosis, abnormal yolk sac remnants and cords encircling a limb [1; 7; 33]. Here UCT was the most common presentation and accounted for 98% of the grouped cases. This proportion of cases attributed to UC pathologies is in line with the previous figures from Newmarket diagnostic laboratories, which range between 38.8%-46.2%, showing no change in 20 years [2; 7]. This is markedly more than the peer-reviewed reports from Kentucky, USA, which attributed only 3.4% of their submitted losses up to 24 hours post parturition to UC pathologies and 22.6% reported in Australia [11; 34]. The limitation of these studies

however is the reporting of submitted case proportions as opposed to a population incidence report and a current lack of a clear definition of what defines UCT with vascular compromise. In this study, the incidence risk of an UC-related pregnancy loss was 1.5%, a finding that can now be compared over time and with other breeding centres.

The diagnosed causes of pregnancy loss, excluding UC-related pathologies, were broadly equal (0.2-0.4%) when evaluating the incidence risk. In contrast to reports from outside the UK, infectious placentitis was not a large contributor to pregnancy loss in this population, [10; 11; 35] for reasons that are not clear. Future work should compare the disease prevalence through gestation between countries in order to ascertain whether the variation is a result of treatment success or a true difference in prevalence. Additionally, the comparative absence in the UK of a number of known causes of placentitis could go some way to explaining the differences. Equine Herpesvirus as a cause of pregnancy loss showed yearly variation, with 2015 conceptions having an increased incidence risk of pregnancy loss with no overlap of confidence interval, reflecting the highly infectious nature of the virus which can result in multiple abortions on a single premises ("abortion storms"). Vaccination, laboratory testing and good management practices have largely minimised the number of pregnancy losses occurring [36], however, elsewhere EHV-1 abortions accounting for as much as 24% of the diagnosed cases have been reported [37]. The proportion of cases which underwent *post mortem* investigation but where no primary diagnosis was made was 11.2%, which is lower than findings reported elsewhere [10; 11; 37], and were a result of incomplete tissue submission, extensive autolysis and absence of pathological findings in the report.

The incidence of pregnancy loss after day 70 of gestation has not changed in the last 15 years, with loss due to UC-related pathologies diagnosed in 1.5% of all day 70 pregnancies, remaining the most commonly diagnosed cause of pregnancy loss in UK Thoroughbred mares. In contrast, the incidence of infectious placentitis was found to be 0.3% and therefore an uncommon cause of pregnancy loss in this population. However, it is unclear if this is due to successful treatment of cases or a lower prevalence compared to other populations. The findings of this study indicate further work is required, exploring the risk factors and underlying mechanisms that lead to pregnancy loss due to UCT in order to improve the reproductive efficiency in the UK Thoroughbred industry. Reporting the incidence of pregnancy losses at a population level with the use of clear case definitions will allow for accurate global comparisons, aiding in identification of risk factors for abortion and the inciting causes.

Authors' declaration of interests

No competing interests have been declared.

Ethical animal research

Ethical approval was granted by the Royal Veterinary College's Clinical Research Ethical Review Board (URN 2017 1660-3).

Informed consent

Informed consent was obtained for inclusion of the animals in this study.

Data accessibility statement

The data that support the findings of this study are openly available in RVC Research Online at http://researchonline.rvc.ac.uk/id/eprint/12701

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Authorship

J. Roach: conceptualisation, methodology, investigation, formal analysis, writing of the original draft manuscript, visualisation. A. de Mestre: conceptualisation, methodology, writing of the original draft manuscript, supervision, funding acquisition**,** project administration. K. Verheyen: conceptualisation, methodology, writing – review and editing, supervision, funding acquisition. A. Foote: resources, methodology, writing – review and editing. K. Smith: conceptualisation, methodology, writing – review and editing, funding acquisition.

Supporting Information

Table S1: Criteria for categorising diagnoses assigned in pathologist written reports of *post mortem* examinations of equine pregnancy losses and perinatal deaths using key descriptors (†not routinely tested for in UK laboratories, ‡not present within the UK)

Manufacturers' addresses

[1]Microsoft Corporation, Redmond, Washington, USA.

