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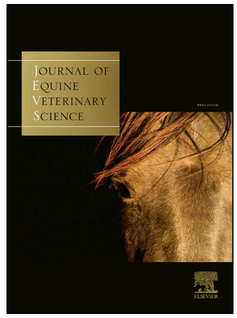

Laminitis: Risk factors and outcome in a group of Danish horses

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Laminitis: Risk factors and outcome in a group of Danish horses

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Abstract

Reasons for performing study: Recent systematic reviews have highlighted the lack of quality information with respect to the epidemiology of equine laminitis.

Objectives : To identify in Denmark the risk factors for new (i.e. not believed to have suffered from laminitis previously) cases of laminitis (NL) and to look at the outcome and incidence of repeated episodes of laminitis in these animals as well as those which had previously suffered an episode of laminitis (i.e. chronic cases) over the following 12 months.

Methods: Information was obtained from 110 veterinary diagnosed cases of laminitis (69 new and 41 chronic) and 80 control animals (the next non-laminitic horse/pony seen by that participating practice). All animals were followed for up to one year. Univariable and multivariable conditional logistic regression was conducted for the NL case control pairs. Variables were retained within the final multivariable models if the likelihood ratio p-value was < 0.05.

Results: There was no association between sex or gender and laminitis. A recent change of grass, being on what was considered high quality grass and being a cold-blooded type, <149cm (i.e. Shetland, Fell, Welsh, or Dartmoor pony, Icelandic horse, Norwegian fjords, or a mix of these breeds) were all significant risk factors for laminitis. Although cresty neck score (CNS), and body condition Score (BCS), were significantly associated with NL at the univariable screening stage, they were found to be confounders of breed and each other during the multivariable model building process. Other factors such as weight, and estimated starch intake were not found to be significant .Thirty three percent of all the laminitis cases had been humanely destroyed within 12 months of diagnosis, mainly for laminitis associated reasons, compared with only 7.5% of the controls (none for laminitis associated reasons).

Conclusions and potential Relevance: This study confirms the importance of grass turn out and breed on laminitis risk. Horses in work at the time of diagnosis as well as those diagnosed in the winter and spring were more likely to be humanely destroyed within the next 12 months than those not in work or diagnosed in the autumn and summer.

Conflicts of interest

The authors do not have any conflict of interest.

Introduction

Laminitis is a systemic condition that manifests in the foot and results in varying degrees of pain, lameness and debilitation (Pollitt 2004). However, laminitis may best be regarded as a syndrome rather than a single disease entity because there are multiple inciting causes and possibly pathophysiological pathways (Harris 2012). Currently it is considered that laminitis can be divided into three main categories (Geor & Harris 2013a): 1) sepsis/systemic inflammatory conditions 2) endocrine/metabolic and 3) mechanical overload. Being able to identify those animals at increased risk of laminitis as well as the potential risk factors is obviously key to reducing the incidence of this condition (Harris et al 2009). Recent systematic reviews, however, have highlighted the lack of quality information with respect to the epidemiology of equine laminitis, including data on prevalence, inciting causes and risk factors (Wylie et al., 2011 a,b). The studies, that are available, suggest that factors associated with the individual animal as well as their management may be key as illustrated by the most recent published UK owner-reported survey (Wylie et al 2013). This work suggested that the risk of laminitis was increased in the summer and winter compared with the spring and autumn and in horses that had recently gained weight, had an owner reported history of previous laminitis, lameness or soreness after farriery or had a concurrent endocrinopathy. In addition, there were certain managemental factors associated with increased risk.

Having suffered a previous bout of laminitis, however, may be a confounding issue in such studies, as it is likely to result in underlying physiological or metabolic changes that may change the risk factors from those associated with naive cases of laminitis. Another potential confounding factor in the previous study by Wylie et al was the use of owner only reporting. The aim of this case-control study, therefore, was to identify risk factors for animals suffering laminitis for the first time in Denmark using veterinarians in equine practice. Additionally animals that had suffered any episode of laminitis, whether for the first time or following one or more previous episodes, were monitored over the subsequent 12 month period in order to record the outcome and incidence of repeated episodes in these two subgroups.

