

Footbathing, formalin and foot trimming

Reeves, Michelle: Prosser, Naomi: Monaghan, Emma: Green, Laura

DOI:

10.1016/j.tvjl.2019.06.002

Creative Commons: Attribution-NonCommercial-NoDerivs (CC BY-NC-ND)

Document Version Peer reviewed version

Citation for published version (Harvard):

Reeves, M, Prosser, N, Monaghan, E & Green, L 2019, 'Footbathing, formalin and foot trimming: the 3Fs associated with granulomas and shelly hoof in sheep', The Veterinary Journal, vol. 250, pp. 28-35. https://doi.org/10.1016/j.tvjl.2019.06.002

Link to publication on Research at Birmingham portal

Publisher Rights Statement:

Checked for eligibility: 26/06/2019

Reeves, M. et al (2019) Footbathing, formalin and foot trimming: the 3Fs associated with granulomas and shelly hoof in sheep, The Veterinary Journal, volume 250, pages 28-35, https://doi.org/10.1016/j.tvjl.2019.06.002

General rights

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes

- •Users may freely distribute the URL that is used to identify this publication.
- •Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
 •User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- •Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.

Download date: 19. Apr. 2024

Original article Footbathing, formalin and foot trimming: The 3Fs associated with granulomas and shelly hoof in sheep 7 M. C. Reeves ^{a,b}, N. S. Prosser ^a, E. M. Monaghan ^{c,*}, L. E. Green ^c ^a School of Life Sciences, University of Warwick, Gibbet Hill Road, Coventry, CV4 7AL, UK ^b Current address: Hatching Egg Producers of Québec, 555 Boul. Roland-Therrien, Longueuil, Québec, J4H 3V6, Montréal, Canada ^c College of Life and Environmental Sciences, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK *Corresponding author. Tel: +44 121 414 2508 Email address: E.Monaghan@bham.ac.uk (E.M.Monaghan)

Abstract

Granulomas and shelly hoof (SH), are lesions of sheep feet. Our objective was to use
data from four questionnaires on lameness sent to English sheep farmers in 2004, 2013, 2014
and 2015 to further understanding of the risks and aetiologies of both lesions.
Granulomas were more likely in flocks where routine foot trimming (odds ratio [OR]
= 3.17 ; 95% confidence intervals [CI] $1.11 - 11.47$) and routine footbathing (OR = 2.38 ; 95%
CI~1.19-4.83) were practised than where these management protocols were not. SH was
more likely in flocks that were footbathed in formalin compared with not footbathing (OR =
1.65; $95%$ CI $1.19-2.30$), and was less common in flocks that stocked ewes at more than
eight vs. four per acre (OR = 0.34 ; 95% CI $0.17 - 0.68$). There were weak associations
between SH and foot trimming. In 2004 only, SH was more likely in flocks where therapeutic
foot trimming was practised than not practised (OR = 2.24 ; 95% CI $1.12 - 4.68$). In 2014
only, SH was marginally less likely in flocks where no feet bled during trimming, compared
with flocks not routinely trimmed (OR = 0.55 ; CI 0.30 - 1.00); SH was not related to foot
trimming once severe footrot was included. We propose that flocks with granulomas and SH
would decrease if farmers stopped footbathing in general, in particular with formalin, and
avoided foot trimming whether as a therapeutic or routine practice. Further work is needed to
understand the role of stocking density.

- Keywords: Contagious ovine digital dermatitis; Footrot; Lameness prevalence; Multivariable
- 42 models; Sheep flock management

Introduction

Lameness in sheep is one of the most important farm animal welfare concerns in the UK (Goddard et al., 2006). It is estimated to cost the sheep industry £24 to £80 million per annum (Nieuwhof and Bishop, 2005; Wassink et al., 2010b; Winter and Green, 2017) due to its significant impact on productivity (Marshall et al., 1991; Glynn, 1993; Wassink et al., 2010b). Footrot (both interdigital dermatitis and severe footrot) is the most common cause of lameness in the United Kingdom. It is present in >95% flocks and causes approximately 70% of lameness (Winter et al., 2015). Contagious ovine digital dermatitis (CODD), another infectious cause of lameness, is present in >50% flocks and causes approximately 30% - 35% of lameness in affected flocks (Angell et al., 2014; Winter et al., 2015).

Granulomas and shelly hoof (SH) are less prevalent causes of lameness in sheep. They are present in 50% - 60% flocks and farmers generally attribute <3% lameness/lesions to these conditions (Kaler and Green, 2008a; Winter et al., 2015). A granuloma is a proliferation of highly vascularised connective tissue that protrudes through disrupted hoof horn at the wall horn junction or through sole horn (Fig.1). It is very painful and sheep are severely lame. Granulomas cause chronic lameness and sheep that have been lame for a long period of time, and not bearing weight on the affected foot, often present with the wall horn grown over the sole with the granuloma hidden from view. Granulomas are very difficult to cure and often lead to premature culling of sheep (Winter, 2008). A professional review suggests that the proliferation is a pathological response to trimming into the sensitive tissue of the foot or as a result of untreated severe footrot (Winter, 2008).

