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Author(s): J. Kaler, G.F. Medley, R. Grogono-Thomas, E.M.H. Wellington, L.A. Calvo-Bado, G.J. Wassink, E.M. King, L.J. Moore, C. Russell and L.E. Green

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1 **Factors associated with changes of state of foot conformation and lameness in a flock of**
2 **sheep**

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4 **J. Kaler^{a*}, G.F. Medley^a, R. Grogono-Thomas^b, E.M.H. Wellington^a, L.A. Calvo-Bado^a,**
5 **G.J. Wassink^a, E.M. King^a, L.J. Moore^b, C. Russell^b, L.E. Green^a**

6
7
8 ^aDepartment of Biological Sciences, University of Warwick, Coventry, CV4 7AL, UK

9
10 ^b Department of Clinical Veterinary Sciences, University of Bristol, Langford House,
11 Langford, Bristol BS40 5DU, UK

12
13 *Corresponding author, postal address as above

14 Tel. +44 2476 575860

15 Email:j.kaler@warwick.ac.uk

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18

19 **Abstract**

20 The aim of this research was to investigate transitions between foot conformation, lameness
21 and footrot in sheep. Data came from one lowland flock of approximately 700 ewes studied for
22 18 months. Multilevel multistate analyses of transitions between good and poor foot
23 conformation states in ewes, and lame and non-lame states in ewes and lambs were conducted.
24 Key results were that the longer sheep had feet in good conformation, the more likely they
25 were to stay in this state; similarly, the longer a ewe was not lame the more likely she was not
26 to become lame. Ewes with poor foot conformation were more likely to become lame (OR:
27 1.83 (1.24-2.67)) and to be > 4 years (OR: 1.50(1.09-2.05)). Ewes with footrot were less likely
28 to move to good foot conformation (OR: 0.48 (0.31-0.75)) and were more likely to become
29 lame (OR: 3.81(2.60-5.59)). Ewes lame for > 4 days and not treated with parenteral
30 antibacterials had a higher risk of developing (OR: 2.00 (1.08-3.61)), or remaining in (OR:
31 0.49 (0.29-0.95)) poor foot conformation compared with ewes never lame. Treatment of ewes
32 lame with footrot with parenteral antibacterials increased the probability of transition from a
33 lame to a non-lame state (OR: 1.46 (1.05-2.02)) and these ewes, even if lame for > 4 days,
34 were not more likely to develop poor foot conformation. The risk of a ewe becoming lame
35 increased when at least one of her offspring was lame (OR: 2.03 (1.42-2.92)) and when the
36 prevalence of lameness in the group was $\geq 5\%$ (OR: 1.42 (1.06-1.92)). Lambs were at
37 increased risk of becoming lame when they were male (OR: 1.42 (1.01-2.01)), single (OR: 1.86
38 (1.34-2.59)) or had a lame dam or sibling (OR: 3.10 (1.81-5.32)). There were no explanatory
39 variables associated with lambs recovering from lameness. We conclude that poor foot
40 conformation in ewes increases the susceptibility of ewes to become lame and that this can
41 arise from untreated footrot. Treatment of ewes lame with footrot with parenteral antibacterials
42 leads to recovery from lameness and prevents or resolves poor foot conformation which then
43 reduces the susceptibility to further lameness with footrot.

- 44 Key words: Multilevel multistate model; Footrot; Lameness; Foot conformation; Sheep;
- 45 *Dichelobacter nodosus*; Discrete-time survival

46 **1. Introduction**

47 Over 90% of sheep farmers in the UK report lameness in their flocks with a within flock
48 prevalence of 8-10% (Grogono- Thomas and Johnston, 1997; Kaler and Green, 2008a). Over
49 90% of lameness in sheep is caused by footrot with or without separation of hoof horn (Kaler
50 and Green, 2008a). The currently accepted pathogenesis of footrot is that, after initial damage,
51 the interdigital skin is invaded by the ubiquitous bacterium *Fusobacterium necrophorum*
52 leading to interdigital dermatitis. This is followed by entry of *Dichelobacter nodosus* (essential
53 for footrot) which can, given a pathogenic strain, a conducive environment and a susceptible
54 host, cause separation of hoof horn (Beveridge, 1941; Egerton and Roberts, 1969). With less
55 pathogenic strains of *D. nodosus*, a dry, hot or cold environment or a resistant host, separation
56 of the hoof horn might not occur and footrot presents as an interdigital inflammation.

