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Unravelling the temporal association between lameness and body condition score in dairy cattle using a multistate modelling approach

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Abstract (400 words)

Recent studies have reported associations between lameness and body condition score (BCS) in dairy cattle, however the impact of change in the dynamics of BCS on both lameness occurrence and recovery is currently unknown. The aim of this study was to investigate in a longitudinal study the effect of change in BCS on the transitions from the non-lame to lame, and lame to non-lame states. A total of 731 cows with 6889 observations from 4 UK herds were included in the study. Mobility score (MS) and body condition score (BCS) were recorded every 13-15 days from July 2010 until December 2011. A multilevel multistate discrete time event history model was built to investigate the transition of lameness over time. There were 1042 non-lame episodes and 593 lame episodes of which approximately 50% (519/1042) of the non-lame episodes transitioned to the lame state and 81% (483/593) of the lame episodes ended with a transition to the non-lame state. Cows with a lower BCS at calving (BCS Group 1 (1.00-1.75) and Group 2 (2.00-2.25)) had a higher probability of transition from non-lame to lame and a lower probability of transition from lame to non-lame compared to cows with BCS 2.50-2.75 i.e. they were more likely to become lame and if lame, they were less likely to recover. Similarly, cows who suffered a greater decrease in BCS (compared to their BCS at calving) had a higher probability of becoming lame and a lower probability of recovering in the next 15 days. An increase in BCS from calving was associated with the converse effect i.e. a lower probability of cows moving from the non-lame to the lame state and higher probability of transition from lame to non-lame. Days of lactation, months of calving and parity was associated with both lame and non-lame transitions and there was evidence of heterogeneity among cows in lameness occurrence and recovery. This study suggests loss of BCS and increase of BCS could influence the risk of becoming lame and the chance of recovery from lameness. Regular monitoring and maintenance of BCS on farms could be a key tool for reducing lameness. Further work is urgently needed in this area to allow a better understanding of the underlying mechanisms behind these relationships.

Keywords: Lameness, Body condition score, Dairy cow, Multilevel multistate model, Discrete time event history model, transitions

1. Introduction

Lameness is one of the most challenging diseases for the dairy industry due to its serious welfare impact and associated economic losses (Kossaibati and Esslemont, 1997; Cha et al., 2010). Lameness in cows leads to discomfort and pain resulting in altered gaits (Whay et al., 1998). There is a significant impact of lameness on milk production, reproductive performances and it results in a higher culling rate (Rajala-Schultz and Grohn, 1999; Green et al., 2002; Bicalho et al., 2007; Peake et al., 2011; Huxley, 2013). In the UK, the estimated average herd prevalence of lameness is 36% (range: 0 to 79%) (Barker et al., 2010; Leach et al., 2010); similar prevalence estimates have been reported from other locations around the world (Hernandez et al., 2005; Dippel et al., 2009; Tadich et al., 2010).

Over the last decade a small number of studies have reported an association between lameness and poor body condition score (BCS) (Espejo et al., 2006; Dippel et al., 2009; Hoedemaker et al., 2009). The area has recently been reviewed (Huxley, 2013); historically it has been assumed that lameness led to cows having a lower BCS because disease meant that cows were more likely to have lower dry matter intakes, decreased feeding time and longer lying time (Bach et al., 2007; Kilic et al., 2007). However, in a cross-sectional study, Bicalho et al. (2009) reported that lame cows were more likely to have thinner digital cushions compared with non-lame cows and reported a significant positive association between BCS and thickness of the digital cushion, i.e. cows with low BCS had thinner digital cushions compared with cows with higher BCS. The authors hypothesized that losing BCS could influence the cows to change from non-lame to lame due to thinning of the digital cushion but could not test this due to the cross-sectional nature of the data. In a longitudinal study conducted on one farm, Green et al. (2013) reported that cows with low BCS (BCS<2.5) in the previous 0-2 months and >2-4 months had a higher risk of treatment for lameness in a 30 day period. However, exploration of the dynamics of change of BCS on both the occurrence and recovery from lameness was not investigated and the study was conducted on a single farm which limited the generalizability of the findings.

Multilevel multistate discrete time event history models can be used to investigate the effects of factors on the likelihood of transitions between states among animals (e.g. disease/healthy) in longitudinal data. Their use is becoming more common in exploring the complex dynamics of diseases on farms (Kaler et al., 2010; Reader et al., 2011; Nielsen et al., 2012) and understanding the interplay of animal level factors. Moreover, they avoid the limitation of fitting a separate model for each state transition (Steele et al., 2004) accounting for the correlation that may exist between the transitions due to heterogeneity. The aim of this longitudinal study was to investigate the temporal effect of changes in BCS in a cow, and other cow level factors, on the transitions from non-lame to lame and lame to non-lame states in a 15-day risk period .

