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INTERPRETIVE SUMMARY

Evaluation of treatments for claw horn lesions in dairy cows. Thomas.

Lameness in dairy cows is a significant health and welfare problem around the world. Diseases affecting the hoof are some of the most common problems. Thousands of animals are treated for these conditions, yet there is little research evidence on the most effective treatments. We tested four treatments in an on-farm trial. A therapeutic trim alone or in combination with either elevating the diseased digit using a glue on block, or a course of anti-inflammatories or both additional treatments. The combination of trimming, elevation of the claw and course of anti-inflammatories was most successful. We recommend its use on-farm.

Evaluation of treatments for claw horn lesions in dairy cows in a randomized controlled trial

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ABSTRACT

Lameness is one of the most significant endemic disease problems facing the dairy industry. Claw horn lesions (principally sole haemorrhage, sole ulcer and white line disease) are some of the most prevalent conditions. Despite the fact that thousands of animals are treated for these conditions every year, there is limited experimental evidence on the most effective treatment protocols.

A randomized, positively controlled clinical trial was conducted to test the recovery of newly lame cows with claw horn lesions. Animals on five farms were locomotion scored every two weeks. Cows were eligible for recruitment if they had two non-lame scores followed by a lame score and had a claw horn lesion on a single claw of a single foot. Following a therapeutic trim, enrolled cows were randomly allocated to one of four treatments: Treatment 1 – no further treatment (positive control; 'TRIM'), Treatment 2 – trim plus a block on the sound claw ('TRIM/BLOCK'), Treatment 3 – trim plus a 3 day course of the non-steroidal anti-inflammatory drug (NSAID) ketoprofen ('TRIM/NSAID'), Treatment 4 – trim plus a block plus ketoprofen ('TRIM/BLOCK/NSAID'). The primary outcome measure was locomotion score 35 days after treatment, by an observer blind to treatment group.

Descriptive statistics suggested that treatment groups were balanced at the time of enrolment i.e. randomization was successful. Based on a sound locomotion score (Score 0) 35 days after treatment, the number of cures was 11 of 45 (24.4%) for TRIM, 14 of 39 (35.9%) for TRIM/BLOCK, 12 of 42 (28.6%) for TRIM/NSAID and 23 of 41 (56.1%) for TRIM/BLOCK/NSAID. The difference between TRIM/BLOCK/NSAID and TRIM was significant.

To test for confounding imbalances between treatment groups, logistic regression models were built with two outcomes, either sound (Score 0) or non-lame (Score 0 or 1) 35

days after treatment. Compared to TRIM, animals which received TRIM/BLOCK/NSAID were significantly more likely to cure to a sound outcome. Farm, treatment season, lesion diagnosis, limb affected, treatment operator and stage of lactation were included in the final models.

Our work suggests that lameness cure is maximised with NSAID treatment in addition to the common practices of therapeutic trimming and elevation of the diseased claw using a block when cows are newly and predominantly mildly lame.

Key words: dairy cow, lameness, claw horn lesion, randomized clinical trial

INTRODUCTION

Lameness in dairy cattle is a significant problem in intensive dairy industries around the world, causing both production losses (Huxley, 2013) and discomfort, undermining animal welfare (Whay et al., 1997). Achieving sustainable reductions in the levels of disease on-farm, requires a combination of two approaches. Firstly, the implementation of effective farm-specific prevention strategies to decrease the rate at which new cases develop, and, secondly, early identification and prompt and effective treatment of clinical cases to reduce the duration of time over which animals are lame. While the emphasis of the majority of recent research has rightly focused on identifying risk factors for lameness and disease prevention, the treatment of animals once they become lame must not be neglected.

Sole haemorrhage, sole ulcer and white line disease (the most common claw horn lesions) are some of the most prevalent conditions causing lameness (Capion et al., 2008, Cramer et al., 2008). Despite the fact that many thousands of animals are routinely treated for these diseases, a recent systematic review of the peer reviewed literature on the prevention and treatment of foot lameness in cattle highlighted the deficit of information in this area (Potterton et al., 2012). In literature published between 2000 and 2011, no papers were identified concerned with the treatment of white line disease and only three with the treatment of sole ulcers. Of these, two were case studies (i.e. not experimental) and whilst the third was composed of primary research it assessed dietary supplementation with Biotin (Lischer et al., 2002) and is of limited use in the field. The authors concluded that virtually all the existing information on the treatment of claw horn lesions appeared to be from anecdotal reports, based on the experience and knowledge of experts working in the field. This does not mean to say that current treatment protocols are ineffective, rather it highlighted the deficit of experimental evidence on the most effective treatment i.e. those that lead to the highest cure rates in the shortest time.

An extension of the literature search described above confirms that very little primary research work has ever been published testing treatments for claw horn lesions, only two other peer reviewed papers were identified. The first describes a randomized study conducted in Australia which tested wooden blocks, rubberised shoes and padded bandages containing copper sulphate for the treatment of a variety of claw horn lesions (Pyman, 1997). Three and seven days after treatment, significantly high number of cows had recovered in the block and shoe groups compared with the bandage group; outcome assessment was limited to 14 days post treatment by which time no differences between groups were apparent. In the second, dairy cows managed under New Zealand's extensive pasture based systems, were randomly treated with a plastic shoe and the non-steroidal anti-inflammatory drug (NSAID) Tolfenamic acid, following corrective trimming (Laven et al., 2008). The authors concluded that there were no significant differences between treatments in either nociceptive threshold or locomotion score over the 100 day outcome period. The objective of the present study was to compare four treatments for claw horn lesions in a randomized study under UK field conditions.