Material and methods

Veterinarians in 20 equine only practices throughout Denmark participated. Following identification of a laminitis case based on clinical examination (backed by clinical guidance from the study website) the veterinarian registered the horse and owner (with their permission) via an online database. The next non-laminitic horse/pony (within +/- 2 years of age of this laminitis case), seen by that participating practice was registered as the matched control. Case-control pairs were therefore matched according to season, age, and geographical region. Unfortunately not all the cases were matched by their reporting veterinarian resulting in information being collected from 110 cases and 80 controls between June 2009 and September 2010 and then followed for up to one year. Animals <1yr of age were excluded from the study as were those that developed laminitis during a stay at an equine hospital.

Information collected by the Consulting Veterinarian

The veterinary surgeon classified the case as either being a new, acute (NL) or a chronic laminitic case. To be included as a NL, the horse/pony had to have suffered an acute onset of lameness in one or more feet accompanied by an increased digital pulse amplitude and/or warm feet without any hoof capsule signs (e.g. concave hoof wall, "founder rings" [growth rings that are wider at the heel than the toe], flat or convex sole and/or widening of the white line in the toe) or history of previous laminitis. All other animals which suffered from laminitis (i.e. with a previous history of laminitis and/or hoof capsule signs with or/without the aforementioned acute signs) were categorised as chronic laminitics. Following guidance text and pictures on the study website www.laminitis.dk (additional information can be provided by contacting the corresponding author) vets scored the clinical signs according the Obel grade (Obel 1948) of laminitis (0-4), and described hoof conformation as either being 'normal' (normal hoof form and quality) or 'abnormal' (e.g. obvious signs of neglected hoof care, diverging rings in the hoof wall etc.). The reporting veterinary surgeon also estimated the Body condition Score (BCS: Henneke et al. 1983) and the cresty neck score (CNS: Carter et al 2009a) again guidance was provided through text and pictures on the website. Hoof conformation, BCS and CNS were reported for the controls in the same way. Weight estimation was undertaken by the owner. All participating cases and controls were sent a commercial weight tape with clear instructions how to measure the weight.

Information collected by telephone interview

Within two weeks of enrollment an owner telephone interview was undertaken (NL/MM) utilizing a standardized questionnaire see Table 1. The owners of laminitis cases were contacted again at 4-6 weeks, 6 months and 12 months after the initial diagnosis and asked about management post-episode, whether there had been any clinical progress or further laminitic episodes, and if the horse was in work or not. . Owners of the case control animals were contacted at 12 months to determine whether the horse had developed laminitis over this period. Details of any euthanasia/death were recorded.

Table 1: *Questions that were asked of the owners of the laminitis cases as well as the control animals at the various time points.*

Table 1 to be inserted here

Statistics

Descriptive statistics were created for all data and where appropriate chi-squared or Fisher exact tests were used to examine specific hypotheses related to level of work at 12 months and level of work at diagnosis or month of diagnosis.

Conditional logistic regression, with veterinary practice or surgeon as the matching variable, was conducted using NL as the outcome variable. All statistical analysis was performed using STATA/SE 12.1 (College Station, Texas, USA). A univariable analysis was initially conducted followed by multivariable forward manual selection process using variables from the univariable analysis for which the p-value was less than 0.2. Variables were retained within the final multivariable models if the likelihood ratio p-value was less than 0.05.