57 Evidence from observational research suggests that farmers who treat individual lame sheep
58 with parenteral and topical antibacterials within 3 days of seeing them lame, have a within
59 flock prevalence of lameness of <2% (Wassink et al., 2003; Kaler and Green, 2008b). This was
60 confirmed in a within flock intervention study where the prevalence of lameness caused by
61 footrot was significantly lower in groups of sheep where individual lame sheep were treated
62 promptly with parenteral and topical antibacterials compared with groups where lame sheep
63 were treated with foot trimming and topical antibacterial spray (Wassink et al., 2010). In
64 addition, over 90% of sheep treated for footrot with parenteral and topical antibacterials
65 without foot trimming recovered within 10 days whilst <30% sheep treated with foot trimming
66 recovered in this time period (Kaler et al., 2010).

67 Beveridge (1941) suggested that after apparent recovery from footrot some sheep have
68 abnormal foot conformation and might continue to harbour *D. nodosus* for several months. In
69 addition, routine trimming of hoof horn (that is, trimming of feet of all sheep in a flock whether
70 they are lame or not) can lead to damage to the hoof horn and permanently misshapen feet

71 (Egerton et al., 1989). No epidemiological studies have been conducted to investigate
72 associations between foot conformation and the occurrence of footrot.

73 Animals might become diseased more than once with some diseases and so move between
74 diseased and non-diseased states over time. Fitting separate models for transitions between
75 each state, i.e. diseased to healthy and *vice versa*, is the traditional approach (Dohoo et al.,
76 2003) but has two major drawbacks: first, by fitting separate models we cannot test explicitly if
77 the effects of predictor variables are state dependent, and, secondly, the assumption of
78 independence between individual random effects for each state might not be correct because
79 there might be unobserved random factors affecting the states (Steele et al., 2004).

80 The aim of this research was to increase our understanding of the occurrence and persistence of
81 footrot. To do this multilevel multistate analyses were used to overcome the limitations of
82 separate state models, (Goldstein, 2004; Steele et al., 2004) and to investigate factors
83 associated with transitions between good and poor foot conformation states in ewes and
84 transitions between lame and non-lame states in ewes and lambs. We explored the complex
85 relationships between these states and the presence of footrot, host and environment factors and
86 the effect of treatment.

87 **2. Materials and methods**

88 *2.1. Source of data*

89 The data were collected as part of an intervention study (Wassink et al., 2010) that tested the
90 efficacy of prompt treatment of sheep lame with footrot, with or without separation of hoof
91 horn, with parenteral and topical antibacterials on a commercial flock. The flock consisted of
92 mainly North Country mules with some Roussin, Suffolk and Hartline breeds. Sheep lambed
93 indoors from the second week of March 2005 and were turned out with their lambs onto
94 lowland pastures from 24 hours after parturition.

95 All ewes and lambs were individually identified. Information on foot conformation and
96 presence of footrot (separation of the hoof horn and a characteristic smell) was collected when

97 the feet of 419 ewes were inspected in March 2005, September 2005 and March 2006. Foot
98 conformation was scored as 0 (undamaged sole, heel or wall area with foot with a perfect
99 shape) or 1 (some damage/misshapen sole, heel or wall of foot) by one of the four observers
100 who were trained by GJW. These data were used in Model 1.

101 Ewes were stratified by age, body condition score, foot conformation and presence of footrot
102 and the family group was allocated to one of four groups (two intervention and two control) by
103 stratified random sampling. Control and intervention groups were matched by pasture type.
104 Data collection started when the youngest lamb in a group was 4 weeks of age.

105 The locomotion of all sheep, in both intervention and control groups, was scored by
106 researchers using a validated locomotion scoring scale (Kaler et al., 2009). In the two
107 intervention groups, all sheep with locomotion score ≥ 2 (visible nodding of head in time with
108 shortened stride and uneven posture) were caught within 3 days of first being seen lame. Sheep
109 with footrot were treated with parenteral and topical antibacterials (Terramycin LA 200mg/ml,
110 Pfizer Ltd; 20 mg per kg bodyweight for ewes; Engemycin LA 200 mg/ml, Intervet/Schering-
111 Plough Animal Health; 15mg per kg bodyweight for lambs, and Terramycin Aerosol Spray,
112 150ml pack, 4g oxytetracycline hydrochloride 3.92% w/w, Pfizer Ltd.). Treated sheep were
113 observed until not lame (no visible nodding of head or uneven posture) or if still lame after 10
114 days, they were retreated. In the two control groups, the farm shepherd (who was blind to the
115 locomotion score) treated the sheep that he considered lame: sheep with footrot were treated by
116 foot trimming and application of topical antibacterials.