Shelly hoof (SH) presents grossly as detachment of the hoof horn wall, typically the abaxial wall, from the underlying epidermis, leaving a cavity between the wall and the sole

horn (Fig.1). SH per se does not cause lameness (Winter et al., 2015), however the impaction of debris in the cavity formed by the detached horn, followed by penetration of a foreign body, such as a thorn or stone, into sensitive tissue can lead to formation of an abscess and then sheep become severely lame (Winter, 2008). Conington et al. (2010a) reported that wall horn in cases of SH presents histologically as poorly keratinised epithelial horn cells with microfissures and 'unzipping' of cell membranes that create microscopic crevices leading deep into the horn. The authors hypothesised that this characteristic structure makes the hoof physically weak, more permeable to moisture and highly vulnerable to entry of water-soluble solutions and organisms that could further contribute to hoof breakdown. Conington et al. (2010a) also reported a genetic component to SH. A professional review hypothesised that physical damage, opportunistic bacteria/fungi or nutritional deficiency may cause SH (Winter and Arsenos, 2009). While many farmers report low SH prevalence, some farmers report high prevalence (Conington et al., 2010b) and the disease is of considerable concern for some farmers (personal observation).

There is a body of published evidence that routine foot trimming and routine footbathing are associated with a higher prevalence of all lameness. Treating individual sheep lame with footrot rather than incorporating foot trimming and footbathing into routine flock management protocols reduces the prevalence of footrot (Kaler and Green, 2009; Winter et al., 2015; Witt and Green 2018). The only evidence of benefit from footbathing is for the treatment of interdigital dermatitis (Clifton and Green, 2016). Which factors are effective in the control of CODD are not well understood. However, recent studies indicate that CODD is typically introduced by newly introduced sheep and that once it is endemic in flocks, CODD can be controlled effectively using the same management protocols that control footrot

(Angell et al., 2016; Dickins et al., 2016). To the authors' knowledge, there are no published studies reporting risk factors for granulomas and SH.

The aim of the current study was to use data from four questionnaires sent to English sheep farmers in 2004, 2013, 2014 and 2015 to investigate associations between management of lameness and farm characteristics with the presence of granulomas and SH to generate hypotheses on the risks for, and possible aetiologies of, these lesions.

Materials and methods

Ethical approval

All questionnaire data used in this paper originates from studies that had ethical approval from when this was required by the University of Warwick's Biomedical and Scientific Research Ethics Committee (BSREC). For the 2013-2014 questionnaires this was BSREC 159-01-12; approved 07 December, 2011. For the 2015 questionnaire this was BSREC REG0-2014-620; approved 02 April, 2014. Ethical approval was not required in 2004.

Questionnaires and responses

In 2004, a postal questionnaire was sent to a random sample of 3000 English sheep farms selected from lists using the RAND function in Microsoft Excel and obtained from the Agriculture and Horticulture Development Board (AHDB) stratified by region of England (South west, South east, Central, North west and North east) and by flock size within each region (Kaler and Green, 2008a, 2009). The questionnaire contained a photograph and a description of granuloma and shelly hoof (Fig.1). Farmers were asked to identify each lesion and estimate its prevalence in their flock, as well as answering questions on the prevalence of

lameness and management of lameness; approximately 6% of the target population was surveyed (Kaler and Green, 2008a, 2009). In 2013, similar questions were posed in a questionnaire sent to 4000 lowland sheep farmers in England with >199 ewes; lists were obtained from the Department for Environment, Food and Rural Affairs (DEFRA) and AHDB who selected flocks randomly stratified by county and size (Winter et al., 2015). In 2004 and 2013, randomization to select farms was achieved by assigning each farm a number using the number autofill function in Microsoft Excel and then generating a second random list of numbers in the same number range and corresponding to the number of farms required using the RAND function in Microsoft Excel. Farms were assigned to the questionnaire group if the number assigned to them was generated in the random number list. The lists for the 2013 questionnaire may have included some of the 809 respondents from 2004. In 2014, an abridged version of the 2013 questionnaire was sent to 1355/4000 compliant farmers who responded to the 2013 questionnaire (Grant et al., 2018). Finally, in 2015, 722 compliant farmers who responded to the 2014 questionnaire were invited to participate in a study which included completing a questionnaire; 192/722 agreed to participate and 144 (75%) completed the questionnaire (Prosser et al., unpublished data). A further 18 farmers from the 2014 study who participated in a clinical trial (Witt and Green, 2018) and an additional five farmers from another clinical trial (Monaghan et al., unpublished data) also completed the questionnaire, resulting in 167 responses to the 2015 questionnaire. Consequently, farmers who responded to the 2015 questionnaire had also responded to the questionnaires in 2014 and 2013 and farmers who responded to the 2014 questionnaire had also responded to the 2013 questionnaire. Data from 2004 were from a separate random sample of English sheep farmers selected from lists using the RAND function in Microsoft Excel with unknown overlap in responses from farmers in 2004 and other years. Data were collected on granulomas in 2004 and 2015 and SH in 2004, 2013 and 2014. Farmer responses to questions in Fig.1 were used