2. Material and methods

2.1. Dataset and study methodology

The data was collected from a convenience sample of four dairy herds in the South West region of the UK. Herds were selected based on their proximity and previous working relationship with the observer (JAW), the quality of their records and their willingness to participate. Animals on the study farms were predominantly Holstein Friesians. The number of animals in milk, average yield and herd calving to conception intervals are outlined in Table 1. On three farms cows were housed through the winter period and had access to pasture during the summer, cows in one herd (Farm 3) were continuously housed throughout the year. All four herds, when housed, used cubicles; herd 4 bedded cows on deep sand, herd 3 bedded cows on mats with straw and the remaining two farms bedded animals on mats with sawdust. In all herds dry cows were loose housed on straw and all farms had loose straw areas available for freshly calved and sick cows.

Animals calving between July 2010 and June 2011 were selected from each herd. One trained observer (JAW) visited all the herds every 13-15 days from July 2010 until December 2011. At every visit, the body condition score (BCS) and mobility score (MS) of selected cows were recorded i.e. the lameness state of selected cows was identified based on a visual assessment every 13-15 days throughout lactation. No treatment interventions were instigated by the observer, consequently no temporal information on the cause of the lameness association with the elevation in mobility score was collected. Body condition score (BCS) was scored according to Edmonson et al. (1989) using a scale of 1-5 with increments of 0.25. Mobility score (MS) was scored according to Whay et al. (2003) on a four point scale (0 to 3). Other information such as parity, age, days of lactation and month of latest calving of selected cows were recorded.

2.2. Statistical analysis

Cows with no information for parity, age, days of lactation, month of latest calving or BCS at calving (0-15 days post-partum) were excluded from the dataset. Any missing observation at the start of the study and end of the study was excluded and if cows had missing visits in the middle of the observation period, the remaining observations following the missing visit were excluded. Only cows with at least 5 observations were used in the analysis. The BCS was grouped into four categories: group1 (BCS G1 1.00-1.75), group 2 (BCS G2 2.00-2.25), group 3 (BCS G3 2.50-2.75) and group 4 (BCS G4 3.00-5.00), while MS was categorized into two groups: non-lame (MS 0 and 1) and lame (MS 2 and 3). Descriptive analyses were conducted in Stata version 12 (StataCorp, USA).

2.3. Multilevel multistate discrete time event history model

A multilevel multistate discrete time event history model (Steele et al., 2004) was set up to investigate the effect of covariates on the probability of transitions between lameness states, in a 15 day risk period. Two origin states were defined for lameness in the multilevel multistate model for each cow *k*: non-lame (MS 0 and 1; coded as 0) and lame (MS 2 and 3; coded as 1). Data were censored at the end of the study. An episode was the continuous period of time (in discrete time intervals) a cow spent in a state until a transition occurred or data was censored. For each episode, the time interval was categorized in discrete periods (15 days) and the number of time intervals (t) was measured as t=1, 2, 3… up to the maximum observed time. For each cow *k,* at the end of each discrete time interval t (15 day) the outcome y was two possible transitions/event occurrences, non-lame to lame or lame to non-lame.

The response variable y was the binary indicator of event occurrence. The event was when a cow transitioned from lame to non-lame or non-lame to lame. The event indicator was coded as 1 or 0 depending on the occurrence of an event: if no event occurred, 0 was coded; 1 was coded if an event occurred (non-lame to lame state or vice versa).

The hazard of transition from origin state i to transition state r_i during discrete-time interval t of episode j for cow k was denoted by $h_{tijk}^{(ri)}$, and the hazard of no transition was denoted by $h_{tijk}^{(0)}$,

The multilevel multistate discrete time model took the form: $\log(h_{tijk}^{(ri)} / h_{tijk}^{(0)}) = \beta_0^{(ri)} + \alpha_t^{(ri)} + \beta x_{tijk}^{(ri)} + \mu_{ik}^{(ri)}$ $r = 0,1; i = 0,1$ where $\beta_0^{(ri)}$ is a state specific intercept, $\alpha_t^{(ri)}$ is an effect of duration which is a piecewise constant step function of time interval with three categories, $\beta x_{tijk}^{(ri)}$ refer to the covariates and $\mu_{ik}^{(ri)}$ represents the random effect of cow level which were assumed to follow a normal distribution with variance σ_u^2 and non-zero correlation between random effects. The model was created in MLwiN version 2.25 (Centre for Multilevel Modelling, University of Bristol) and estimation was carried out by quasi-likelihood methods and followed by Monte Carlo Markov chain (MCMC) methods with 500,000 iterations and a burn in of 5,000. The chain mixing and stability were then evaluated visually in the MCMC trajectories window and MCMC diagnostic window (Browne, 2009).