117 These data were used for Models 2 and 3. They included 692 ewes (including the 419 ewes
118 above) and their 1217 lambs which were observed between 3rd May and 19th Sep 2005; lambs
119 were weaned on 20/08/2005 and were not monitored after this time

120

121 *2.2. Defining states, transitions and episodes*

122 For Model 1, a sheep were defined as in a state of good foot conformation when the maximum
123 conformation score on all feet was 0 and poor when any foot had a conformation score ≥ 1 . For
124 Models 2 and 3, sheep were categorised into two states; non-lame, locomotion score < 2 and
125 lame when a ewe or lamb had a locomotion score ≥ 2 . An episode for Models 1, 2 & 3 was a
126 continuous period of time spent in a state until a transition occurred to another state.

127 *2.3. Discrete –time data structure (Table 1)*

128 For Model 1 on foot conformation, the length of each discrete time interval was 6 months and
129 there were two intervals per sheep. For Models 2 and 3 on lameness, the length of the discrete
130 time interval was 10 days; there were up to 12 intervals per sheep. For each episode j for sheep
131 k there was an original state i (coded as 1= good conformation, 2= poor conformation for
132 Model 1, and 1= non-lame, 2= lame for Models 2 and 3), the duration spent in that state was
133 categorised into discrete time intervals t_i (measured as $t=1, 2, \dots, n$ with n being the maximum
134 duration of an episode) and an outcome event at the end of the discrete time interval, y , with 0
135 = no change in state, and 1 = occurrence of a change in state. For example, for a sheep that
136 started an episode in a non-lame state that changed state to lame at the 4th discrete time
137 interval; there would be four discrete time intervals for that sheep-episode (1, 2, 3, 4) with
138 outcomes, that is change in state, (0, 0, 0, 1) which would then lead to the start of a new
139 episode. Explanatory variables were interacted with the original indicator state variable in the
140 model to give state specific effects. See Table 1 for an example of the data structure.

141

142 *2.4. Multilevel multistate discrete time models*

143 The discrete -time analysis is a modified logistic regression that models hazard probability in a
144 discrete time intervals. The hazard probability is a conditional probability that an event occurs
145 in a particular time period, given that it has not occurred in the previous time period and is
146 described by an odds ratio. In the analysis, the probability or hazard of a change in state (π) at
147 time interval t in episode j is expressed as in equation (1):

148 $\pi_{ijk} = \Pr \{y_{ijk(t)} = 1 \mid y_{ijk(t-1)} = 0\}$ (1)

149 i = original state, j = episode, k = sheep /lamb

150 Models 1 and 2 had two hierarchical levels, level 2 (k), ewes and level 1, discrete time interval
 151 within episodes. Model 3 had 3 levels, level 3 (l), the family group (lambs and ewe), level 2
 152 (k), the lamb and level 1, the discrete time interval within episodes. The majority of ewes and
 153 lambs had one or two episodes so a random term for variation between episodes within ewes /
 154 lambs was not included in the models. A logit link function was used to express the ratio of
 155 probability of a change in state to probability of no change in the state as expressed in
 156 equations 2 & 3. Models 1 and 2 took the form:

157 $\text{logit} [\pi_{ik(t)}] = \beta_0 + \alpha_i(t) + \beta x_{ik(t)} + u_k^{(i)}$ (2)

158 and Model 3 took the form:

159

160 $\text{logit} [\pi_{ikl(t)}] = \beta_0 + \alpha_i(t) + \beta x_{ikl(t)} + u_k^{(i)} + u_l^{(i)}$ (3)

161 where β_0 is a state specific intercept, $\alpha_i(t)$ a set of dummy variables for the discrete time
 162 interval t depicting duration of state, $\beta x_{ik(t)}$ covariates includes a vector of explanatory
 163 variables varying by time or sheep with a dummy variable for original foot conformation or
 164 lameness state (explanatory variables are described in Tables 2 & 3). Covariate effects and
 165 random variability indexed at level 2 ($u_k^{(i)}$) and 3 ($u_l^{(i)}$) varied by original state. The random
 166 effects were assumed to have a multivariate normal distribution with an unspecified covariance
 167 matrix and a non zero correlation between random effects. Models were assumed to have a
 168 binomial error distribution. The models were run in MLwiN 2.10 (Rasbash et al., 2000) and
 169 fitted with MCMC for 500,000 iterations with a burn in of 5000. Chain mixing and stability
 170 were evaluated visually.