MATERIALS AND METHODS

Study Design and Reporting

A positively controlled, randomized clinical trial (RCT) with blind outcome observations was designed to test the recovery of dairy cows with claw horn lesions, treated using different protocols. The study hypothesis stated that the likelihood of claw horn lesion recovery depended on the treatment administered. Based on a binary primary outcome measure (lame or not lame) post treatment, a power calculation suggested that treatment group sizes of 58 would detect a 25% difference in recovery rate between treatments (power value of 0.8, $P \leq$

118 0.05). A difference of 25% was selected as it was considered clinically meaningful and likely
119 to be large enough to warrant the additional cost of the treatments tested should they prove
120 superior.

121 The study was positively controlled (i.e. no animals were left untreated) and
122 conducted under the Veterinary Surgeons Act 1966, which regulates acts of veterinary
123 surgery in the UK. The protocol was reviewed and approved by the University of
124 Nottingham's School of Veterinary Medicine and Science Ethical Review Committee prior to
125 study instigation.

126 The study manuscript has been prepared in accordance with the guidelines outlined in
127 the REFLECT statement for reporting randomized controlled trials in livestock (O'Connor et
128 al., 2010).

129

130 ***Herd Selection***

131 A convenience sample of five commercial dairy farms was recruited in the East Midlands
132 area of the UK, within close proximity to the University of Nottingham. To be eligible for
133 enrolment, farms were required to have a herd lameness prevalence of above 20% at the start
134 of the study and be undertaking routine measures to control digital dermatitis at the herd level
135 (e.g. regular foot bathing). Farms were either known to the trial coordinators or were
136 recruited through their veterinary surgeons' who were asked to nominate clients they
137 considered met the criteria and would be willing to participate. A short list of suggested farms
138 were approached and visited to discuss the trial and to assess their lameness prevalence.
139 Following an introductory phone call, one farm elected not to participate as they considered
140 the trial would interfere with their day to day farm management.

141 The five farms were between 187 and 353 (median 241) cows in size with 305-d
142 adjusted milk yields ranging from 7,394 to 11,579L (median 10,381L). Three of the farms

143 (Farms 2, 4 and 5) housed lactating cows continuously, the other two farms managed cows at
144 pasture during the summer (~March – October) and in housing over winter. On all farms,
145 lactating cows were accommodated in stalls with mats, mattresses or waterbeds. Two farms
146 (Farms 2 and 4) milked cows in an automatic milking system, the remaining farms milked
147 cows in conventional parlours, two times daily. All walkways and standing areas were
148 concrete on all farms except Farm 2 which had rubber matting throughout and Farm 3 which
149 had rubber matting at the feed face of the high yielding group. All farms undertook routine
150 foot trimming, although scheduling ranged from as required to weekly sessions; two farms
151 (Farms 1 and 2) used an external professional foot trimmer, on the other farms trimming was
152 conducted by farm staff. All the farm routines were that lame cows were treated as soon as
153 they were identified or at weekly or fortnightly routine health sessions, depending on disease
154 severity and staff availability. Farmers were advised to continue their normal procedures for
155 identifying and treating lame cows throughout the study period.
156
157 ***Cow Selection and Enrolment Criteria***
158 Beginning in December 2011, locomotion scoring of all cows in the lactating herd was
159 undertaken at fortnightly intervals, by trained experienced observers (HT, GMP, NJB), as
160 cows exited the milking parlour (Farms 1, 3 and 5) or in a passageway with a firm, level
161 surface (Farms 2 & 4). All animals in all herds were uniquely identified by freeze brand,
162 which was used to distinguish individual cows. Dry cows and young stock were not scored.
163 Cows were scored on a 6 point scale adapted from the Great Britain industry standard scoring
164 system (Table 1); for animals considered lame (> 1), the lame limb was identified and
165 recorded.
166 Animals were considered for enrolment if they presented with a new case of lameness
167 in a single hind limb i.e. two successive non-lame scores (0 or 1) followed by a lame score (>

168 1). Animals were excluded if they had received treatment for lameness in the same foot
169 within 120 days, treatment for lameness in another foot within 90 days or had completed a
170 course of parenteral antibiotics or NSAIDs within the previous 14 days.