2.4. Covariates (Predictor variables) used in the model

The covariates with fixed effects used in the analysis were: parity group (1^{st}, 2^{nd}, 3^{rd} and $>3^{rd}$), herd (Herd 1, 2, 3 and 4), month of calving (January-March, April-June, July-September and October-December) and BCS at calving (BCS G1: 1.00-1.75, BCS G2: 2.00-2.25, BCS G3: 2.50-2.75 and BCS G4: 3.00-5.00). Days of lactation and changes of BCS at the current visit compared with calving were included in the model as time-varying effects. Days of lactation referred to the days which compared the current visit with the latest calving date and were categorized into three categories: 0-90 days, 91-120 days and more than 120 days. Likewise, the change in BCS at the current visit compared with BCS at calving was categorized into five categories:

i) no change (C1)

ii) decrease in 2 or 3 categories of BCS compared with calving (C2) (e.g. BCS G4 drop to BCS G2 or BCS G1)

iii) decrease in 1 category of BCS compared with calving (C3) (e.g. BCS G4 drop to BCS G3)

iv) increase in 1 category of BCS compared with calving (C4) (e.g. BCS G2 increase to BCS G3)

v) increase in 2 categories of BCS compared with calving (C5) (e.g. BCS G2 increase to BCS G4).

3. Results

3.1. Descriptive results

There were a total of 8351 observations obtained from 731 cows across the four herds. Of these, a total of 1462 observations were excluded for reasons described in the methodology. The final dataset had 6889 observations, these included 110 (1100 observations), 329 (2953 observations), 166 (1626 observations) and 126 (1210 observations) cows from Herd 1, 2, 3 and 4 respectively. There were 214 (29%), 145 (20%), 113 (16%) and 259 (35%) cows in parity 1, 2, 3 and 4 or greater respectively. A total of 166 (23%), 115 (16%), 258 (35%) and 192 (26%) cows calved within Jan-March, April-June, July-Sep and Oct-Dec respectively. The frequencies of variables at the cow level by herd are presented in Table 2.

Out of 1635 episodes, 1042 were non-lame episodes and 593 were lame episodes. Approximately 50% (519/1042) of non-lame episodes transitioned to the lame state and 81% (483/593) of lame episodes ended with a transition to the non-lame state. For transitions from the non-lame to the lame state, approximately 65% occurred within 45 days, 84% within 90 days and the remaining (16%) occurred after 90 days. Approximately 88% of transitions from the lame to the non-lame state occurred within 45 days, 97% within 90 days and 3% after 90 days.

3.2. Multilevel multistate model

The multistate model results are presented in Table 3 and 4. Cows in BCS G1 (1.00-1.75) and BCS G2 (2.00-2.25) at calving had a significantly higher probability of transition from the non-lame to the lame state in a 15 day period (OR: 7.73, CI: 3.37-17.71; OR: 1.54, CI: 1.11-2.14) and a lower probability of transition from the lame to the non-lame state in a 15 day period (OR: 0.21,CI: 0.08-0.52; OR: 0.31,CI: 0.19-0.51) compared with the cows with BCS G3 (2.50-2.75) respectively.

When comparing the BCS at the current visit with the BCS at calving; cows where the BCS had decreased by 2 or 3 groups had a higher probability of transition from the non-lame to the lame state over the next 15 day period (OR: 2.07,CI:1.30-3.29) and a lower probability of transition from lame to non-lame over the next 15 day period (OR: 0.44, CI: 0.23-0.82), compared with cows with no change in BCS. Similarly, cows where BCS decreased 1 group had a lower probability of transition from the lame to the non-lame state over the next 15 day period compared with cows where BCS did not change (OR: 0.66, CI: 0.44-0.98); there was no significant effect of this change in the transition from non-lame to lame.

Cows in BCS G1 (1.00-1.75), G2 (2.00-2.25) or G3 (2.5-2.75) that had increased one BCS category at the current visit had a lower probability of transition from the non-lame to the lame state (OR: 0.53, CI: 0.33-0.83) and a higher probability of transition from the lame to the non-lame state (OR: 2.49, CI:1.37-4.53) over the next 15 day period, compared with the cows with no change in BCS.