171 **3. Results**

172 *3.1. Descriptive results*

173 *3.1.1. Model 1- foot conformation of ewes*

174 The final dataset for Model 1 had 419 ewes with a total of 275 episodes of good foot
175 conformation and 308 of poor foot conformation. With two 6-month discrete time intervals
176 there were 838 records. Ewes had a maximum of two transitions, one between March 2005 and
177 September 2005 and one between September 2005 and March 2006. Approximately 50%
178 (141/275) of episodes with good foot conformation had a transition to poor; 119 / 141 episodes
179 started with a good conformation in March 2005, approximately 80% (94) had a transition
180 within 6 months and the rest in 7-12 months. Approximately 60% (187/308) of episodes with
181 poor foot conformation had a transition to good; 117/187 episodes started with a poor
182 conformation in March 2005; 52% (68) had a transition within the first 6 months and the rest in
183 7-12 months. Significantly more good to poor (67% versus 33%; $p < 0.05$) foot conformation
184 transitions occurred in the first time interval than in the second; and significantly more poor to
185 good transitions (64% versus 36%; $p < 0.05$) occurred in the second time interval than the first.

186 *3.1.2. Model 2-lameness in ewes*

187 The dataset for Model 2 had 692 ewes contributing 1120 episodes of which 863 were non-lame
188 and 257 were lame episodes; there were a total of 7571, 10-day discrete time intervals. A total
189 of 222/863 episodes in non lame sheep ended with a transition to lame. Approximately 24% of
190 these occurred within 10 days, 38% within 20, 49% within 30, 77% within 60, 93% within 90
191 and the rest (7%) after 90 days. A total of 244/257 episodes in lame sheep had a transition to
192 non-lame. The majority (77%) of the lame to non-lame transitions occurred within 10 days,
193 with 91% within 20 days, 95% within 30 days, and the remaining 5% within 31 - 60 days.

194 *3.1.3. Model 3- lameness in lambs*

195 The dataset for Model 3 had a total 1217 lambs (707 sibling groups). There were 1379 non-
196 lame episodes and 204 lame episodes; with a 10-day discrete time interval the final dataset had

197 10542 records. There were 194/1379 episodes when non-lame lambs had a transition to lame;
198 19% within 10 days, 31% within 20, 43% within 30, 88% within 60 days and the remaining
199 12% occurring after 60 days. The majority (202/204) of episodes in lame lambs had a
200 transition to non-lame, with 86% occurring within 10 days and 97% within 20 days and the
201 remaining 3% within 21 - 30 days.

202

203 3.2. *Multilevel multistate models*

204 3.2.1. *Model 1- foot conformation of ewes (Table 4)*

205 The probability of a transition from good to poor foot conformation decreased in the second
206 time interval if the ewe had spent the first six months in a state of good foot conformation,
207 however, the first six month spent in poor foot conformation did not significantly affect the
208 transition from poor to good foot conformation. Ewes that had footrot at the start of a time
209 interval had a significantly lower probability of changing from poor to good foot conformation.
210 Ewes that were lame for > 4 days and were not treated with parenteral antibacterials were
211 significantly more likely to change from good to poor foot conformation and less likely to
212 change from poor to good compared with sheep that were not lame. There was no significant
213 association between ewes lame for ≤ 4 days, whether they were treated with antibacterials or
214 not, and ewes lame for > 4 days and treated with parenteral antibacterials and the probability of
215 transition from good to poor or poor to good foot conformation compared with non lame ewes.

216 3.2.2. *Model 2 – lameness in ewes (Table 5)*

217 The greater the number of 10-day intervals a ewe spent lame the less likely she was to move to
218 a non-lame state and vice versa. Ewes with poor foot conformation, footrot or > 4 years of age
219 at the start of the study were significantly more likely to move from a non-lame to lame state
220 compared with ewes with good foot conformation, no footrot or ≤ 4 years of age respectively.
221 A prevalence of lameness of $\geq 5\%$ in the group or at least one lame offspring at the start of the
222 time interval significantly increased the probability of a non-lame to lame transition compared

223 with a prevalence of lameness of <5% or when there were no lame offspring. The only variable
224 with a significant effect on lame to non-lame transitions in ewes was treatment with parenteral
225 antibacterials.

226 3.2.3. Model 3- lameness in lambs (Table 6)

227 The time a lamb spent in a lame or non-lame state did not significantly affect its probability of
228 having a transition to a non-lame or lame state respectively (Table 6). Male lambs had a
229 significantly higher probability of changing from a non-lame to a lame state compared with
230 female as did lambs born as singles compared with twins. Lambs grazing flood plain pasture
231 had a significantly increased risk of changing from non-lame to lame compared with those on
232 parkland but there was no significant effect of pasture type on transitions from lame to non-
233 lame. A lame sibling or mother at the start of the time interval significantly increased the
234 likelihood of a lamb moving from non-lame to lame. There were no significant factors
235 associated with lame to non-lame transitions in the lambs.