171 Selected cows were examined within 48 hours of the locomotion scoring. Animals
172 were assessed for body condition score (BCS) according to Edmonson et al. (1989) using a
173 scale of 1-5 with increments of 0.5. The lame foot was inspected with the animal restrained in
174 a foot trimming crush. Animals were excluded if they were diagnosed with interdigital
175 necrobacillosis, active digital dermatitis (an M1, M2 or M4.1 lesion (Berry et al., 2012)),
176 substantial inter-digital hyperplasia or a significant hock lesion. Identification of the painful
177 claw was attempted by lateral rotation of the claw resulting in a withdrawal reflex and the
178 application of hoof testers. Each animal received a therapeutic trim of the whole foot (i.e.
179 both claws) consisting of a standard trim, investigation and trimming out of any lesions
180 identified, removal of diseased and under-run horn and rebalancing the claw height to reduce
181 weight bearing on the diseased claw (Toussaint Raven, 2002). Animals were excluded from
182 the study where lesions were identified in both claws i.e. only animals with a claw horn
183 lesion(s) on one claw of a single lame hind leg were eligible for inclusion.

184 Animals which did not meet these enrolment criteria were treated but not enrolled.
185 They took no further part in the study, but they could be considered again in the future
186 providing the minimum lag periods since treatment had elapsed. Animals could only be
187 enrolled onto the study once; if they presented with lameness on the same or a different leg in
188 the future they were excluded.

189

190 ***Lesion Classification***

191 Claw lesions identified during examination of the feet of enrolled animals were classified into
192 one of three groups:

193 1. Sole haemorrhage / sole ulceration (SH/U): Lesion(s) composed of haemorrhage or an
194 ulcer of the sole in any location
195 2. White line disease (WLD): Lesion(s) of any severity (haemorrhage through to complete
196 separation) at any location on the white line
197 3. Other claw horn lesion: Any other claw horn lesion(s) that could not be categorised as
198 SH/U or WLD or two or more different lesions on the same claw (e.g. SH/U and WLD)
199
200 ***Randomization and Treatments Administered***
201 Enrolled animals were randomly allocated to one of four treatment groups (Table 2), using a
202 computer generated randomization plan (www.randomization.com, work conducted by HT)
203 created in blocks of four, with each of the four treatment groups included once in each block.
204 Randomization was further blocked by farm and lesion type (SH/U, WLD or 'Other'), to
205 ensure approximate temporal matching of equal numbers of cows with each diagnosis within
206 each study farm. Group 1 (Therapeutic trim only; 'TRIM') was considered the positive
207 control group. Following completion of the therapeutic trim, animals were allocated to
208 treatment group by drawing consecutively numbered cards from a card index box which had
209 the treatment written on the reverse side.
210 Drawing of the randomization cards and administration of treatments were conducted
211 by trained veterinary surgeons familiar with the treatment of lame cows and predominantly
212 undertaken by a single operator (HT) with vacation cover (SA, OM, JH and JR). Operators
213 administering treatments were not blind to the treatment administered. Enrolled animals were
214 identified with a leg band on both hind limbs. Farmers were asked to continue managing
215 them in accordance with normal farm management practices but were requested not to treat
216 them for lameness and to notify the researcher if they felt that further intervention was
217 necessary. Farmers were not blind to treatment group, whilst they were not provided with a

218 list of treatments administered, the presence of a therapeutic blocks could be observed and
219 treatment with NSAID was recorded in their medicine records.
220
221 ***Treatment Follow Up and Outcome Observations***
222 Animals were re-examined eight days (± 3 days) after treatment. If a foot block had been
223 applied as part of the treatment protocol (Treatment 2 ('TRIM/BLOCK') and Treatment 4
224 (TRIM/BLOCK/NSAID')) and it was no longer present, it was reapplied. If their locomotion
225 score had deteriorated from that at the time of enrolment, animals were retreated.
226 Animals in groups TRIM/BLOCK and TRIM/BLOCK/NSAID were re-examined for
227 a second time, 28 days (± 3 days) after treatment. If the block was still present, it was
228 manually removed using trimming pincers and careful leverage. This was the only action
229 undertaken at this time point i.e. no additional treatment(s) were administered.
230 The primary outcome measure, locomotion score 35 days (± 4 days) after treatment,
231 was conducted by an independent observer (GMP) blind to treatment group. That observer
232 collected outcome scores with cows walking in isolation, on a firm level surface. For animals
233 considered lame (> 1), the lame limb was identified and recorded. Following the blind
234 outcome score animals were body conditioned scored using the method previously described
235 and the treated limb was elevated and examined for digital dermatitis and any other
236 conditions.
237
238 ***Additional Data Collected***
239 Data on parity, monthly milk yield and calving date were collated from farm records.
240 Animals which were sold, culled or died before assessment of the primary outcome measure
241 were recorded and withdrawn from the study.
242

243 ***Data Collation and Statistical Analysis***

244 Data collected for each cow at each visit were recorded onto data capture forms and
245 then transcribed and stored in a relational database (Access 2007, Microsoft Corporation).
246 Data analysis was conducted in Minitab 16 (Minitab Inc.). Data were audited for validity and
247 spurious records using entry rules set up in the database and by manually scanning for
248 outlying data following sorting within each data category. For analysis locomotion scores 2a
249 and 2b, and 3a and 3b were amalgamated to 2 and 3 respectively.

250 Differences between treatment groups at the time of enrolment were assessed by
251 analysis of variance (days in milk and last recorded monthly yield) and using the Kruskal-
252 Wallis test (lameness score at treatment, body condition score at treatment and parity).