Results

Descriptive

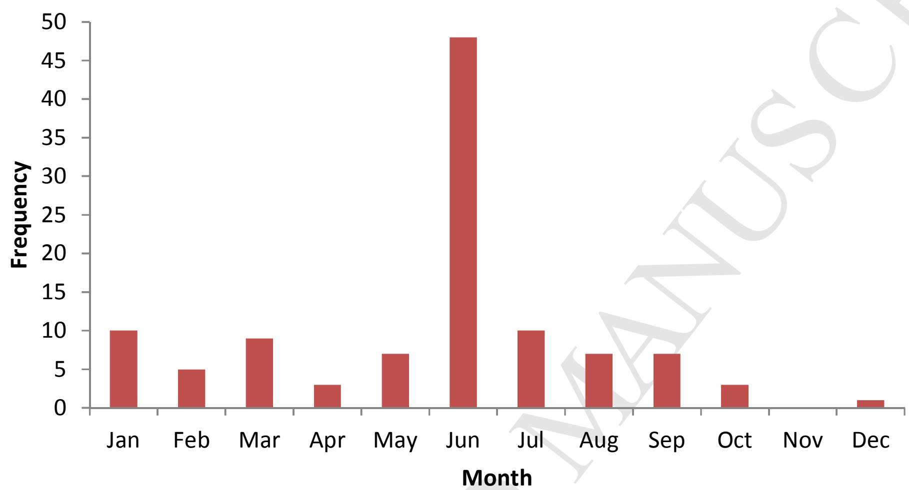
One hundred and ten laminitis cases were recruited (61 female: 49 male; average age 13.5yrs: range 2-34years) and 80 control animals (33 female: 47 male; average age 12.2yrs range 2-25 years). There was no significant difference in age or gender between cases and controls.

There were 69 NL and 41 chronic cases. 60.5% of the laminitics were obese compared with 33% of the controls (BCS of ≥ 7/9: Dugdale et al 2011).

Time of year of diagnosis

The majority of the cases of laminitis were diagnosed in June (see Figure 1).

Figure 1: Number of laminitis cases reported each month.



Outcome

Within 12 months from enrolment six of 80 (7.5%) control horses had been humanely destroyed (euthanized) compared with 36/109 cases (33%). Seventy-three cases (67%) were still alive with one unknown (loss of owner contact). The majority of cases (33/36) were euthanized for laminitis associated reasons; 10 (30%) within one month of diagnosis and a further 12 (36%) between one and three months following diagnosis. The most common reasons given were persistent signs (6), persistent signs with deterioration (12) or a relapse (12). Fourteen additional animals had suffered another episode of laminitis within the year but were not euthanized.

Only one of the control horses and none of the laminitic cases were in hard work at enrolment. Of the 73 NL horses still alive at 12 months: 38 (51%) were not lame but were not working; 31 (44%) were not lame and were back working at their previous level and four (5%) had improved but still had some clinical issues and were not yet in work. Horses not in any work at the time of diagnosis were significantly less likely to be euthanized within 12 months than those in mild (Chi squared p-value = 0.002) or moderate work (Fisher exact p-value = 0.01) at the time of diagnosis. There was no statistically significant difference in the likelihood of euthanasia within 12 months between horses in mild or moderate work at the time of diagnosis (Fisher exact p-value = 0.4).

With respect to obel severity grade at diagnosis: 2/9 (22%); 24/66 (36%); 8/26 (31%) and 2/7 (29%) were euthanized within 12 months for obel grade 1, 2, 3, and 4 respectively. The likelihood of being euthanized within 12 months of diagnosis was not associated with initial obel severity score when comparing horses with grade 4 with; all others, those with grades 1 or 2 or those with grade 1 (Fisher exact p-value = 1.0 for all three comparisons). In addition, the likelihood of being euthanized within 12 months of diagnosis was not associated with initial obel severity score when comparing horses diagnosed as grade 3 or 4 with those with grade 1 or 2 (Chi squared test p-value = 0.66) or with those horses diagnosed as grade 1 (Fisher exact p-value = 1.0).