236 All the models (Tables 4, 5, 6) converged with visually stable chain mixing.

237

238 4. Discussion

239 The results from the current study assist in elucidating risks and posing hypotheses for
240 persistence of footrot in this flock. The models allow us to consider transitions between foot
241 conformation (Model 1, Table 4) and lameness states (Models 2 and 3, Tables 5 and 6) that
242 occurred over time in these sheep. This flock was studied closely and the dataset collected is a
243 rare resource. Over 90% of lameness in sheep that were inspected (all sheep with locomotion
244 score >1) in the intervention group was footrot (Hawker, 2008). Based on this finding it was
245 assumed that all lame sheep (in both the groups) had footrot. In support of this assumption is
246 the finding that over 90% of lameness in sheep flocks in the UK is attributed to footrot (Kaler
247 and Green, 2008a). Whilst it is not possible to be certain that the results are generalisable to all

248 flocks with footrot in a temperate climate, it is likely that the biological patterns are externally
249 valid.

250 The use of multilevel multistate analysis (Steele et al., 2004) is an informative approach to
251 investigate the state specific effects of exposures with certain variables affecting transitions
252 between states, some in only one direction. Steele et al. (2004) reported little impact on model
253 parameter estimates when the discrete intervals were increased in length. In the current model,
254 testing 5 and 8 day time intervals for lameness state transitions gave similar results to the 10-
255 day interval (results not shown). Foot conformation was observed at 6 month intervals, so there
256 is a possibility that two transitions, e.g. a sheep moving from good to poor to good
257 conformation, were missed. However, hoof horn grows at approximately 3 mm per month
258 (unpublished data) and it seems likely therefore that missed transitions would be a rare
259 occurrence because hoof horn damage would take months to resolve. For the sceptic, the
260 results from the analysis in the current paper at least provide evidence for factors associated
261 with a change in foot conformation after 6 months.

262 There were two periods of transition in the foot conformation model, March to September 2005
263 and September 2005 to March 2006. In the first time period when *D. nodosus* was probably
264 surviving on pasture and spreading between sheep the majority of transitions were good to
265 poor. The majority of transitions from poor to good foot conformation occurred between
266 September 2005 and March 2006 which included winter, when the ground and air temperature
267 were below that postulated for survival of *D. nodosus* on pasture (Egerton et al., 1989),
268 especially in January and February when ewes in this study were outdoors and so exposed to
269 this cooler climate. Assuming *D. nodosus* invades or recrudesces in damaged feet, the lack of
270 exposure to *D. nodosus* and the cold environment in this winter period, might have favoured
271 healing of skin and horn and so a transition from poor to good foot conformation. Once housed
272 in mid- February 2006, this flock was on deep straw (40 – 50cm of dry straw underfoot) until
273 March 2006. This dry environment might also have helped foot conformation to improve.

274 The presence of detectable footrot at the start of a time interval significantly reduced the
275 likelihood of a change from poor to good foot conformation (Table 4), suggesting that *D.*
276 *nodosus* prevented healing or was continuously damaging the foot. In addition, in many cases
277 it was the individual foot with poor conformation at the start of the interval (with or without
278 detectable footrot) that was later diagnosed with footrot (data not shown), suggesting that feet
279 with poor conformation either increased susceptibility to footrot or that they covertly harboured
280 *D. nodosus* as suggested by Beveridge, (1941) or both.

281 The fact that sheep lame for > 4 days and not treated with parenteral antibacterials had an
282 increased risk of changing from good to poor foot conformation suggests that either the foot is
283 more chronically damaged if disease persists for >4 days or that these sheep remained covertly
284 infected or both. Those lame sheep treated with parenteral antibacterials were protected from
285 this effect, even if lame for > 4 days, suggesting that parenteral antibacterials contributed
286 towards retaining a normal foot conformation, possibly because this treatment reduced the risk
287 of *D. nodosus* becoming or remaining quiescent in the foot. This protection of good
288 conformation was not observed in sheep treated with foot trimming and topical spray.
289 *Dichelobacter nodosus* penetrates deep into the hoof (Egerton et al., 1969) so that systemic
290 treatment is more likely to clear infection than topical treatment. This highlights the importance
291 of prompt parenteral antibacterial treatment which is the only current therapy for which there is
292 evidence for rapid recovery from foot lesions and lameness (Kaler et al., 2010).

293 Susceptibility to lameness, but not poor foot conformation, increased with age in ewes
294 suggesting some reduction in resistance to footrot with increasing age (Tables 4, 5). In ewes,
295 the probability of transition from non-lame to lame and from good to poor foot conformation
296 decreased with increased duration spent in a non-lame state or a state of good foot
297 conformation respectively. This suggests that the host foot conformation plays an important
298 role in resistance to footrot. Given that these sheep were all in a similar environment it might
299 indicate host heterogeneity with some sheep less susceptible to *D. nodosus* than others.