253 A successful treatment at study outcome (35 days after treatment) was defined as
254 either: i. a sound locomotion score (Score 0) or ii. a non-lame score (Score 0 or 1). The
255 proportions of successful treatments in animals which received TRIM/BLOCK,
256 TRIM/NSAID (Treatment group 3) and TRIM/BLOCK/NSAID were each compared to
257 TRIM using the χ^2 test. A Bonferroni corrected *P* value was calculated to account for multiple
258 comparisons; the significance probability was set at $P \leq 0.05$ for a two tailed test.

259 To test for confounding effects in the results, a multivariable analysis was conducted.
260 Logistic regression models were built in MLwiN (Version 2.1, Centre for Multilevel
261 Modelling, University of Bristol), with the same outcomes described above: i. a sound
262 locomotion score (Score 0) 35 days after treatment and ii. a non-lame score (Score 0 or 1) 35
263 days after treatment. Farm and treatment were forced into the models as categorical fixed
264 effects. Other variables and plausible interactions were investigated by forwards selection, for
265 inclusion stepwise. Variables were eliminated from the model based on the Wald test if $P \leq$
266 0.05. Variables tested included parity (1, 2, 3, $\geq$ 4), days in milk, calving season (winter,
267 spring, summer, autumn), season of treatment, locomotion score at treatment, lame leg at

treatment, BCS at treatment and outcome, lesion classification (SH/U, WLD, Other), active DD at outcome (Yes/No), retreatment required at 8 day recheck visit (Yes/No), reapplication of block required at eight day recheck visit (Yes/No), treatment operator (principal operator (HT) or 'other' operators (SA, OM, JH, JR)) and milk yield at the last two monthly recordings. DIM was tested as a linear mean centred variable, a categorical variable in 30 d increments, and as a non-linear variable; $e^{(-0.065 * DIM)}$ (Silvestre et al., 2006).

To assess fit, model predictions were compared to the observed data in groups stratified by categorical variables in the model, such as treatment group. Predictions were generated by simulation. The models were deemed adequate if observed values were within 95% confidence intervals of prediction.

RESULTS

Study Inclusions

Between the 10th of January 2012 and the 31st January 2013 a total of 512 cows met the initial selection criteria and were examined. Enrolment of cows on Farm 3 was suspended on the 24th of April 2012 due to the very low numbers of animals which were becoming eligible for enrolment (i.e. the number of new cases of lameness had dropped substantially from the start of the study). Farm 5 was recruited as a replacement; enrolment began on the 17th of July 2012 and continued to the end of the study. Selection of cows on Farm 3 recommenced on the 16th of November 2012 and continued to the end of the study. Of the selected and examined cows, 183 met all of the inclusion criteria and were enrolled into the RCT. The remaining 329 animals were not enrolled for the following reasons: 227 (68.9%) had a lesion on both claws; 27 (8.2%) had no visible lesion on either claw and no painful claw could be identified; two (0.6%) were no longer lame, 41 (12.5%) had active digital dermatitis, three (0.9%) had interdigital necrobacillosis, one (0.3%) had an inter-digital hyperplasia, six (1.8%) had a hock

293 lesion, 14 (4.3%) had been treated by farm staff and eight (2.4%) were not compliant with
294 the study protocol.
295 The number of cows allocated to each of the treatment groups by lesion diagnosis and
296 farm is outlined in Table 3. In total 47 cows received TRIM, 46 TRIM/BLOCK, 45
297 TRIM/NSAID and 45 TRIM/BLOCK/NSAID. Of the enrolled cows, 171 (93.4%) presented
298 with a locomotion score of 2 and 12 (6.6%) with a score of 3.
299
300 ***Study Exclusions***
301 Sixteen enrolled cows were withdrawn before the primary outcome was assessed. One
302 animal (Fm 1, TRIM/NSAID) was culled; five animals (Fm 2, TRIM/BLOCK x2; Fm 4,
303 TRIM/BLOCK/NSAID; Fm 5, TRIM/BLOCK x1 & TRIM/BLOCK/NSAID x1) were
304 withdrawn for non-compliance with the study protocol after enrolment (e.g. becoming unduly
305 stressed or repeated collapsing in the crush); four animals (Fm 2, TRIM/NSAID x1 &
306 TRIM/BLOCK/NSAID x1; Fm 4, TRIM/BLOCK x1 & TRIM/BLOCK/NSAID x1) were
307 retreated by the farmer without informing the researcher and six animals (Fm 1,
308 TRIM/BLOCK x1 & TRIM/NSAID x1; Fm 2, TRIM/BLOCK; Fm 4, TRIM x1 &
309 TRIM/NSAID x1; Fm 5, TRIM) were lost to the study or were unavailable for reassessment
310 for other reasons (e.g. moved to a distant location or incorrectly identified). Of the remaining
311 167 enrolled animals, six animals (Fm 1, TRIM x1 & TRIM/BLOCK x1; Fm 2,
312 TRIM/BLOCK x1 & TRIM/NSAID x1; Fm 4 TRIM/BLOCK x1 & TRIM/BLOCK/NSAID
313 x1) required retreatment at the eight day recheck visit. Two received additional trimming,
314 two had their foot block removed and repositioned, one was treated for digital dermatitis with
315 topical oxytetracyline spray (Alamycin aerosol 3.58% w/w cutaneous spray solution,
316 Norbrook) and one received treatment for a hock lesion by cleaning and the application of
317 topical oxytetracyline spray. Seventeen animals that received TRIM/BLOCK (seven animals)

and TRIM/BLOCK/NSAID (10 animals) required the reapplication of a foot block at the eight day recheck visit because it was no longer present. One hundred and forty four cows were treated by the principal operator (HT) and 23 cows were treated by other operators (SA, JR, JH or OM).