Of 35 horses diagnosed with laminitis in the winter or spring, 16 (46%) were subject to euthanasia within 12 months of diagnosis. Of 76 horses diagnosed in summer or autumn 14 (18%) were euthanized within 12 months of diagnosis. Horses diagnosed in winter or spring were significantly more likely to have been euthanized within 12 months than horses diagnosed in summer or autumn (Chi squared p-value = 0.003).

Risk factors for new laminitis cases:

Table 2 shows details of the final multivariable conditional logistic regression model for NL. An abrupt change in grass (i.e. going from a restricted number of hours per day to *adlibitum* turnout, changing from a small restricted area of turnout within a much larger paddock to the larger paddock, or a sudden change to a new paddock) within the previous 14 days was associated with a 40.5 fold increase (95% confidence interval (CI) 2.6-639.6) in the likelihood of having a NL episode. Being a cold blooded (CB) pony had an eighteen fold increase (95%CI 2.3-148.0) in the likelihood of developing laminitis. Horses kept on paddocks deemed by the owner to be of high quality (dense grass, well managed, fertilized and with high growth rate) were 19 times (95% CI 2.1-179.3) more likely to be diagnosed with NL.

Table 2. Multivariable conditional logistic regression model (matching on practice/veterinary surgeon) for new cases of laminitis (NL).

Variable	Odds ratio	P-value	95% Confidence Intervals
Change of grass (compared to no change of grass)*	40.5	0.009	2.6 – 639.6
CB ‘pony’ <149cm (compared to other breed types)	18.4	0.006	2.3 – 148.0
High paddock quality (compared to moderate or poor)	19.3	0.009	2.1 – 179.3

* Days since change of grass: Range = 1-14 days; mean = 8 days and median = 7 days; 25th%tile = 5; 75th%tile = 12 days. CB ‘pony’ <149cm high (i.e. Shetland, Fell, Welsh, or Dartmoor pony, Icelandic horse, Norwegian fjords, or a mix of these breeds)

Discussion

This study looked at the risk factors for new episodes of laminitis and also monitored the outcome of any animal suffering from laminitis over the 12 months following the initial diagnosis and enrolment.

Risk Factors

A common factor in both this study and in the recent study in the UK (Wylie et al 2013) is new access to grass. In the UK study it was access to grass within the past month whereas in this study it was an abrupt change in grass intake within the past 14 days (although for the majority of cases the change was considerably more recent than this). All the NL cases in this study were out at pasture for at least 2 hrs a day, and for the majority the change in grass intake reflected a sudden increase in the number of hours at pasture, or a marked increase in the size of the grazing area suggesting an increase in the amount of grass available. This suggests that grass intake may either be the cause or the final triggering actor for many animals developing NL. This might be linked to increased intake of water-soluble carbohydrates (WSC: which include the simple sugars as well as the more complex storage carbohydrates/sugars: fructans) and/or starch (Geor & Harris 2013). However, it is not clear whether this may be due to disturbances to the gut microflora, insulin dynamics, and a combination of both or some other factors (Geor & Harris 2013). In addition, in this study there was an apparent increased risk if the paddock's grass quality was considered to be high (i.e. the paddocks had plenty of grass, were well managed etc.). This suggests that the nature of such grass and/or the herbage yield may be important. Certainly ponies may ingest 4% and even 5% BW in dry matter out at grass (Longland et al 2011) and recent survey work (Longland et al unpublished data) has shown that of 245 samples of pasture grasses (perennial ryegrass, timothy and fescue) harvested throughout a growing season approximately 20 percent contained > 20 percent WSC on a DM basis, ~. 5% > 25% WSC and ~ 3% >30% WSC. If a 250 kg pony was turned onto grass with a 27.5 % fructan content it would only need to ingest 4.5 kg DM grass (1.8% BW DM) in order to ingest the amount of fructan used by Kalck and co-workers to induce laminitis in some of their non-laminitis prone animals (Kalck et al 2009). Even if large intakes of high NSC grass do not result in the 'typical carbohydrate or fructan' overload as in the experimental models it is possible that they could result in large and/or persistent peaks of insulin (Byrd et al 2006, Geor & Harris 2013). However, why some but not all animals out on such pastures develop laminitis is still an unknown question and may relate to their genetic predisposition or inherent insulin dynamics (Harris et al 2006, Borer et al 2013).