The probability of cows transitioning from the non-lame to the lame state was lower the longer a cow remained non-lame (OR: 0.53, CI: 0.40-0.71; OR: 0.33, CI: 0.21-0.51). In contrast, the longer the cow was in the lame state, the lower the probability (OR: 0.42, CI: 0.18-0.96) of transition from the lame to the non-lame state (i.e. they were more likely to remain lame). Cows between 91-120 days of lactation (OR: 1.64, CI: 1.17-2.29) and greater than 120 days of lactation (OR: 2.11, CI: 1.58-2.82) were more likely to change from the non-lame to the lame state compared with cows less than 91 days of lactation. Cows between 91-120 days of lactation were less likely to change from the lame to the non-lame state compared with cows less than 91 days of lactation (OR: 0.67, CI: 0.44-1.00). Cows that calved between Oct-Dec had a higher probability of transition from the lame to the non-lame state compared with cows that calved during Jan-March (OR: 1.79, CI: 1.05-3.06); the month of calving did not have a significant effect on transition from the non-lame to the lame state.

Cows in parity 3 and above had a higher probability (OR: 3.00, CI: 1.95-4.60; OR: 3.51, CI: 2.39-5.17) of transition from the non-lame to the lame state and a lower probability (OR: 0.50, CI: 0.25-1.00; OR: 0.36, CI: 0.19-0.67) to transition from the lame to the non-lame state compared with cows in parity 1. Cows in parity 2 did not show any significant differences in both transitions compared with cows in parity 1.

Herd 2 (OR: 3.18, CI:1.98-5.11) and Herd 3 (OR: 1.94, CI:1.19-3.15) had a significantly higher probability of transition from the non-lame to the lame state compared with Herd 1; Herd 2 had a significantly lower probability of transition from the lame to the non-lame state compared with Herd 1 (OR: 0.23, CI:0.10-0.53).

Estimated random effects covariance matrices for the models with duration effects only and duration with all covariates are presented in Table 5. For the model with duration effects only, there was significant moderate negative correlations (-0.76) between the probability of both transitions from non-lame to lame and lame to non-lame. It indicated that the cows with a high (low) probability of switching from non-lame to lame had a low (high) probability of changing from the lame to the non-lame state. Equally, cows with a longer (shorter) duration of the non-lame state were likely to have a shorter (longer) duration in the lame state. The correlation between both transitions after adding covariates was not significant. The model converged visually with stable chain mixing.

4. Discussion

The key finding from the study reported here is that loss of BCS increased a cow's probability of becoming identifiably lame and decreased her likelihood of recovery, over the next 15 days; the effect was apparent after controlling for body condition score at calving. Furthermore, cows with a greater decrease of BCS had a higher (lower) probability of transition from non-lame to lame (lame to non-lame) compared with cows that had a relatively lower decrease in BCS i.e. the effect was greater in animals which lost more condition. Our findings demonstrate that in this dataset loss of BCS preceded an animal being identified as lame by mobility scoring.

The findings from this longitudinal study shed no light on the causality of this relationship, however they add further evidence in support of a previous cross-sectional study that has demonstrated that BCS is associated with the thickness of the digital cushion (Bicalho et al., 2009). The digital cushion is thought to absorb part of the load and protecting the corium during locomotion, lowering the incidence of claw horn lesions (sole haemorrhage, sole ulcers and white line disease) and lameness (Räber et al., 2004; Räber et al., 2006; Bicalho et al., 2009). Results from the current study support the hypothesis that a greater loss of BCS leads to a higher risk of lameness possibly due to the thinning effects on the digital cushion. They also suggest that body condition score loss decreases an animal's chance of recovery i.e. animals which lose weight are less likely to recover from any lameness events which do occur. Alternatively, thinner cows may have lower social rank and therefore be less able to compete with other cows for resources such as lying space and access to feed (Hohenbrink and Meinecke-Tillmann, 2012). Being out competed in the environment could but them at greater risk of becoming lame and make them less likely to recover once a lameness event occurs.

Our findings support the work of Green et al. (2013) who demonstrated that low BCS (<2.5) was associated with an increased risk of treatment for lameness in the following four months. Additionally they extend the previous findings by exploring the dynamics of changes in BCS and lameness both in terms of lameness occurrence and recovery in a 15 day period. The work described here suggests that a) in addition to low BCS per se being a risk for lameness, any significant loss of BCS has an added detrimental effect on the occurrence and recovery from lameness in a 15 day risk period, b) thinner cows at calving who gain BCS have a lower chance of becoming lame and a higher chance for recovery compared with their counterparts who stay thin. That is the interrelationship between BCS and BCS change and lameness are bidirectional.