117

118

119

120

121

122

123

124

125

126

127

128

129

130

131

132

133

134

135

136

137

138

139

140

to identify flocks where granulomas and SH were present and to estimate the percentage of granulomas and SH that farmers observed. Farmers were asked whether they practised therapeutic and routine foot trimming in all four questionnaires; in addition, for 2013-2015, the proportion of sheep that bled when trimmed was requested. Careful trimming is defined here, as in Winter et al. (2015), as trimming where no sheep in a flock bled when routinely trimmed.

Data preparation and analysis

All four datasets were clean because they had been used in previous analyses (Kaler and Green, 2008a, 2009; Winter et al., 2015, Grant et al., 2018; Prosser et al., unpublished data). The data were stored in Microsoft Excel. Responses were excluded if there were no data on the presence of granulomas or SH. Explanatory variables were selected from the questionnaires to test the following hypotheses. For granulomas, treatment variables e.g. treated footrot with foot trimming, were used to test the hypothesis that management protocols used for footrot were associated with presence of granulomas. Farm characteristics, e.g. stocking rate, were used to test the hypothesis that certain types of farms had a higher risk of granulomas. In addition, for SH, biosecurity variables e.g. the flock mixed with other flocks, were used to test the hypothesis that SH is an infectious disease (Supplementary Tables 1 and 2, respectively).

The global mean period prevalence of granulomas, SH and all lameness were estimated and prevalence of lameness in flocks with and without granulomas and SH were calculated. Previous work has reported that farmers recognise lameness (Kaler and Green, 2008b; King and Green, 2011) and foot lesions, but do not necessarily identify lesions correctly (Kaler and Green, 2008a). Consequently, the prevalence of granulomas and SH by

correct (identifying the lesion in the photograph; Fig.1) and incorrect (identifying the lesions as anything else, but most commonly footrot) identifying the lesions were investigated using Mann Whitney tests. Binomial logistic regression models in R version 3.4.1 (R Core Team 2018) were used to investigate univariable and multivariable associations between the presence of granulomas and SH and management protocols and farm characteristics. The data from 2004 and 2015 were used to investigate granulomas and data from 2004, 2013 and 2014 were used to investigate SH; each year was modelled separately. The models took the following form:

175
$$y_i \sim \alpha + \beta_i X_i + e_i$$

where y_j is the probability that a flock has granulomas / SH, \sim is a logit link function, α is the intercept and β_j represents the series of vectors of coefficients of explanatory variables for X_j that vary by farm j and e_j is the residual random error that follows a binomial distribution.

The results were assessed using Wald's test for significance, that is 95% confidence intervals did not include unity. Variables significant at $P \le 0.05$ in the univariable analysis were tested in the multivariable model using manual forward stepwise selection. All variables were then retested using manual forward stepwise selection regardless of their significance in the univariable analysis to check for residual confounding (Cox and Wermuth, 1996) and were included in the model if significant. Where two variables were highly correlated, the most biologically relevant was kept in the model. Presence of other lesions (interdigital dermatitis, severe footrot and CODD) in the flock were tested in the models to investigate residual confounding. Correlations between the variables in the multivariable models and

¹ See: R Core Team, 2018. R: A language and environment for statistical computing. R Foundation for Statistical Computing. https://www.R-project.org (accessed 30 May 2019).

between lesions were investigated using chi-square tests. The model fit was investigated by visually comparing the ranked expected values against the observed values.

Results

Farmer response proportions

Granulomas

Of the 809 (27%) and 922 (68%) farmers that responded to questionnaires in 2004 and 2015, 89-95% answered questions regarding granulomas and flock size. Granulomas were reported in 54-63% flocks (Supplementary Table 3). The median flock size was 220 (interquartile range [IQR], 90-450) in 2004 and 400 (IQR, 223-600) in 2015. The geometric mean (95% confidence intervals [CI]) farmer reported prevalence of lameness was 8.1% (8.0-8.1%) in 2004 and 4.1% (3.7-4.7%) in 2015. The prevalence of granulomas was right skewed meaning the distribution was positive on the x axis with a long tail to the right. Flock prevalence in affected flocks ranged from 0.0-8.0% (upper quartile range, 1.0-8.0% in 2004; 1.2-7.0% in 2015; Supplementary Table 3).