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Table 1: *Incidence risk of pregnancy outcomes, the day of diagnosis and form of investigation of pregnancy losses between day 70 of gestation and 24 hours post parturition in a cohort of 3,516 Thoroughbred pregnancies managed by UK based farms over the 2013-2017 breeding seasons. (Brackets contain n number and binomial exact 95% confidence interval [CI], †denotes one-sided 97.5% confidence interval).*

Pregnancy outcome	**2013**	**2014**	**2015**	**2016**	**2017**	**Total**
Live foal % (n, CI)	**94.0 (601, 91.9-95.8)**	**93.1 (474, 90.6-95.2)**	**92.3 (710, 90.2-94.1)**	**91.9 (739, 89.8-93.7)**	**92.5 (735, 90.4-94.2)**	**92.7 (3259, 91.8-93.5)**
No Live Foal % (n, CI)	**5.9 (38, 4.2-8.1)**	**6.9 (35, 4.8-9.4)**	**7.7 (59, 5.9-9.8)**	**8.1 (65, 6.3-10.2)**	**7.5 (60, 5.8-9.6)**	**7.3 (257, 6.5-8.2)**
70-300 days gestation	3.1 (20, 1.9-4.8)	3.5 (18, 2.1-5.5)	4.6 (35, 3.2-6.3)	3.5 (28, 2.3-5.0)	5.0 (40, 3.6-6.8)	4.0 (141, 3.4-4.7)
No abortus material	*0.9 (6, 0.3-2.0)*	*0.6 (3, 0.1-1.7)*	*1.7 (13, 0.9-2.9)*	*1.0 (8, 0.4-2.0)*	*2.1 (17, 1.3-3.4)*	*1.3 (47, 1.0-1.7)*
Full post mortem	*2.0 (13, 1.1-3.5)*	*2.8 (14, 1.5-4.6)*	*2.2 (17, 1.3-3.5)*	*2.2 (18, 1.3-3.5)*	*2.4 (19, 1.4-3.7)*	*2.3 (81, 1.8-2.9)*
EHV PCR with vet notes	*0.0 (0, 0.0-0.6†)*	*0.2 (1, 0.0-1.1)*	*0.1 (1, 0.0-0.7)*	*0.1 (1, 0.0-0.7)*	*0.4 (3, 0.1-1.1)*	*0.2 (6, 0.1-0.4)*
No known diagnostic investigation	*0.2 (1, 0.0-0.9)*	*0.0 (0, 0.0-0.7†)*	*0.5 (4, .1-1.3)*	*0.1 (1, 0.0-0.7)*	*0.1 (1, 0.0-0.7)*	*0.2 (7, 0.1-0.4)*
301-315 days gestation	0.3 (2, 0.0-1.1)	*0.4 (2, 0.0-1.4)*	*0.1 (1, 0.0-0.7)*	0.5 (4, 0.1-1.3)	*0.4 (3, 0.1-1.1)*	0.3 (12, 0.2-0.6)
No abortus material	*0.0 (0, 0.0-0.6†)*	*0.2 (1, 0.0-1.1)*	*0.0 (0, 0.0-0.5†)*	*0.0 (0, 0.0-0.5†)*	*0.0 (0, 0.0-0.5†)*	*0.0 (1, 0.0-0.2)*
Full post mortem	0.3 (2, 0.0-1.1)	*0.2 (1, 0.0-1.1)*	*0.0 (0, 0.0-0.5†)*	0.5 (4, 0.1-1.3)	*0.4 (3, 0.1-1.1)*	*0.3 (10, 0.1-0.5)*
EHV PCR with vet notes	*0.0 (0, 0.0-0.6†)*	*0.0 (0, 0.0-0.7†)*	*0.1 (1, 0.0-0.7)*	*0.0 (0, 0.0-0.5†)*	*0.0 (0, 0.0-0.5†)*	*0.0 (1, 0.0-0.2)*
No known diagnostic investigation	*0.0 (0, 0.0-0.6†)*	*0.0 (0, 0.0-0.7†)*	*0.0 (0, 0.0-0.5†)*	*0.0 (0, 0.0-0.5†)*	*0.0 (0, 0.0-0.5†)*	*0.0 (0, 0.0-0.1†)*
316 days gestation-24 hours post parturition	0.6 (4, 0.2-1.6)	0.8 (4, 0.2-2.0)	2.1 (16, 1.2-3.4)	2.0 (16, 1.1-3.2)	1.3 (10, 0.6-2.3)	1.4 (50, 1.1-1.9)
No abortus material	*0.0 (0, 0.0-0.6†)*	*0.0 (0, 0.0-0.7†)*	*0.1 (1, 0.0-0.7)*	*0.2 (2, 0.0-0.9)*	*0.3 (2, 0.0-0.9)*	*0.1 (5, 0.0-0.3)*