Previous work has demonstrated that the thickness of the digital cushion is influenced by age, parity and days of lactation (Räber et al., 2004; Bicalho et al., 2009). It is noteworthy that these factors also had a significant effect on lameness transitions in the current study. The thickness of the digital cushion increases to the third parity and then reduces after the third parity (Räber et al., 2004; Bicalho et al., 2009). Cows in parity three and greater were more likely to become lame and less likely to recover in the current study. Alternatively, previous work has demonstrated that animals which have experienced a lameness event in previous lactations are at greater risk of future cases of lameness (Hirst et al., 2002) The increased risk of lameness in older cows could have been caused by their lameness history. For days of lactation, the thickness of the digital cushion has been reported to decrease from early lactation until 120 days post calving and then slowly increase in thickness after 120 days (Bicalho et al., 2009). Our results demonstrate that cows were more likely to become lame and less likely to recover between 91 and 120 days of lactation, this coincides with the period that the digital cushion is thinnest. Equally this finding could be due to injuries to the corium around the time of parturition and in early lactation taking a period of time to cause an identifiable lameness event.

The duration that cows spent in a particular lameness state influences the risk of lameness and recovery (Reader et al., 2011). Our results suggest that cows that have been lame for longer are less likely to recover. Equally, the longer that cows remain non-lame the less likely they are to become lame. This was further confirmed by the significant moderate correlations observed between lameness transitions. This could be due to the effect of cow heterogeneity or genetic resistance to lameness, where cows with inherently thinner digital cushion will have a higher risk of lameness and a lower chance of recovery compared with other animals. A recent study (Oikonomou et al., 2013) reported that the heritability estimate for digital cushion thickness was moderate (0.33) and it was genetically correlated with claw horn disruption lesions. Alternatively the observed effects could be mediated via the impacts of lameness on nutrition. Lame cows have shorter feeding times and suffer reduced feed intakes (Bach et al., 2007; Kilic et al., 2007) which could further reduce the thickness of the digital cushion exacerbating the problem i.e. lameness state is a vicious (or virtuous) cycle. Finally this increase in lameness risk could be due to some failure in the efficacy of treatments. Since lameness was only measured by mobility score, no information was captured on the causes of lameness or if, when and how animals were treated on farm. Reader et al. (2011) reported that cows with a history of treatment for sole ulcer and digital dermatitis were more likely to become lame compared with non-treated cows, suggesting that current treatments may not be fully healing the lesion or leaving the animal with changes to the foot which increase the risk of recurrence in the future.

In the current study, the chance of incorrect animal identification was minimised by identifying cows whilst they were stationary in the milking parlour. Moreover, all the observations for BCS and MS score were made by a single trained and experienced observer to reduce between observer bias, although the possibility of intra-observer bias remains. We believe this approach is likely to have reduced the chance of data misclassification and the authors have no reason to suspect that what misclassifications did occur were not randomly distributed through the data set. Although the 4 herds selected for the study were not randomly selected we have no reason to believe that they are not representative of typical UK dairy herd w.r.t. range and change of body condition and mobility scores. Given the consistency of our results with previous literature, we consider that the results are likely to be generalisable to other similar cattle herds.

5. Conclusion

In conclusion, our results suggest that both a decrease and an increase in BCS influences the risk of becoming lame and the chance of recovery, possibly due to the impact of body weight change on the thickness of the digital cushion. Further longitudinal studies with detailed measurements of the digital cushion alongside BCS and MS would help to explore these complex interactions. Regular monitoring and maintenance of BCS on farms could be a key tool for managing the risk of lameness on farm.

6. Conflicts of interest

The authors declare that they have no competing interests.

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References

Bach, A., Dinares, M., Devant, M., Carre, X., 2007. Associations between lameness and production, feeding and milking attendance of Holstein cows milked with an automatic milking system. J. Dairy Res. 74, 40-46.

Barker, Z.E., Leach, K.A., Whay, H.R., Bell, N.J., Main, D.C., 2010. Assessment of lameness prevalence and associated risk factors in dairy herds in England and Wales. J. Dairy Sci. 93, 932-941.

Bicalho, R.C., Machado, V.S., Caixeta, L.S., 2009. Lameness in dairy cattle: A debilitating disease or a disease of debilitated cattle? A cross-sectional study of lameness prevalence and thickness of the digital cushion. J. Dairy Sci. 92, 3175-3184.

Bicalho, R.C., Vokey, F., Erb, H.N., Guard, C.L., 2007. Visual locomotion scoring in the first seventy days in milk: impact on pregnancy and survival. J. Dairy Sci. 90, 4586-4591.

Cha, E., Hertl, J.A., Bar, D., Grohn, Y.T., 2010. The cost of different types of lameness in dairy cows calculated by dynamic programming. Prev. Vet. Med. 97, 1-8.