Shelly hoof (SH)

There were 809 (27%), 1354 (34%) and 922 (68%) responses from farmers who received a questionnaire in 2004, 2013 and 2014, respectively. Of these, 84-86% answered questions on shelly hoof and flock size, with 58-76% reporting shelly hoof in their flock (Supplementary Table 3). The median flock size ranged from 225 ewes (IQR, 95-460) in 2004, to 340 ewes (IQR, 220-540) in 2013 and 320 ewes (IQR, 220-518) in 2014. The geometric mean (95% CI) farmer reported prevalence of lameness was 6.9% (6.4-7.3%), 3.7% (3.3-3.9%) and 3.3% (3.1-3.5%) in 2004, 2013 and 2014, respectively. In flocks with SH, the prevalence of lesions was mostly <5%, however, in each year, some flocks had very

215 high prevalence. The upper quartile flock prevalence range was 3.8-37.5% in 2004, 5.0-216 70.0% in 2013 and 5.0-95.0% in 2014 (Supplementary Table 3). 217 218 Farmer identification and prevalence of granuloma and shelly hoof 219 Granuloma 220 In 2004 and 2015, 56% (n=288/516) and 98% (n=155/158) of farmers identified 221 granulomas correctly from a photograph (Fig. 1). There was no significant difference in 222 median flock prevalence of lameness by farmer identification of granuloma (Table 1). 223 224 Shelly hoof 225 In 2004, 2013 and 2014, 28% (n=134/477), 73% (n=787/1079) and 76% (n=605/800) 226 farmers, respectively, identified SH correctly from the photograph (Fig.1). Only 55% 227 (n=356/642) farmers correctly identified SH in both 2013 and 2014; 7% (n=43/642)228 identified SH incorrectly in both years, and 37% farmers identified SH correctly once in 2013 229 or 2014. However, the median prevalence of SH was not significantly different between 230 flocks where farmers correctly and incorrectly identified SH and identification of SH was not 231 significantly associated with flock prevalence of lameness (Table 1). 232 233 Univariable and multivariable binomial logistic regression models of factors associated with 234 the presence of granulomas and SH 235 Granulomas 236 The univariable associations between management variables and presence of 237 granulomas in 2004 and 2015 are listed in Supplementary Table 1 and the multivariable 238 models are presented in Table 2. In 2004, granulomas were more likely to be present in 239 flocks where routine footbathing (odds ratio [OR] = 1.71; 95% CI 1.26 – 2.32) was practised

compared with those where routine footbathing was not practised and in flocks where farmers practised therapeutic foot trimming of lame sheep (OR = 2.07; 95% CI 1.03 - 4.32) compared with flocks where farmers did not practise therapeutic foot trimming. In 2015, granulomas were more likely to be present in flocks where routine footbathing (OR = 2.38; 95% CI 1.19 - 4.83) and routine trimming (OR = 3.17; 95% CI 1.11 - 11.47) were practised compared with flocks where these management protocols were not practised. When other foot lesions were added to the models, only CODD in 2015 was significantly associated with the presence of granulomas; all management variables remained significant in this model (data not shown).

Shelly hoof

The univariable associations between management variables and the presence of SH in 2004, 2013 and 2014 are listed in Supplementary Table 2 and the multivariable models are in Table 3. Approximately 94% farmers practised therapeutic foot trimming in 2004 (Table 4) and SH was significantly more likely to be present in flocks where farmers practised therapeutic foot trimming compared with flocks where this was not practised (OR = 2.24; 95% CI 1.12 - 4.68). Approximately 65% farmers practised routine footbathing of sheep (Table 4) and SH was more common in flocks where footbaths were used compared to where they were not used (OR = 1.81; 95% CI 1.33 - 2.46). In 2013, SH was more likely to be present in flocks where sheep were routinely footbathed, and this was significantly associated with flocks footbathed in formalin (OR = 1.65; 95% CI 1.19 - 2.30) compared with flocks never footbathed or footbathed with other products. The likelihood of SH was lower as stocking density increased from fewer than four to more than eight ewes per acre (OR = 0.34; 95% CI 0.17 - 0.68). In 2014, routine foot trimming was associated with increased likelihood of SH (data not shown). However, SH was less likely to be present (Wald's P =

0.047; OR = 0.55; 95% CI 0.30 - 1.00) in flocks where farmers reported that no feet bled during trimming (these were carefully, but not excessively, trimmed), compared with flocks that were not routinely trimmed. When other foot lesions were tested in the models, ID, CODD and severe footrot were significantly associated with the presence of SH in 2004, 2013 and 2014. The only change in the management variables was in 2014 when careful foot trimming became non-significant (P = 0.44).

Correlations between explanatory variables in the multivariable models and with footrot and

CODD

There were significant ($P \le 0.05$) correlations between variables in the multivariable models. Typically, there were positive correlations between routine and therapeutic foot trimming and footbathing. Stocking density was positively associated with footbathing and positively and negatively associated with foot trimming in different models (Supplementary Table 4). All lesions that were recorded in a single year were positively correlated with each other.

Model fit

The model fits were reasonable, with predicted values following the pattern of observed for both granulomas and SH (Supplementary Figs.1-5).