300 Poor foot conformation and presence of footrot also increased the risk of sheep becoming lame,
301 however, no variables other than treatment of ewes with parenteral antibacterials significantly
302 influenced the likelihood of lame to non-lame transitions in ewes, suggesting that once a sheep
303 is lame the former factors do not influence recovery but that treatment does assist recovery.

304 No variables at all were significantly associated with recovery from lameness in lambs. It is
305 possible that the lack of a significant positive effect of parenteral antibacterials in lambs was
306 because of the short duration of lameness episodes in lambs compared with ewes or the
307 presence of less severe footrot lesions than ewes (Hawker, 2008), or because lambs recovered
308 through their own immune response or possibly because of lack of power. The lack of
309 association between treatment with foot trimming and the likelihood of ewes and lambs
310 moving from lame to non-lame states is probably because foot trimming lame sheep increases
311 the time to recovery from lameness and foot lesions. In Kaler et al. (2010) >90% ewes treated
312 with parenteral antibacterials recovered within 10 days whilst <30% of those foot trimmed
313 recovered in this time period. In fact, the non significant (probably due to lack of power)
314 negative coefficients suggest that foot trimming might exacerbate lameness, perhaps because of
315 damage to the foot as indicated by the negative effect of foot trimming on foot conformation
316 (Model 1).

317 The significantly increased likelihood of male (vs. female) and single born (vs. twin) lambs
318 becoming lame might be due to the fact that male and single lambs are more likely to be
319 heavier which has been suggested to increase their susceptibility to lameness (Egerton et al.,
320 1989).

321 As with conformation states, there were environmental factors associated with a change in state
322 from non-lame to lame. The association between a prevalence of lameness in the group $\geq 5\%$
323 and non-lame to lame transitions in ewes suggests that *D. nodosus* was more abundant in these
324 groups which would either lead to more frequent or more intense exposure resulting in an
325 increased dose of *D. nodosus*. The strong link between lambs on flood plain pasture and a

326 higher probability of non-lame to lame transitions might be because this pasture type is wetter
327 and so could damage the lambs' interdigital skin and so increase their susceptibility to footrot,
328 or increase the suitability of the habitat for *D. nodosus*. In addition, sheep and lambs were more
329 likely to move from non-lame to lame if any member of the family was lame at the start of a
330 time interval. This might be due to contamination of the local environment with *D. nodosus*,
331 shed by a lame family member(s), increasing the likelihood of disease, or it might indicate a
332 genetic effect, where certain families are more susceptible to footrot than others, or it might be
333 a result of interactions between host genetics and pathogen strain.

334

335 **5. Conclusions**

336 There are complex interactions between factors in the host, the environment and the group of
337 sheep that alter the risks for changing conformation state and lameness in individual sheep. We
338 conclude that there is a dynamic interaction between lameness, footrot and foot conformation.
339 Footrot increases the risk of poor foot conformation, which increases the risk of further footrot
340 and further lameness, which then increases the risk of poor foot conformation. There are
341 relatively few factors that influence good to poor foot conformation and lame to non-lame
342 transitions. Good to poor foot conformation occurs principally a result of environmental
343 conditions and presence of footrot and lame to non-lame transitions occur after appropriate
344 treatment. Appropriate treatment, parenteral and topical antibacterial therapy, leads to recovery
345 from lameness and reduces the risk of poor foot conformation this in turn reduces susceptibility
346 to further episodes of footrot by preventing / reversing poor foot conformation.

347

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352 **Conflict of interest statement**

353 The authors declare no conflict of interests.

354

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403 Table 1: An example of lameness data in discrete-time format with one record for 10 day
 404 interval for multistate analysis

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sheep	episode	duration	Original state	Outcome	State indicator variables		Explanatory variable	Interactions between indicator and explanatory variables		
k	j	t	i	Y_{ijkt}	I_1	I_2	X	$I_1 * X$	$I_2 * X$	
1	1	1	1	0	1	0		0	0	0
1	1	2	1	0	1	0		0	0	0
1	1	3	1	0	1	0		0	0	0
1	1	4	1	1	1	0		0	0	0
1	2	1	2	0	0	1		1	0	1
1	2	2	2	0	0	1		1	0	1
1	2	3	2	1	0	1		1	0	1
1	3	1	1	0	1	0		0	0	0
1	3	2	1	0	1	0		0	0	0
1	3	3	1	0	1	0		0	0	0
1	3	4	1	0	1	0		0	0	0
1	3	5	1	0	1	0		0	0	0
2	1	1	2	0	0	1		0	0	0
2	1	2	2	0	0	1		0	0	0
2	1	2	2	0	0	1		0	0	0
2	1	4	2	0	0	1		0	0	0
2	1	5	2	1	0	1		1	0	1
2	2	1	1	0	1	0		0	0	0
2	2	2	1	0	1	0		0	0	0
2	2	3	1	0	1	0		0	0	0
2	2	4	1	0	1	0		1	1	0
2	2	5	1	0	1	0		1	1	0
2	2	6	1	0	1	0		1	1	0
2	2	7	1	1	1	0		1	1	0