Descriptive Results and Univariate Analysis

The parity, days in milk, last recorded milk yield and body condition score and lameness score at treatment of enrolled cows by treatment group are outlined in Table 4. Differences between groups were not significant.

The locomotion scores of enrolled cows at outcome, 35 days after treatment, are outlined in Table 5. Based on a sound score (Score 0) the number (and percentage) of successful treatments was 11 of 45 (24.4%) for TRIM, 14 of 39 (35.9%) for TRIM/BLOCK, 12 of 42 (28.6%) for TRIM/NSAID and 23 of 41 (56.1%) for TRIM/BLOCK/NSAID. The difference between TRIM/BLOCK/NSAID and TRIM was significant (Bonferroni corrected $P = 0.01$).

Based on a non-lame score (Score 0 or 1), the number (and proportion) of successful treatment was 31 of 45 (68.8%) for TRIM, 28 of 39 (71.8%) for TRIM/BLOCK, 32 of 42 (76.2%) for TRIM/NSAID and 35 of 41 (85.3%) for TRIM/BLOCK/NSAID. The differences between groups were not significant.

Of the lame animals 35 days after treatment, the number (and proportion) of animals lame on the leg that was treated at enrolment was eight of 14 (57.1%) for TRIM, four of 11 (36.4%) for TRIM/BLOCK, five of 10 (50%) for TRIM/NSAID and five of six (83.3%) for TRIM/BLOCK/NSAID.

Logistic Regression Analysis

343 Of the enrolled cows, 85 and 66 had missing milk recording records in the preceding one and
344 two months respectively. Milk recording records in the two months preceding treatment were
345 tested in models based on subsets of the dataset with no missing records. Eight animals had
346 missing records for DIM and were discarded.
347 Model fit to the data was acceptable, and results of the logistic regression models are
348 outlined in Table 6. In the first model testing cure to outcome i. (Score 0), animals in the
349 TRIM/BLOCK/NSAID group were significantly more likely to cure compared to cows in the
350 TRIM group ($P \leq 0.05$). Cows treated on Farm 5, compared to other study farms, and
351 treatments in Spring and Autumn, compared to treatments in winter, were less likely to cure.
352 In the second model testing cure to outcome ii. (Score 0 or 1), treatment group was
353 not significant, however there was a trend for animals in the TRIM/BLOCK/NSAID group to
354 be more likely to cure compared to cows in the TRIM group (odds ratio 3.2, 95% CI 0.9-
355 11.3). Cows with 'Other' lesions had lower odds of cure compared to cows treated for SH/U
356 and animals treated by 'Other' operators were less likely to cure than those treated by the
357 principal operator.
358 In both models, animals treated on the left hind limb were more likely to cure
359 (compared to those treated for lameness on the right hind limb) and cows were more likely to
360 recover when treated in early lactation with exponential decay in the relationship with time
361 after calving.
362
363 **DISCUSSION**
364 In this study, lame cows treated for a claw horn lesion in a single claw of a single leg
365 recovered at different rates depending on the treatment administered. Cows treated with a
366 therapeutic trim, block and NSAIDs were more likely to recover to a sound locomotion score
367 than those treated with a therapeutic trim alone.

One of the surprising findings from our study was how small the differences in treatment success were between therapeutic trim and the application of a block to the sound claw and therapeutic trim alone. Only when a NSAID was added to the block and trim were significant differences in outcome seen. The application of a block to the sound claw as a treatment for lameness is a common practice around the world. In a recent review of text books and grey literature (e.g. reports and control plans) (Potterton et al., 2012), 85% of sources advocated their use for claw horn lesion. Behind a therapeutic trim, therapeutic blocks were the next most common treatment option described. Similarly in a recent survey of UK dairy farmers over 90% reported using blocks and 70% considered trim and block an effective treatment for claw horn lesions (Horseman et al., 2013).

The aetiology of claw horn lesions has not been fully elucidated; whatever the underlying cause, compression of the sole corium leads to vascular compromise, ischaemia, haemorrhage and ultimately interruption of keratogenesis and the development of lesions. The application of a block to the sound claw is thought to reduce load bearing and hence compression of the corium in the diseased claw and allow the compromised tissues to heal. It is noteworthy that only marginal, non-significant differences in cure rates were observed following the administration of NSAID without a block or a block without NSAID. This suggests that reduction in load bearing and NSAID action were synergistic in this study. We propose two hypotheses for this observation. Firstly the NSAID could be having a direct effect at the corium, reducing inflammation and assisting the corium to heal if loading is reduced by a block. Alternatively it seems credible that blocks may cause some discomfort following application, this may modify behaviour (e.g. changing lying or feeding time) or cause a redistribution of weight bearing between the claws and limbs leading to a reduction in the rate of healing of the diseased claw. Administration of a NSAID in combination with a block may mitigate these possible changes. Our results provide some circumstantial evidence