Discussion

This is the first study to provide evidence that the associations between therapeutic foot trimming and routine footbathing and all lameness (Kaler and Green, 2009; Winter et al., 2015) are associated with specific lesions, granulomas and SH, in addition to footrot

(Wassink et al., 2003; Kaler and Green, 2009) and CODD (Dickins et al., 2016). These findings are discussed in detail below.

291

292

293

294

295

296

297

298

299

300

301

302

303

304

305

306

307

308

309

310

311

289

290

Granuloma data was available from 2004 and 2015. These data came from two independent randomly selected samples of English sheep farmers, the degree of overlap in farmers between these two samples is unknown, but it is likely to be low given a population of >35,000 sheep farmers in England². Additionally, given the time interval of 13 years, even if some of the farmers were the same, practices changed (Winter et al., 2015), so it seems reasonable to assume that the datasets were independent. Consequently, the consistency between results for both years (Table 2) provides confidence in their robustness. We hypothesised that foot trimming could damage the foot structure and so lead to proliferation of connective tissue i.e. a granuloma. The results indicate that routine and therapeutic foot trimming are associated with the presence of granulomas (Table 2) and support the hypothesis that damaging connective tissue in the foot is associated with trimming. In both questionnaires, therapeutic and routine foot trimming were positively correlated and so the presence of one or the other in the final models is in part because the degree of correlation was sufficient to exclude the other. There is insufficient statistical power in the 2015 dataset to explore whether excessive routine foot trimming vs. all routine foot trimming, was associated with granulomas. Despite this, we conclude that granulomas are associated with the practice of foot trimming. Granulomas were also more likely to be present in flocks that were footbathed in both datasets. It is not clear why this might be. However, if formalin was the main footbathing product in 2004 and 2015, as it was in 2013 (73% farmers; Winter et al., 2015), and formalin can cause neoplasia and damage cells (see below), then either reduced

² See: AHDB, 2018. UK Sheep Yearbook 2018. Agriculture and Horticulture Development Board. http://beefandlamb.ahdb.org.uk/wp-content/uploads/2018/10/UK-Sheep-Yearbook-2018.pdf (Accessed 14 March 2019).

regrowth of excessively trimmed hoof horn, or proliferation of digit connective tissue, or both, could lead to granuloma. This requires further study.

314

315

316

317

318

319

320

321

322

323

324

325

326

327

328

329

330

312

313

SH data were available for 3 years, 2004 and 2013 and 2014; respondents from 2014 were a subset of those who replied in 2013. In all 3 years, routine footbathing was associated with increased risk of SH, providing a consistent association. In 2013, we identified increased risk associated with formalin footbaths. Formalin is carcinogenic, causing nasopharyngeal cancer in animals and humans (Swenberg et al., 1980; Hauptmann et al., 2004) and at concentrations >5% in footbaths it causes skin inflammation in cattle (Cornelisse et al., 1982) and sheep (Ross, 1983), and hard keratinous-like material in the interdigital skin (Pyror, 1959). Formalin is also used post mortem to fix tissues. It acts by dehydrating cells which harden and form cross-links to create an insoluble meshwork (Thavarajah et al., 2012). The combination of inflammation of living skin and tough dead cells in the outer layers of skin and horn could exacerbate the micro- and macro-disintegration of the white line observed in SH (Conington et al., 2010a). The association between SH and formalin could possibly be reverse causality, with farmers with SH in their flock using formalin footbaths. However, footbaths are not a recommended treatment for SH and farmers rarely change their behaviour (Wassink et al., 2005; Wassink et al., 2010a), so it is likely that these farmers had been using formalin footbaths for many years and are still reporting SH.

331

332

333

334

335

336

The associations between foot trimming and SH were inconsistent; therapeutic foot trimming was a risk in 2004 but not in other years and all routine foot trimming was not associated with SH in any study, although careful routine foot trimming with no bleeding, was only associated with reduced risk in 2013, but this association was confounded by the presence of severe footrot in the flock. Many observational and interventional studies have

reported that foot trimming is detrimental. It increases the flock prevalence of all lameness (Kaler and Green, 2009; Winter et al., 2015), severe footrot (Wassink et al., 2003) and CODD (Dickins et al., 2016), delays healing (Kaler et al., 2010) and increases the reoccurrence of footrot (Kaler et al., 2010). We consider that the inconsistent and weak association and confounding associated with the presence of severe footrot indicates that foot trimming is not a potential cause of SH and that the recommendation to avoid foot trimming sheep is still robust.