Dippel, S., Dolezal, M., Brenninkmeyer, C., Brinkmann, J., March, S., Knierim, U., Winckler, C., 2009. Risk factors for lameness in freestall-housed dairy cows across two breeds, farming systems, and countries. J. Dairy Sci. 92, 5476-5486.

Edmonson, A.J., Lean, I.J., Weaver, L.D., Farver, T., Webster, G., 1989. A body condition scoring chart for Holstein dairy cows. J. Dairy Sci. 72, 68-78.

Espejo, L.A., Endres, M.I., Salfer, J.A., 2006. Prevalence of lameness in high-producing Holstein cows housed in freestall barns in Minnesota. J. Dairy Sci. 89, 3052-3058.

Galindo, F., Broom, D.M., 2000. The relationships between social behaviour of dairy cows and the occurrence of lameness in three herds. Res. Vet. Sci. 69, 75-79.

Galindo, F., Broom, D.M., Jackson, P.G.G., 2000. A note on possible link between behaviour and the occurrence of lameness in dairy cows. Appl. Anim. Behav. Sci. 67, 335-341.Green, L.E., Hedges, V.J., Schukken, Y.H., Blowey, R.W., Packington, A.J., 2002. The impact of clinical lameness on the milk yield of dairy cows. J. Dairy Sci. 85, 2250-2256.

Green, L.E., Huxley, J.N., Banks, C., Green, M.J., 2013. Temporal associations between low body condition, lameness and milk yield in a UK dairy herd. Prev. Vet. Med. 113, 63-71.

Hirst, W.M., Murray, R.D., Ward, W.R., French, N.P., 2002. A mixed-effects time-to-event analysis of the relationship between first-lactation lameness and subsequent lameness in dairy cows in the UK. Prev. Vet. Med. 54, 191-201.Hernandez, J.A., Garbarino, E.J., Shearer, J.K., Risco, C.A., Thatcher, W.W., 2005. Comparison of the calving-to-conception interval in dairy cows with different degrees of lameness during the prebreeding postpartum period. J. Am. Vet. Med. Assoc. 227, 1284-1291.

Hoedemaker, M., Prange, D., Gundelach, Y., 2009. Body condition change ante- and postpartum, health and reproductive performance in German Holstein cows. Reprod. Domest. Anim. 44, 167-173.

Hohenbrink, S., Meinecke-Tillmann, S., 2012. Influence of social dominance on the secondary sex ratio and factors affecting hierarchy in Holstein dairy cows. J. Dairy Sci. 95, 5694-5701.

Huxley, J.N., 2013. Impact of lameness and claw lesions in cows on health and production. Livest. Sci. 156, 64-70.

Kaler, J., Medley, G.F., Grogono-Thomas, R., Wellington, E.M., Calvo-Bado, L.A., Wassink, G.J., King, E.M., Moore, L.J., Russell, C., Green, L.E., 2010. Factors associated with changes of state of foot conformation and lameness in a flock of sheep. Prev. Vet. Med. 97, 237-244.

Kilic, N., Ceylan, A., Serin, I., Gokbulut, C., 2007. Possible interaction between lameness, fertility, some minerals, and vitamin E in dairy cows. Bull. Vet. Inst. Pulawy 51, 425–429.

Kossaibati, M.A., Esslemont, R.J., 1997. The costs of production diseases in dairy herds in England. Vet. J. 154, 41-51.

Leach, K.A., Whay, H.R., Maggs, C.M., Barker, Z.E., Paul, E.S., Bell, A.K., Main, D.C., 2010. Working towards a reduction in cattle lameness: 1. Understanding barriers to lameness control on dairy farms. Res. Vet. Sci. 89, 311-317.

Nielsen, B.H., Thomsen, P.T., Green, L.E., Kaler, J., 2012. A study of the dynamics of digital dermatitis in 742 lactating dairy cows. Prev. Vet. Med. 104, 44-52.

Oikonomou, G., Banos, G., Machado, V., Caixeta, L., Bicalho, R.C., 2013. Short communication: Genetic characterization of digital cushion thickness. J. Dairy Sci. 97, 1-5.

Peake, K.A., Biggs, A.M., Argo, C.M., Smith, R.F., Christley, R.M., Routly, J.E., Dobson, H., 2011. Effects of lameness, subclinical mastitis and loss of body condition on the reproductive performance of dairy cows. Vet. Rec. 168, 301.

Räber, M., Lischer, C.J., Geyer, H., Ossent, P., 2004. The bovine digital cushion – a descriptive anatomical study. Vet. J. 167, 258-264.

Räber, M., Scheeder, M.R.L., Ossent, P., Lischer, C.J., Geyer, H., 2006. The content and composition of lipids in the digital cushion of the bovine claw with respect to age and location – A preliminary report. Vet. J. 172, 173-177.