393 of this effect. At outcome (35 days after treatment), six, seven and five cows were lame on
394 the contralateral hind leg in the TRIM, TRIM/BLOCK and TRIM/NSAID groups
395 respectively, this compares to just one cow in the TRIM/BLOCK/NSAID group. Lame cows
396 in the TRIM, TRIM/BLOCK and TRIM/NSAID groups may have increased loading on the
397 contralateral hind limb predisposing it to lesion progression and lameness. Cows in the
398 TRIM/BLOCK/NSAID group may have been comfortable to bear weight evenly on the lame
399 limb, whilst at the same time the block allowed the diseased claw to heal. Further work is
400 required to confirm our findings and better understand the mechanisms of action and benefits
401 of different treatment options in cows with claw horn lesions.
402 Our results disagree with those reported by Laven et al (2008), who saw no difference
403 in outcomes between lame cows with claw horn lesions treated with blocks and the NSAID
404 Tolfenamic acid in addition to a therapeutic trim alone. Whilst the study designs are not
405 directly comparable they have a range of similarities making comparisons between outcomes
406 legitimate. The differences in outcome observed could be due to differences in case selection
407 (identified by an external observer as soon as lame vs identified by farm staff and therefore
408 likely to be more chronically lame), management system (more intensive predominantly
409 housed vs more extensive predominantly pasture based), cow type (predominantly higher
410 yielding Holstein type vs predominantly lower yielding Friesian and Jersey type) or other
411 unidentified factors.
412
413 The study population recruited to this RCT was a convenience sample. That said we have no
414 reason to suspect that it was not broadly representative of both cow and farm types common
415 in the UK (all be it that two of the study farms used automatic milking systems). Enrolled
416 cows selected from this population were predominantly newly and mildly lame. A previous
417 study reported a median lag of 65 days between when cows can first be identified as lame by

418 an external observer and when they were identified for treatment by farmers (Leach et al.,
419 2012). This may be because, as recent work suggests, many farmers do not identify or refer to
420 milder cases as '*lame'* (i.e. score 2 in this study). It appears they reserve the term 'lame' for
421 more severe cases (i.e. score 3 in this study) (Horseman et al., 2014). Consequently if farmers
422 do not consider that milder cases are 'lame' it stands to reason that they would not necessarily
423 be considered for treatment. In our study, animals were locomotion scored every two weeks
424 and treated as soon as they became identifiably lame. The period of time which could have
425 elapsed between animals first becoming lame and being treated ranged between two and 16
426 days (fortnightly locomotion scoring plus lag to treatment visit). The majority of cows (93%)
427 presented with the mildest lameness classification (Score 2). This population was selected
428 firstly because we considered it ethically questionable to identify and then knowingly leave
429 lame animals for a number of weeks before they were treated and secondly because we
430 believe that these are the animals which the industry should be targeting for treatment.
431 Readers should note that our study population, and consequently our results, may not reflect
432 the cases which many farmers routinely identify and present for treatment and at this stage it
433 is not possible to say whether our results are generalisable to more severe and / or chronic
434 cases managed in different farm systems. Further studies are needed to replicate this type of
435 clinical trial to test treatment protocols in more chronically and severely lame animals,
436 providing this work does not encourage or condone delayed treatment on-farm.
437 A range of other variables were significant in the final models (i.e. they significantly
438 impacted on cure), including farm, limb treated, days in milk, season of treatment, diagnosis
439 and operator. Of note, cure rates to soundness on one farm (Farm 5) were significantly worse
440 than on other study farms. Despite identical case selection criteria, an unidentified factor(s)
441 significantly affected outcome following all treatments on this unit. Clinically, it is important
442 that farms with poor cure rates are identified and the reasons for poor responses are explored

443 to limit the impacts of this painful disease on health and welfare. It is also interesting to note
444 that cows were more likely to recover from lameness when treated in early lactation and that
445 there was an exponential decay in the relationship with time after calving. Whilst animals
446 were not enrolled until at least 120 days had elapsed since their last treatment on the same
447 limb, the reduction in treatment success could reflect lower recovery rates in feet with more
448 chronic lesions from previous lameness events. Finally, the reasons for the difference in cure
449 rates between left and right limbs is unclear, it could reflect an operator bias based on the
450 relative ease of trimming left and right feet, depending on the dominant hand of the worker.
451 Logistically, this was a complex, expensive and time consuming study protocol to
452 conduct; this may explain why so few of these studies have been conducted previously. The
453 low proportion of cows which met all the selection criteria was particularly challenging, over
454 500 animals had to be examined and trimmed to enrol 183 cows. The principal reason,
455 making up nearly 70% of exclusion, were animals with lesions on both claws, i.e. even if the
456 claw causing the lameness was obvious, large numbers of animals had mild lesions on the
457 contralateral claw. Whilst in practice, therapeutic blocks are often applied to claws with
458 visible but mild lesions we felt it important that this was not the case in a RCT. The use of
459 blocks as part of treatment also necessitated an additional crush restraint intervention to
460 remove blocks from treatment groups which had received them. We considered this
461 necessary firstly to blind treatment group from the outcome observer and secondly because
462 work suggests that cows alter their gait whilst walking on blocks (Higginson Cutler, 2012).
463 Workers wishing to undertake studies such as this may wish to consider their selection
464 criteria, case definitions and study methodology carefully to avoid some of the logistical
465 problems we encountered.
466 The study of lameness treatment protocols has lagged behind that of similarly
467 important endemic diseases such as mastitis and infertility. In these fields clinical decision