In our study, SH was more likely to occur in flocks at stocking densities of fewer than four ewes per acre compared with more than eight ewes per acre. This is consistent with SH being more common in flocks on poor quality pasture. Winter and Arsenos (2009) suggested that physical damage was a risk factor for SH. Features of poor quality pasture include uneven surfaces, stones, or very dry or wet pasture, which might increase the risk of physical damage to the white line and predispose to formation of SH. The presence of farm tracks are a risk factor for white line disease in dairy cattle (Barker et al., 2009) and so give some credence to this hypothesis by analogy (Bradford Hill, 1965). Additionally, if the grass was poor quality, sheep could be malnourished and develop poor quality horn, as hypothesised by Conington et al. (2010a). Sheep kept at low stocking densities are often different breeds from those farmed at higher stocking densities; this might indicate breed differences in susceptibility to SH, as well as the within-breed differences reported by Conington et al. (2010b). However, there are a plethora of other management factors associated with low vs. high stocking densities that could act as risk factors for SH.

There were no significant associations and varying patterns of positive and negative coefficients between biosecurity variables and granulomas and SH between the years of study

(Supplementary Tables 1 and 2). This indicates that there were no strong or consistent risks with biosecurity variables and we hypothesise that granulomas and SH are unlikely to be of infectious origin, introduced into flocks by incoming sheep. Additionally, the distribution of granulomas and SH within flocks provides further clues, as many flocks did not have lesions, most affected flocks had very low prevalence and only a few had very high prevalence (Kaler and Green, 2008a). This is not typical of infectious disease and suggests that granulomas and SH are non-infectious diseases and that where there is a high prevalence there is a farm-specific risk.

In studies by Conington et al. (2010a; 2010b), the prevalence of SH in 27 flocks ranged from 0-76%. In the current study, the range of SH was 0% to 37-95%, indicating there were some flocks with a similar prevalence of SH to those reported by Conington et al. (2010a; 2010b), but many hundreds with low prevalence. The within-flock prevalence of lesions was a farmer estimate from recollection of foot examinations. It is therefore likely to be an underestimate of the true prevalence of SH, since the farmers are unlikely to have examined all feet simultaneously. Even if the prevalences reported here and elsewhere are not representative of the within-flock prevalence of granulomas and SH across the population of English sheep flocks, our data are robust enough to estimate the risk of granulomas and SH in flocks, as long as the presence of a lesion did not bias farmers' responses. This seems unlikely but cannot be determined from our data. When findings were consistent across the questionnaires, the robustness of the results is greater. However, because farmers from 2013-2015 were the same, the robustness is less than for independent studies.

Conclusions

This is the first study to associate footbathing, formalin and foot trimming with granulomas and SH in sheep flocks. These management protocols were associated with reduced risk of SH, but less consistently. We conclude that the current recommended management protocols of avoiding footbathing and foot trimming to minimise lameness and footrot and CODD also contribute to reduced risk of granulomas. Further work is required to understand whether granulomas are more likely to occur when formalin is used and to investigate the role of formalin footbaths and low stocking density on the occurrence of SH.

Conflict of interest statement

None of the authors has any other financial or personal relationships that could inappropriately influence or bias the content of the paper.

Acknowledgements

We thank the authors from the original studies for provision of the data and Dr Rachel Clifton for statistical support. Data collection was funded by DEFRA and the Biotechnology and Biological Sciences Research Council (BBSRC). Naomi Prosser holds a BBSRC studentship with AHDB as the Collaborative Awards in Science and Engineering (CASE) partner.

Appendix A: Supplementary material

Supplementary data associated with this article can be found, in the online version at doi:

References

Angell, J.W., Duncan, J.S., Carter, S.D., Grove-White, D.H., 2014. Farmer reported prevalence and factors associated with contagious ovine digital dermatitis in Wales: A questionnaire of 511 sheep farmers. Preventive Veterinary Medicine 113, 132-138.

- 414 Angell, J.W., Grove-White, D.H., Williams, H.J., Duncan, J.S., 2016. Whole-flock, 415 metaphylactic tilmicosin failed to eliminate contagious ovine digital dermatitis and 416 footrot in sheep: a cluster randomised trial. Veterinary Record 179, 308-344.
- Barker, Z.E., Amory, J.R., Wright, J.L., Mason, S.A., Blowey, R.W., Green, L.E., 2009. Risk factors for increased rates of sole ulcers, white line disease, and digital dermatitis in dairy cattle from twenty-seven farms in England and Wales. Journal of Dairy Science 92, 1971-1978.
- Bradford Hill, A., 1965. The Environment and Disease: Association or Causation?
 Proceedings of the Royal Society of Medicine 58, 295-300.