In the study by Menzies-Gow et al. (2010), univariate analysis revealed that animals ≥ 14.3 (~149cm) hands in height were at reduced risk of laminitis and in the Wylie et al. 2013 study increasing height appeared to be protective. In this study apparently being a cold blooded type pony < 149 cms (ie Shetland, Fell, Welsh, or Dartmoor pony, Icelandic horse, Norwegian fjords, or a mix of these breeds) but not a warm blooded type pony of <149 cms (i.e. Danish Sport Pony, Dutch Sport Pony, Arabs or a mix of these breeds) were associated with an increased risk of NL. There was, however, no apparent protective effect of being one or other of the horse groups. This may suggest that breed or breed: height interaction may be key perhaps because certain breeds are more metabolically efficient, more likely to have abnormal insulin dynamics in response to a dietary NSC challenge, more likely to be or become obese and potentially more at risk of laminitis (Geor et al 2013, Goer & Harris 2013, Bamford et al 2014). Interestingly in the Menzies-Gow 2010 study, in multivariate analysis, weight but not height was a significant risk factor. In a prospective study of pasture-associated laminitis, the majority of affected animals (89 of 107 cases) were overweight/obese (Menzies-Gow et al., 2010b). Additionally, overweight animals were at increased risk of severe clinical signs and were less likely to survive; such findings were consistent with earlier reports that identified obesity as a risk factor for laminitis (Alford et al., 2001). However, in this current study neither BCS nor cresty neck score were significant in the multivariable model, even though they were significant at the univariable modelling stage. BCS and CNS were correlated and both were confounders for breed which was retained in the final multivariable model. In several other studies a CNS score of ≥ 3/5 has been associated with an increased risk of laminitis (Bailey et al 2008, Carter et al 2009b, and Geor & Harris 2013). In an inbred herd of Welsh and Dartmoor ponies, for example the presence of obesity (generalized or regional, i.e. cresty neck), hyperinsulinemia (insulin >32 mU/L when sampled on winter pasture) or hyperleptinemia (>7.3 ng/ml) were useful predictors of laminitis episodes when ponies were exposed to high carbohydrate pasture (Carter et al., 2009b). It may be that having a high cresty neck score may increase the risk of laminitis purely due to the additional fat present in this particular adipose tissue depot (Burns et al 2010, Bruynstein et al 2013) or this could be a proxy for increased abdominal fat and/or increased risk of having insulin dysregulation etc. In a published consensus statement from the American College of Veterinary Internal Medicine (Frank et al 2010) the equine metabolic syndrome (EMS) phenotype was defined by 3 criteria including a predisposition towards laminitis and generalised obesity and/or increased adiposity in specific locations (regional adiposity). Since then the features that define EMS have been widely debated and it is clear that not all of these components, in particular obesity, may be present in all individuals having underlying metabolic derangements and an increased risk of laminitis (Geor et al 2013) and obesity does not automatically mean that an individual will be insulin resistant and have abnormal insulin dynamics (Bamford et al 2015). Although, much more work is needed to understand the relationship between obesity, a high cresty neck score and laminitis risk it is important to note that obesity and/or cresty neck and/or recent gain in weight have been important risk factors for laminitis in several studies. .