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419 Table 2: Sheep level variables in foot conformation multistate model (Model 1), lameness
 420 multistate models for ewes (Model 2) and lambs (Model 3)
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Variables	Categories	Model 1		Model 2		Model 3	
		N	Percent	N	Percent	N	Percent
Ewes age at start of study :	≤ 4 years	252	60	332	48	-	-
	> 4 years	167	40	360	52	-	-
Foot conformation at start of study:	Good	-	-	469	68	-	-
	Poor	-	-	224	32	-	-
Presence of footrot at start of study:	No	-	-	548	79	-	-
	Yes	-	-	145	21	-	-
Sex of lamb:	Male	-	-	-	-	629	52
	Female	-	-	-	-	588	48
Litter size born :	Single	-	-	-	-	224	18
	Twin	-	-	-	-	993	82

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Table 3: Number of observations for discrete –time variables included in foot conformation model for ewes (Model 1) and lameness models for ewes (Model 2) and lambs (Model 3)

Discrete time variables	Categories	Model 1		Model 2		Model 3	
		Good	Poor	Non-Lame	Lame	Non-Lame	Lame
Treated with parenteral antibacterials in time t :	No	-	-	-	279	-	193
	Yes	-	-	-	90	-	48
Treated with foot trim in time t :	No	-	-	-	357	-	235
	Yes	-	-	-	12	-	6
Presence of footrot at start of t :	No	-	334	-	-	-	-
	Yes	-	115	-	-	-	-
Lameness and treatment in time t :							
	Not lame	213	179	-	-	-	-
	Lame ≤ 4 days & treated with parenteral antibacterials	60	99	-	-	-	-
	Lame >4 days & treated with parenteral antibacterials	18	32	-	-	-	-
	Lame >4 days & treated with foot trimming	3	6	-	-	-	-
	Lame ≤ 4 days & no treatment	72	83	-	-	-	-
	Lame > 4 days & no treatment	23	50	-	-	-	-
Prevalence of lameness in pasture at start of t :	$< 5\%$	-	-	4309	109	5873	241
	$\geq 5\%$	-	-	2893	260	4428	0
Offspring(s) lame at start of t :	No	-	-	7010	325	-	-
	Yes	-	-	192	44	-	-
Mother or sibling lame at start of t :	No	-	-	-	-	9701	180
	Yes	-	-	-	-	600	61
Pasture type in t :	flood plain	-	-	4073	222	6102	141
	clover lay	-	-	979	46	1686	56
	parkland	-	-	2150	101	2513	44

Table 4: Model 1. Multilevel multistate model for transitions between foot conformation states in ewes

Variable	Categories	Good to poor foot conformation ^{a,b,c}		Poor to good foot conformation ^{a,b,c}	
		OR	95% C.I.	OR	95% C.I.
Duration spent in a state (months)					
	0 - 6	ref.	-	ref.	-
	7 - 12	0.50	0.31-0.79	0.95	0.68-1.32
Footrot at start of time t :					
	No	-	-	ref	-
	Yes	-	-	0.48	0.31-0.75
Age at the start of study:					
	≤ 4 years	ref	-	ref	-
	> 4 years	1.04	0.72-1.49	0.83	0.62-1.13
Lameness and treatment in time t :					
	Not lame	ref	-	ref	-
	Lame ≤ 4 days & treated with parenteral antibacterials	1.03	0.62-1.71	1.19	0.81-1.77
	Lameness >4 days & treated with parenteral antibacterials	1.27	0.58-2.57	1.09	0.58-2.04
	Lameness >4 days & treated with foot trimming	2.93	0.40-22.26	0.56	0.09-3.41
	Lameness ≤ 4 days & no treatment	1.17	0.70-1.94	0.95	0.62-1.45
	Lameness > 4 days & no treatment	2.00	1.08-3.61	0.49	0.29-0.95

OR- Odds ratio; ^a Constant (Coefficient (standard error): good to poor foot conformation: -2.68 (0.50); poor to good foot conformation : -2.41 (0.36) ^b Random variability between sheep : good to poor foot conformation: 0.05 (0.04); poor to good foot conformation: 0.07 (0.06) ^c Covariance: 0.002 (0.03)