Rajala-Schultz, P.J., Grohn, Y.T., 1999. Culling of dairy cows. Part III. Effects of diseases, pregnancy status and milk yield on culling in Finnish Ayrshire cows. Prev. Vet. Med. 41, 295-309.

Reader, J.D., Green, M.J., Kaler, J., Mason, S.A., Green, L.E., 2011. Effect of mobility score on milk yield and activity in dairy cattle. J. Dairy Sci. 94, 5045-5052.

Steele, F., Goldstein, H., Browne, W., 2004. A general multilevel multistate competing risks model for event history data, with an application to a study of contraceptive use dynamics. Statistical Modelling 4, 145-159.

Tadich, N., Flor, E., Green, L., 2010. Associations between hoof lesions and locomotion score in 1098 unsound dairy cows. Vet. J. 184, 60-65.

Whay, H.R., Main, D.C.J., Green, L.E., Webster, A.J.F., 2003. Assessment of the welfare of dairy caftle using animal-based measurements: direct observations and investigation of farm records. Vet. Rec. 153, 197-202.

Whay, H.R., Waterman, A.E., Webster, A.J., O'Brien, J.K., 1998. The influence of lesion type on the duration of hyperalgesia associated with hindlimb lameness in dairy cattle. Vet. J. 156, 23-29.

Tables

Table 1. Descriptive data collected from 7/10/2010 to 12/11/2011 on 4 study farms located in southwest region of UK

Table 2. The frequency of the covariates at the cow level by herd used in multilevel multistate model

Table 3. Frequency of observations for each covariate/predictor variable in the multilevel multistate model by state (Lame/Non-Lame)

Table 4. Multilevel multistate model of factors associated with transition of cows from the non-lame to the lame and the lame to the non-lame state in dairy cows on 4 herds

Table 5. Random effects covariance matrix for a multilevel multistate model looking into transitions from the non-lame to the lame and the lame to the non-lame state in cows

Table 1

	Herd 1	Herd 2	Herd 3	Herd 4
Number of cows in milk*	164	359	220	138
Milk Production (kg / 305d lactation)	5,889	8,057	9,171	9,005
Calving-Conception interval (d)	93	148	138	115

***Breed of cows: Predominantly Holstein Friesians**

Table 2.

Herd	1		2		3		4		Total
	Freq.	**%**	**Freq.**	**%**	**Freq.**	**%**	**Freq.**	**%**	**Freq.**
Cows	110	15.05	329	45.01	166	22.71	126	17.23	731
Parity group									
1	25	22.73	100	30.40	48	28.92	41	32.54	214
2	15	13.64	48	14.59	55	33.13	27	21.43	145
3	19	17.27	50	15.20	21	12.65	23	18.25	113
>3	51	46.36	131	39.81	42	25.30	35	27.78	259
Month of calving									
Jan-March			81	24.62	49	29.52	36	28.57	166
Apr-June			83	25.23	18	10.84	14	11.11	115
July-Sep	84	76.36	82	24.92	58	34.94	34	26.98	258
Oct-Dec	26	23.64	83	25.23	41	24.70	42	33.34	192
BCS at calving									
BCS G1 (1.00-1.75)			16	4.86	3	1.81	2	1.59	21
BCS G2 (2.00-2.25)	23	20.91	116	35.26	46	27.71	41	32.54	226
BCS G3 (2.50-2.75)	81	73.64	163	49.54	105	63.25	72	57.14	421
BCS G4 (3.00-5.00)	6	5.45	34	10.34	12	7.23	11	8.73	63

Table 3.

Covariates	Categories	State			
		Non-lame (%)		**Lame (%)**	
Duration spent in state (days)	≤45	2062	(37.50)	974	(70.07)
	46-90	1618	(29.42)	240	(17.27)
	≥90	1819	(33.08)	176	(12.66)
Herd					
	1	1028	(18.69)	72	(5.18)
	2	1989	(36.17)	964	(69.35)
	3	1402	(25.50)	224	(16.12)
	4	1080	(19.64)	130	(9.35)
Days of lactation					
	0-90	3136	(57.03)	684	(49.21)
	91-120	923	(16.78)	238	(17.12)
	>120	1440	(26.19)	468	(33.67)
Month of calving					
	Jan-March	1104	(20.08)	398	(28.63)
	Apr-June	671	(12.20)	251	(18.06)
	July-Sep	2211	(40.21)	484	(34.82)
	Oct-Dec	1513	(27.51)	257	(18.49)
Parity group					
	1	1818	(33.06)	145	(10.43)
	2	1239	(22.53)	159	(11.44)
	3	809	(14.71)	278	(20.00)
	>3	1633	(29.70)	808	(58.13)
BCS at calving					
	BCS G3 (2.50-2.75)	3413	(62.07)	549	(39.50)
	BCS G1 (1.00-1.75)	74	(1.35)	104	(7.48)
	BCS G2 (2.00-2.25)	1517	(27.58)	640	(46.04)
	BCS G4 (3.00-5.00)	495	(9.00)	97	(6.98)
BCS (Comparing current visit with calving)					
	No change	2860	(52.01)	574	(41.29)
	Decrease by 2,3 groups	341	(6.20)	210	(15.11)
	Decrease by 1 group	1801	(32.75)	517	(37.19)
	Increase by 1 group	467	(8.49)	87	(6.26)
	Increase by 2 groups	30	(0.55)	2	(0.14)