In some other studies, females have been suggested to be at a greater risk (Menzies- Gow 2010, Alford et al., 2001). The reason for the apparent increased laminitis risk in mares is not known. However, in this study gender was not apparently a significant factor. Neither season nor age were significantly associated with the likelihood of NL but this reflects the study design which matched on both of these factors. Nevertheless it is interesting to note that more cases were diagnosed in June than any other month which is similar to the retrospective study in the South of England which noted that over a 6-year period, the highest prevalence (2.6%) and incidence (16 cases/1000 animals) of laminitis occurred in May. The recent UK study (Wylie et al 2013) suggested that that animals were approximately four times more likely to have laminitis in both summer (June–August) and winter (December–February) months compared to spring (March–May). Evidence of seasonality has been said to be inconsistent (Wyllie et al., 2011b) and this may reflect different environmental factors (perhaps influencing rate and extent of grass growth) in the different studies in different locations. Anthelmintic treatment and transportation were not evaluated in this study so a comparison with the Wylie et al 2013 findings on these aspects cannot be made.

Outcome

In this study approximately 30 % of the animals which suffered an episode of laminitis had been euthanized within a year of the diagnosis. Of these the majority were for laminitis related reasons (e.g. deterioration/relapse and/or persistent signs) and in the majority of cases they were euthanized within three months of diagnosis due to signs becoming more pronounced or having another episode of laminitis. Menzies-Gow et al. (2010b) also observed that approximately one-third of animals diagnosed with laminitis had at least one more episode over a 6yr period with about a quarter of them having a repeat episode in the same year as the original diagnosis. In this current study a slightly higher percentage of animals (~11%) were euthanized for repeated laminitis and 27% of those that were not euthanized within the year also had a further episode. Such findings support the clinical impression that some animals are prone to repeated episodes of laminitis and suggest that there may be phenotypic or genetic factors associated with susceptibility and/or they are repeatedly being exposed to environmental factors that keep them at increased risk.

Of interest is that proportionally more animals were euthanized that were in mild or moderate work (compared to no work) before the laminitis incident. This perhaps suggests that the owners of such animals were less tolerant of the situation and less willing to keep more active horses alive. Further work on the decision making process at the end of life for laminitic horses may be of value.

Conclusion

This veterinarian led study into laminitis risk factors highlights the importance of grass turn out and breed. Further work is needed to evaluate the interaction between these two key factors. It also highlight the important role that a change in grass intake, both type and particularly amount may play at any time of the year not only the spring as commonly thought.

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Interview #1 **(2 weeks after laminitis episode)**	**Interview #2** **(4-6 weeks after laminitis episode)**	**Interview #3** **(6 months after laminitis episode)**	**Interview #4** **(12 months after laminitis episode)**
Horse data : e.g. age, gender, breed, estimated weight	Euthanized – Y/N	Euthanized – Y/N	Euthanized – Y/N
Date of laminitis	Reason for any euthanasia	Reason for any euthanasia	Reason for any euthanasia
	Clinical signs • Better • Same • Worse	Clinical signs • Better • Same • Worse	Clinical signs • Better • Same • Worse
Interval between shoeing • Date of last shoeing	• Use of therapeutic shoeing Y/N • Farriery intervals	• Use of therapeutic shoeing Y/N • Farriery intervals	• Use of therapeutic shoeing Y/N • Farriery intervals
Details of Veterinary treatment: • Were NSAIDs used, Y/N and if so which • were pads used pads Y/N, • was a change of bedding recommended and made Y/N – if yes to what, • was box rest recommended Y/N	Continued use of box rest – Y/N If No : Duration of box rest after laminitis • In days	Continued use of box rest – Y/N	Continued use of box rest – Y/N
	Duration of treatment with NSAID	Continued use of NSAIDs – Y/N	Continued use of NSAIDs – Y/N
Diet and feeding management prior to laminitis (including type and amount of complementary feed per meal/day)	Diet and feeding management after laminitis	Diet and feeding management currently	Diet and feeding management currently
Information regarding grass turnout prior to laminitis: • Size of the paddock, • no. of horses on paddock, • height of grass (where the horses graze) • quality of grass: poor (e.g dry/mature), moderate or lush (eg dense grass, well managed, fertilized and with high growth rate).	Is the horse back out at grass again Y/N If yes • Size of paddock • Quality of paddock (grass, sand, dirt)	Information regarding any current grass turn out • Size of paddock • Quality of paddock (grass, sand, dirt)	Information regarding any current grass turn out • Size of paddock • Quality of paddock (grass, sand, dirt)