making is based on a plethora of research studies which have tested different treatments and identified the most effective protocols. It is incumbent on the industry and research community to find ways of ensuring that more studies such as this are conducted to provide a robust evidence base to support the effective treatments of this prevalent, costly and painful endemic disease.

CONCLUSIONS

In the RCT described here, dairy cows with claw horn lesions treated with a therapeutic trim, a foot block on the sound claw and a three day course of the NSAID Ketoprofen were most likely to be sound five weeks post treatment. Our work suggests that cows benefit from NSAID treatment in addition to the common practices of therapeutic trimming and elevation of the diseased claw using a foot block even when they are newly and mildly lame.

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536 claw lesions and nociceptive threshold in dairy heifers during the peri-partum period. Vet. J.
537 154:155-161.

538 Table 1. Locomotion scoring descriptors employed in a randomized clinical trial to test the
539 recovery of dairy cows from claw horn lesions

Locomotion Score[1]	Descriptor
0	Walks with even weight bearing and rhythm on all four feet, with a flat back. Long fluid strides possible.
1	Steps uneven (rhythm or weight bearing or strides shortened; affected limb or limbs not immediately identifiable).
2a	Mild asymmetry in hind-limb movement. Decreased stride length on affected limb and slightly decreased stance duration with a corresponding increase in limb flight velocity on the non-affected side. Walking velocity remains normal. Back may be raised.
2b	Moderate asymmetry in hind-limb movement. Decreased stride length on affected limb and a distinct decrease in stance duration. Limb flight on the non-affected limb is correspondingly faster and the overall walking velocity is reduced. Back usually raised.
3a	Severe asymmetry in hind-limb movement. Marked decrease in stride length on affected limb and very short stance duration. Limb flight on non-affected limb rapid and walking velocity reduced such that cannot keep up with healthy herd. Back raised.
3b	Minimal or non-weight bearing on affected limb. Back raised. Reluctant to walk without encouragement.

540 [1]Adapted from the DairyCo Mobility Score system, the GB industry standard. Scores 2a and 2b and 3a and 3b
541 can be amalgamated back to scores 2 and 3 in this system respectively.
542

543 Table 2. Treatment administered in a randomized clinical trial designed to test the recovery of
544 dairy cows from claw horn lesions

Treatment group	Treatment	Description
1 ('TRIM')	Therapeutic trim only (Positive control group)	1. Therapeutic trim applicable to the lesion
2 ('TRIM/BLOCK')	Therapeutic trim plus foot block	1. Therapeutic trim applicable to the lesion 2. Application of a foot block[1] (Demotec 95, Demotec) to the unaffected claw
3 ('TRIM/NSAID')	Therapeutic trim plus NSAID	1. Therapeutic trim applicable to the lesion 2. Administration of a three day course of ketoprofen (Ketodale 100mg/ml, Richter Pharma AG) administered by deep intramuscular injection at 3mg ketoprofen / kg bodyweight
4 ('TRIM/BLOCK/NSAID')	Therapeutic trim plus foot block plus NSAID	1. Therapeutic trim applicable to the lesion 2. Application of a foot block (Demotec 95, Demotec) to the unaffected claw 3. Administration of a three day course of ketoprofen (Ketodale 100mg/ml, Richter Pharma AG) administered by deep intramuscular injection at 3mg ketoprofen / kg bodyweight

545 [1]Approximately 110mm long, 55mm wide and 23mm deep. The block was positioned based on the experience
546 of the worker in an attempt to replicate 'normal' claw placement and weight distribution. Where necessary the
547 block was positioned towards the heel (away from the toe) to ensure weight was borne on the flat of the block.

548 Table 3. Number of cows allocated to each of 4 treatment groups by lesion diagnosis and farm in a randomized clinical trial designed to test the

549 recovery of dairy cows from claw horn lesions

	Lesion Diagnosis												
	Sole Haemorrhage / Ulcer				White Line Disease				'Other' Lesion[1]				
Farm ID	T[2]	T/B	T/N	T/B/N	T	T/B	T/N	T/B/N	T	T/B	T/N	T/B/N	Total
1	6	6	5	5	1	1	1	1	3	4	3	3	39
2	4	5	5	5	4	4	3	4	3	2	3	3	45
3	1	1	1	1	2	2	1	2	2	2	2	2	19
4	8	7	8	8	2	2	2	1	4	4	4	4	54
5	2	2	2	1	1	0	1	1	4	4	4	4	26
Total	21	21	21	20	10	9	8	9	16	16	16	16	183
Grand Total	83				36				64				