Full post mortem	*0.5 (3, 0.1-1.4)*	*0.4 (2, 0.0-1.4)*	*1.3 (10, 0.6-2.4)*	*0.4 (3, 0.1-1.1)*	*0.9 (7, 0.4-1.8)*	*0.7 (25, 0.5-1.0)*
EHV PCR with vet notes	*0.0 (0, 0.0-0.6†)*	*0.4 (2, 0.0-1.4)*	*0.3 (2, 0.0-0.9)*	*0.7 (6, 0.3-1.6)*	*0.0 (0, 0.0-0.5†)*	*0.3 (10, 0.1-0.5)*
No known diagnostic investigation	*0.2 (1, 0.0-0.9)*	*0.0 (0, 0.0-0.7†)*	*0.4 (3, 0.1-1.1)*	*0.6 (5, 0.2-1.4)*	*0.1 (1, 0.0-0.7)*	*0.3 (10, 0.1-0.5)*
Unknown	0.9 (6, 0.3-2.0)	1.2 (6, 0.4,2.5)	0.7 (5, 0.2-1.5)	1.5 (12, 0.8-2.6)	0.5 (4, 0.1-1.3)	0.9 (33, 0.6-1.3)
Mare died	0.9 (6, 0.3-2.0)	1.0 (5, 0.3-2.3)	0.3 (2, 0.0-0.9)	0.6 (5, 0.2-1.4)	0.4 (3, 0.1-1.1)	0.6 (21, 0.4-0.9)
Total (n)	**639**	**509**	**769**	**804**	**795**	**3516**

Table 2: *Incidence risk of causes of equine pregnancy losses between day 70 of gestation and 24 hours post parturition in a cohort of 3,516 Thoroughbred pregnancies managed by UK based farms over the 2013-2017 breeding seasons (brackets contain n number and binomial exact 95% confidence interval [CI], †excluding Equine Herpesvirus infections, ‡denotes one-sided 97.5% confidence interval).*

Diagnosis % (n, CI)	**2013**	**2014**	**2015**	**2016**	**2017**	**Population incidence risk**
Umbilical cord related pathology	1.7 (11, 0.9-3.1)	1.6 (8, 0.7-3.1)	0.8 (6, 0.3-1.7)	1.5 (12, 0.8-2.6)	1.9 (15, 1.1-3.1)	**1.5 (52, 1.1-1.9)**
Infectious placentitis†	0.5 (3, 0.1-1.4)	0.2 (1, 0.0-1.1)	0.4 (3, 0.1-1.1)	0.1 (1, 0.0-0.7)	0.5 (4, 0.1-1.3)	**0.3 (12, 0.2-0.6)**
Non-infectious placental disease	0.3 (2, 0.0-1.1)	0.4 (2, 0.0-1.4)	0.5 (4, 0.1-1.3)	0.4 (3, 0.1-1.1)	0.3 (2, 0.0-0.9)	**0.4 (13, 0.2-0.6)**
Equine Herpesvirus infection	0.0 (0, 0.0-0.6‡)	0.0 (0, 0.0-0.7‡)	0.9 (7, 0.4-1.9)	0.1 (1, 0.0-0.7)	0.4 (3, 0.1-1.1)	**0.3 (11, 0.2-0.6)**
Pathology of fetal origin	0.0 (0, 0.0-0.6‡)	0.2 (1, 0.0-1.1)	0.3 (2, 0.0-0.9)	0.1 (1, 0.0-0.7)	0.3 (2, 0.0-0.9)	**0.2 (6, 0.1-0.4)**
No primary diagnosis	0.3 (2, 0.0-1.1)	0.1 (5, 0.3-2.3	0.0 (0, 0.0-0.5‡)	0.5 (4, 0.1-1.3)	0.3 (2, 0.0-0.9)	**0.4 (13, 0.2-0.6)**
No written laboratory report	0.0 (0, 0.0-0.6‡)	0.0 (0, 0.0-0.7‡)	0.7 (5, 0.2-1.5)	0.4 (3, 0.1-1.1)	0.1 (1, 0.0-0.7)	**0.3 (9, 0.1-0.5)**
Total incidence	**2.8 (18, 1.7-4.4)**	**3.3 (17, 2.0-5.3)**	**3.5 (27, 2.3-5.1)**	**3.1 (25, 2.0-4.6)**	**3.6 (29, 2.5-5.2)**	**3.3 (116, 2.7-3.9)**
Total pregnancies (n)	**639**	**509**	**769**	**804**	**795**	**3516**