417

422

429

433

437

448

452

- Clifton, R., Green, L.E., 2016. On the treatment, control and elimination of ovine footrot: A
 comparative review. CAB Reviews: Perspectives in Agriculture, Veterinary Science,
 Nutrition and Natural Resources 11, 1-9.
- Conington, J., Nicoll, L., Mitchell, S., Bunger, L., 2010a. Characterisation of white line
 degeneration in sheep and evidence for genetic influences on its occurrence.
 Veterinary Research Communications 34, 481-489.
- Conington, J., Speijers, M.H.M., Carson, A., Johnston, S., Hanrahan, S., 2010b. Foot health in sheep prevalence of hoof lesions in UK and Irish sheep. Advances in Animal Biosciences 1, 340-340.
- Cornelisse, J.J., Peterse, D.J., Raven, E.T., 1982. Formalin foot baths in the prevention of interdigital dermatitis in cattle. Tijdschrift Voor Diergeneeskunde 107, 835-840.
- Cox, D.R., Wermuth, N., 1996. Statistical analysis. In: Multivariate Dependencies. Models,
 Analysis and Interpretation, First Edn. Chapman & Hall, London, UK, pp.92-122.
- Dickins, A., Clark, C.C.A., Kaler, J., Ferguson, E., O'Kane, H., Green, L.E., 2016. Factors associated with the presence and prevalence of contagious ovine digital dermatitis: A 2013 study of 1136 random English sheep flocks. Preventive Veterinary Medicine 130, 86-93.
- Glynn, T., 1993. Benign footrot an epidemiologic investigation into the occurrence, effects on production, response to treatment and influence of environmental factors.

 Australian Veterinary Journal 70, 7-12.
- Goddard, P., Waterhouse, T., Dwyer, C., Stott, A., 2006. The perception of the welfare of sheep in extensive systems. Small Ruminant Research 62, 215-225.
- Grant, C., Kaler, J., Ferguson, E., O'Kane, H., Green, L.E., 2018. A comparison of the efficacy of three intervention trial types: postal, group and one-to-one facilitation, prior management and the impact of message framing and repeat messages on the flock prevalence of lameness in sheep. Preventative Veterinary Medicine 149, 82-91.
- Hauptmann, M., Lubin, J.H., Stewart, P.A., Hayes, R.B., Blair, A., 2004. Mortality from
 solid cancers among workers in formaldehyde industries. American Journal of
 Epidemiology 159, 1117-1130.

Kaler, J., Daniels, S.L.S., Wright, J.L., Green, L.E., 2010. Randomized clinical trial of long acting oxytetracycline, foot trimming, and flunixine meglumine on time to recovery in
 sheep with footrot. Journal of Veterinary Internal Medicine 24, 420-425.

468 469

470

Kaler, J., Green, L.E., 2008a. Naming and recognition of six foot lesions of sheep using written and pictorial information: A study of 809 English sheep farmers. Preventive Veterinary Medicine 83, 52-64.

471 472

Kaler, J., Green, L.E., 2008b. Recognition of lameness and decisions to catch for inspection among sheep farmers and specialists in GB. BMC Veterinary Research 4, doi: 10.1186/1746-6148-4-41.

476

Kaler, J., Green, L.E., 2009. Farmers' practices and factors associated with the prevalence of all lameness and lameness attributed to interdigital dermatitis and footrot in sheep flocks in England in 2004. Preventive Veterinary Medicine 92, 52-59.

480

King, E.M., Green, L.E., 2011. Assessment of farmer recognition and reporting of lameness in adults in 35 lowland sheep flocks in England. Animal Welfare 20, 321-328.

483

Marshall, D.J., Walker, R.I., Cullis, B.R., Luff, M.F., 1991. The effect of footrot on bodyweight and wool growth of sheep. Australian Veterinary Journal 68, 45-49.

486

Nieuwhof, G.J., Bishop, S.C., 2005. Costs of the major endemic diseases of sheep in Great Britain and the potential benefits of reduction in disease impact. Animal Science 81, 23-29.

490

Pyror, W.J., 1959. Two foot syndromes in sheep following excessive foot bathing. The Australian Veterinary Journal 35, 493-494.

493

494 Ross, A.D., 1983. Formalin and footrot in sheep. New Zealand Veterinary Journal 31, 170-495 172.

496

Swenberg, J.A., Kerns, W.D., Mitchell, R.I., Gralla, E.J., Pavkov, K.L., 1980. Induction of squamous-cell carcinomas of the rat nasal cavity by inhalation exposure to formaldehyde vapor. Cancer Research 40, 3398-3402.

500 501

Thavarajah, R., Mudimbaimannar, V.K., Elizabeth, J., Rao, U.K., Ranganathan, K., 2012. Chemical and physical basics of routine formaldehyde fixation. Journal of Oral Maxillofacial Pathology 16, 400-405.

503504

502

Wassink, G.J., George, T.R.N., Kaler, J., Green, L.E., 2010a. Footrot and interdigital dermatitis in sheep: Farmer satisfaction with current management, their ideal management and sources used to adopt new strategies. Preventive Veterinary Medicine 96, 65-73.

509

Wassink, G.J., Grogono-Thomas, R., Moore, L.J., Green, L.E., 2003. Risk factors associated with the prevalence of footrot in sheep from 1999 to 2000. Veterinary Record 152, 351-358.