Table 4.

Transitions	Non-lame to lame [a,b,c]					Lame to non-lame [a,b,c]				
Covariates	**Freq.**	**OR.**	**95%**	**C.I.**	**P-value**	**Freq.**	**OR.**	**95%**	**C.I.**	**P-value**
Duration spent in state (days)										
≤45	339	Ref.				427	Ref.			
46-90	98	0.53	0.40	0.71	<0.001	43	0.64	0.40	1.04	0.07
≥90	82	0.33	0.21	0.51	<0.001	13	0.42	0.18	0.96	0.04
Herd										
1	55	Ref.				49	Ref.			
2	272	3.18	1.98	5.11	<0.001	247	0.23	0.10	0.53	<0.001
3	115	1.94	1.19	3.15	0.01	113	0.64	0.28	1.47	0.29
4	77	1.36	0.82	2.28	0.24	74	0.83	0.34	2.01	0.68
Days of lactation										
0-90	284	Ref.				267	Ref.			
91-120	84	1.64	1.17	2.29	<0.001	66	0.67	0.44	1.00	0.05
>120	151	2.11	1.58	2.82	<0.001	150	0.72	0.50	1.03	0.07
Month of calving										
Jan-March	132	Ref.				130	Ref.			
Apr-June	81	0.71	0.45	1.11	0.13	70	1.19	0.67	2.12	0.55
July-Sep	184	0.95	0.66	1.38	0.79	164	0.81	0.50	1.33	0.41
Oct-Dec	122	0.82	0.56	1.20	0.31	119	1.79	1.05	3.06	0.03
Parity group										
1	88	Ref.				80	Ref.			
2	78	1.26	0.83	1.91	0.28	76	1.08	0.52	2.25	0.83
3	109	3.00	1.95	4.60	<0.001	95	0.50	0.25	1.00	0.05
>3	244	3.51	2.39	5.17	<0.001	232	0.36	0.19	0.67	<0.001
BCS at calving										
BCS G3 (2.50-2.75)	266	Ref.				242	Ref.			
BCS G1 (1.00-1.75)	29	7.73	3.37	17.71	<0.001	24	0.21	0.08	0.52	<0.001
BCS G2 (2.00-2.25)	173	1.54	1.11	2.14	0.01	173	0.31	0.19	0.51	<0.001
BCS G4 (3.00-5.00)	51	0.92	0.56	1.51	0.74	44	1.51	0.73	3.10	0.27
BCS (Comparing current visit with calving)										
No change	253	Ref.				207	Ref.			
Decrease by 2,3 groups	64	2.07	1.30	3.29	<0.001	62	0.44	0.23	0.82	0.01
Decrease by 1 group	169	1.12	0.86	1.46	0.41	165	0.66	0.44	0.98	0.04
Increase by 1 group	31	0.53	0.33	0.83	0.01	48	2.49	1.37	4.53	<0.001
Increase by 2 groups	2	0.50	0.07	3.37	0.48	1	5.85	0.12	276.25	0.37

[a] Intercept (coefficient (standard error)): Non-lame to lame: -3.80 (0.34); Lame to non-lame :2.44 (0.61)

[b] Random variability between cows: Non-lame to lame : 0.80 (0.27) ; Lame to non-lame: 0.87 (0.36)

[c] Covariance : -0.32(0.25); Freq.: frequency, OR.: odd ratios, C.I.: credible interval, P-value.: significant value, Ref.: reference

Table 5.

Model	Coefficient	SE
Duration effects only		
Non-lame to lame	2.45*	0.55
Lame to non-lame	1.63*	0.65
Covariance between both transitions	-1.51*	0.58
Correlation between random effects	-0.76	
Duration+covariates		
Non-lame to lame	0.80*	0.27
Lame to non-lame	0.87*	0.36
Covariance between both transitions	-0.32	0.25
Correlation between random effects	-0.38	

*Significant at 5% level, SE: standard error.