Table 5: Model 2. Multilevel multistate model for transitions between lameness states in ewes

Variable	Categories	Non-Lame to Lame ^{a,b,c}		Lame to Non- Lame ^{a,b,c}	
		OR	95% C.I.	OR	95% C.I.
Duration spent in a state (days)	0-10	ref.	-	ref.	-
	11-20	0.76	0.52-1.29	0.76	0.51-1.12
	21-30	0.50	0.24-0.99	0.50	0.24-0.98
	31-60	0.69	0.46-1.04	0.76	0.40-1.45
	61-90	0.60	0.36-0.99	-	-
	>90	0.40	0.21-0.77	-	-
Foot conformation of ewe at start of the study :	Good	ref.	-	ref.	-
	Poor	1.83	1.24-2.67	0.93	0.65-1.34
Presence of footrot at start of the study:	No	ref.	-	ref.	-
	Yes	3.81	2.60-5.59	0.85	0.60-1.20
Age of ewe at start of study :	≤ 4 years	ref.	-	ref.	-
	> 4 years	1.50	1.09-2.05	1.07	0.81-1.40
Treated with a parenteral antibacterials in time <i>t</i> :	No	-	-	ref.	-
	Yes	-	-	1.46	1.05-2.02
Treated with a foot trim in time <i>t</i> :	No	-	-	ref.	-
	Yes	-	-	0.34	0.09-1.25
Prevalence of lameness in field at start of time <i>t</i> :	<5%	ref.	-	ref.	-
	≥ 5 %	1.42	1.06-1.92	1.03	0.76-1.39
Lame offspring(s) at start of time <i>t</i> :	No	ref.	-	ref.	-
	Yes	2.03	1.42-2.91	0.85	0.62-1.17
Pasture type in time <i>t</i> :	parkland	ref.	-	ref.	-
	clover lay	0.79	0.49-1.30	0.97	0.60-1.54
	flood plain	1.02	0.73-1.42	0.95	0.65-1.30

OR- Odds ratio; ^a Constant (Coefficient (standard error): non-lame to lame: -7.21(0.38); lame to non-lame : -2.68(0.32) ^b Random variability between sheep : non-lame to lame: 0.50 (0.19); lame to non-lame: 0.03 (0.02) ^c Covariance: -0.06 (0.07)

Table 6: Model 3. Multilevel multistate model for transitions between lameness states in lambs

Variable	Categories	Non-Lame to Lame ^{a,b,c,d,e}		Lame to Non- Lame ^{a,b,c,d,e}	
		OR	95% C.I.	OR	95% C.I.
Duration of time spent in a state (days)					
	0-10	ref.	-	ref.	-
	11-20	0.77	0.44-1.33	1.00	0.61-1.63
	21-30	0.85	0.48-1.51	0.34	0.54-3.32
	31-60	1.43	0.89-2.28	-	-
	>60	0.62	0.31-1.28	-	-
Sex of the lamb:					
	Female	ref.	-	ref.	-
	Male	1.42	1.01-2.01	0.92	0.67-1.25
Litter :					
	Twin/Triplet	ref.	-	ref.	-
	Single	1.86	1.34-2.59	1.07	0.77-1.48
Treated with a parenteral antibacterials in time <i>t</i> :					
	No	-	-	ref.	-
	Yes	-	-	1.03	0.68-1.56
Treated with a foot trim in time <i>t</i> :					
	No	-	-	ref.	-
	Yes	-	-	0.96	0.25-3.57
Prevalence of lameness in field at start of time <i>t</i> :					
	< 5%	ref.	-	-	-
	≥ 5%	0.81	0.47-1.40	-	-
Lame sibling lamb or mother at start of time <i>t</i> :					
	No	ref.	-	ref.	-
	Yes	3.10	1.81-5.32	1.06	0.78-1.43
Pasture type in time <i>t</i> :					
	parkland	ref.	-	ref.	-
	clover lay	1.61	0.81-3.08	1.08	0.67-1.75
	flood plain	1.59	1.02-2.49	0.82	0.52-1.27

OR- Odds ratio; ^a Constant (Coefficient (standard error): non-lame to lame: -6.61 (0.50); lame to non-lame : -2.25(0.36) ^b Random variability between sibling group : non-lame to lame: 0.49 (0.28); lame to non-lame: 0.02(0.02) ^c Covariance: -0.01 (0.06) ^d Random variability between lambs within a sibling group : non-lame to lame: 1.12 (0.38); lame to non-lame: 0.02 (0.03) ^e Covariance -0.02 (0.07)