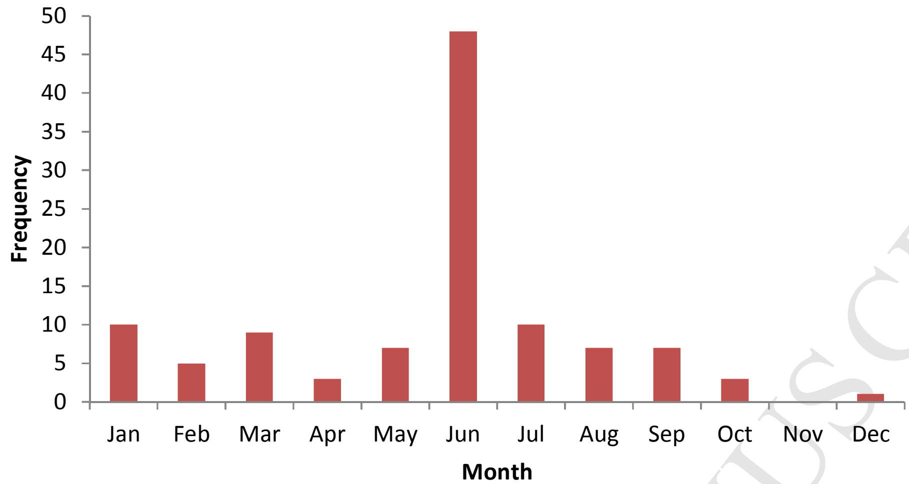
• How many hours out at grass : never, <2hrs, 2-<4hrs, 4hrs, >4-8hrs, >8-12hrs, Ad libitum			
Had there been any abrupt change in grass intake (from restricted hours to ad libitum; opening up from restricted areas to the whole; moved to a new paddock) in the 14 days prior to the laminitis episode : Y/N • If yes how many days prior to laminitis episode			
Workload prior to laminitis: **None** : (less than once a week); **Light work** (1-3x per week); **Moderate work** (>4 x per week at a low intensity); **hard work**(>5 times per week at high intensity)	Is the horse back to work Y/N If yes: • less • same • more	Is the horse back to work Y/N If yes: • less • same • more	Is the horse back to work Y/N If yes: • less • same • more

Controls

Interview #1 **(Within 2 weeks of enrolment)**	**Interview #2** **(12 months after enrolment)**
Horse data : e.g. age, gender, breed, estimated weight	Euthanized – yes or no
Reason for Veterinary consultation (other than laminitis)	Reason for euthanasia
Workload prior to enrolment	Any episode of laminitis during the last 12 months
Diet and feeding management prior to enrolment (including type and amount of complementary feed per meal/day)	
Information regarding grass turnout prior to enrolment: • Size of the paddock, • no. of horses on paddock, • height of grass (where the horses	

graze) • quality of grass: poor (ie dry/mature), moderate or lush. • How many hours out at grass : never, <2hrs, 2-<4hrs, 4hrs, >4-8hrs, >8-12hrs, Ad libitum	
Interval between shoeing • Date of last shoeing	

Figure 1: Number of laminitis cases reported each month.



- We identify risk factors for new cases of laminitis in Denmark based on 110 cases and 80 controls
- Outcome and incidence of repeated episodes is obtained by following cases for 12 months
- Significant risk factors are recent change in grass, high quality paddock and breed
- 33% of all laminitis cases were euthanized within 12 months of diagnosis
- The likelihood of euthanasia following a diagnosis of laminitis depends on the type of work and the time of year of diagnosis