550 [1]Predominantly a combination of both sole haemorrhage / ulcer and white line disease

[2]Treatment Group: T – Therapeutic trim only; T/B – Therapeutic trim plus block on the sound claw; T/N – Therapeutic trim plus 3d course of NSAID; T/B/N – Therapeutic trim plus block plus NSAID

553 Table 4 Descriptive statistics of animals in each of 4 treatment groups in a randomized

554 clinical trial designed to test the recovery of dairy cows from claw horn lesions

	Treatment Group			
	TRIM	TRIM/BLOCK	TRIM/NSAID	TRIM/BLOCK/NSAID
Parity (Median (Interquartile range)) [1]	3 (2-4)	3 (2-4)	3 (2-3)	2.5 (2-3)
Days in milk (Mean (SE)) [1]	205 (126)	180 (111)	168 (100)	182 (102)
Last recorded milk yield (Mean (SE)) [1]	36.2 (10.8)	37.4 (10.8)	43.1(9.1)	37.6 (9.4)
Body condition score at treatment (Median (Interquartile range)) [1]	3 (2.5-3)	3 (2.5-3)	2.5 (2.5 – 3.375)	2.5 (2.5 – 3.5)
Lameness Score at treatment (Median (Interquartile range)) [1]	2 (2-2)	2 (2-2)	2 (2-2)	2 (2-2)

555 [1]Differences between treatment groups were not significant

556 [2]TRIM – Therapeutic trim only; TRIM/BLOCK – Therapeutic trim plus block on the sound claw;

557 TRIM/NSAID – Therapeutic trim plus 3d course of NSAID; TRIM/BLOCK/NSAID – Therapeutic trim plus

558 block plus NSAID

559 Table 5. Locomotion score 35 days after treatment in dairy cows recruited to a randomized

560 clinical trial designed to test recovery from claw horn lesions

	Locomotion score 35 days after treatment			
Treatment	0[1]	1[1]	2	3
TRIM[2] (n=45)	11 (24.4%)	20 (44.4%)	14 (31.1%)	0
TRIM/BLOCK (n= 39)	14 (35.9%)	14 (35.9%)	10 (25.6%)	1 (2.6%)
TRIM/NSAID (n=42)	12 (28.6%)	20 (47.6%)	10 (23.8%)	0
TRIM/BLOCK/NSAID (n=41)	23 (56.1%)	12 (29.3%)	6 (14.6%)	0

561 [1]Score 0 = Sound; Scores 0 & 1 = Non-lame

562 [2]TRIM – Therapeutic trim only; TRIM/BLOCK – Therapeutic trim plus block on the sound claw;

563 TRIM/NSAID – Therapeutic trim plus 3d course of NSAID; TRIM/BLOCK/NSAID – Therapeutic trim plus

564 block plus NSAID

565 Table 6. Outcomes from logistic regression models in a randomized clinical trial designed to
566 test the recovery of dairy cows from claw horn lesions (odds ratio scale unless shown
567 otherwise)

	Outcome i. Sound locomotion score (Score 0) 35 days after treatment			Outcome ii. Non-lame locomotion score (Score 0 or 1) 35 days after treatment		
		95% CI			95% CI	
Model term	Odds ratio	2.5%	97.5%	Odds ratio	2.5%	97.5%
Intercept	-1.08	-2.14	-0.05	3.28	0.82	13.1
TRIM[1]	Reference			Reference		
TRIM/BLOCK[1]	2.1	0.8	5.8	1.2	0.4	3.8
TRIM/NSAID[1]	1.2	0.4	3.2	1.3	0.4	4.3
TRIM/BLOCK/NSAID[1]	6.4*	2.4	18.0	3.2	0.9	11.3
Farm 1	Reference			Reference		
Farm 2	0.6	0.2	1.8	0.7	0.2	2.5
Farm 3	1.3	0.4	4.3	3.6	0.6	21.9
Farm 4	1.2	0.5	3.5	1.1	0.3	4.0
Farm 5	0.1*	0.0	0.4	0.7	0.2	2.8
Right hind limb	Reference			Reference		

Left hind limb	4.8*	2.3	10.5	2.3*	1.0	5.5
$e^{-0.065 * DIM}$ (logit scale)	8.5*	3.5	13.9	7.8*	2.3	13.3
Winter treated[2]	Reference					
Spring treated[2]	0.2*	0.1	0.4			
Summer treated[2]	0.4	0.1	1.1			
Autumn treated[2]	0.1*	0.0	0.3			
Sole ulcer / haemorrhage				Reference		
White line disease				0.8	0.2	2.6
'Other' lesion(s)				0.3*	0.1	0.9
Principal Treatment Operator (HT)				Reference		
'Other' Treatment Operators				0.3*	0.1	0.8

568 * $P \leq 0.05$

569 [1]TRIM – Therapeutic trim only; TRIM/BLOCK – Therapeutic trim plus block on the sound claw;
570 TRIM/NSAID – Therapeutic trim plus 3d course of NSAID; TRIM/BLOCK/NSAID – Therapeutic trim plus
571 block plus NSAID

572 [2]Spring – March, April and May; Summer – June, July and August; Autumn – September, October and
573 November; Winter – December, January and February