514 Wassink, G.J., King, E.M., Grogono-Thomas, R., Brown, J.C., Moore, L.J., Green, L.E., 515 2010b. A within farm clinical trial to compare two treatments (parenteral 516 antibacterials and hoof trimming) for sheep lame with footrot. Preventive Veterinary 517 Medicine 96, 93-103. 518 519 Wassink, G.J., Moore, L.J., Grogono-Thomas, R., Green, L.E., 2005. Footrot and interdigital 520 dermatitis in sheep: farmers' practices, opinions and attitudes. Veterinary Record 157, 521 761-U731. 522 523 Winter, A.C., 2008. Lameness in sheep. Small Ruminant Research 76, 149-153. 524 525 Winter, A.C., Arsenos, G., 2009. Diagnosis of white line lesions in sheep. In Practice 31, 17-526 21. 527 528 Winter, J.R., Green, L.E., 2017. Cost-benefit analysis of management practices for ewes lame 529 with footrot. Veterinary Journal 220, 1-6. 530 531 Winter, J.R., Kaler, J., Ferguson, E., KilBride, A.L., Green, L.E., 2015. Changes in 532 prevalence of, and risk factors for, lameness in random samples of English sheep 533 flocks: 2004-2013. Preventive Veterinary Medicine 122, 121-128. 534 535 Witt, J., Green, L., 2018. Development and assessment of management practices in a flock-536 specific lameness control plan: A stepped-wedge trial on 44 English sheep flocks. 537 Preventive Veterinary Medicine 157, 125-133. 538

Table 1
Median (interquartile range) flock prevalence of lameness, granuloma and shelly hoof (SH)
identified by farmers from questionnaires completed by sheep farmers in England in 2004,
2013, 2014 and 2015.

	Granuloma	Granuloma		SH	SH				
Year	correctly	incorrectly	P^{a}	correctly	incorrectly	P^{a}			
	identified	identified		identified	identified				
Lameness %									
2004	8 (5-10)	8 (5-10)	0.88	10 (5-15)	10 (5-15)	0.25			
2013	-	-		4 (2-5)	4 (2-6)	0.88			
2014	-	-		3 (2-5)	3 (2-5)	0.53			
2015	5 (2-7)	15 (1.5-15)	0.28	-	-				
Granuloma %									
2004	0.25 (0.0-1.0)	0.5 (0.0-1.1)	< 0.01	0.6 (0.3-1.1)	0.8 (0.3-1.5)	0.72			
2013	-	-		-	-				
2014	-	-		-	-				
2015	0.9 (0.0-1.0)	5 (0.0-10.0)	0.68	-	-				
		ı	Shelly hoof %	, 0					
2004	0.6 (0.0-2.0)	0.5 (0.0-2.1)	0.40	10 (5-40)	20 (10-50)	0.03			
2013	-	-		2.0 (1.0-5.0)	3.0 (1.0-5.0)	0.78			
2014	-	-		2.0 (1.0 -5.0)	3.0 (1.4-5.0)	0.11			
2015	-	-		-	-				

- Data not collected

^a *P* calculated from Mann-Whitney tests comparing prevalence of SH and granulomas by correct and incorrect farmer identification of lesions.

Table 2
 Binomial regression models of factors associated with the presence of granulomas in 2004
 and 2015

Model term	Category	Number of	%	OR	95% CI	
		flocks				
2004						
Footbathing ^a	No	265	34.42	1.00		
	Yes	500	64.94	1.71	1.26	2.32
Trim to treat sheep	No	35	4.55	1.00		
lame with footrot	Yes	723	93.90	2.07	1.03	4.32
2015						
Routine footbathing ^a	No	68	43.04	1.00		
	Yes	90	56.96	2.38	1.19	4.83
Routine foot trim	No	131	82.91	1.00		
	Yes	27	17.09	3.17	1.11	11.47

OR, odds ratio; 95% CI, 95% confidence interval

^a Footbathing product data not collected

Table 3
 Binomial regression models of factors associated with the presence of shelly hoof (SH) in
 sheep flocks in 2004, 2013 and 2014

Model term	Category	Flocks,	%	OR	95%	CI
		n				
2004						
Footbathing ^a	No	261	34.71	1.00		
	Yes	486	64.63	1.81	1.33	2.46
Trim to treat sheep lame	No	35	4.65	1.00		
with footrot	Yes	705	93.75	2.24	1.12	4.68
2013						
Ewe stocking rate	<4/acre	385	42.73	1.00		
	4-8/acre	451	50.06	0.75	0.55	1.02
	>8/acre	36	4.00	0.34	0.17	0.68
Footbathing ^a	No	341	37.85	1.00		
	Yes: formalin used	411	45.62	1.65	1.19	2.30
	Yes: formalin not	145	16.09	1.38	0.90	2.16
	used					
2014						
Routine foot trim	No trim	295	48.92	1.00		
	Trim: no bleeding	53	8.79	0.55	0.30	1.00
	Trim: bleeding	244	40.46	1.13	0.78	1.64

OR, odds ratio; 95% CI, 95% confidence interval

- ^a Footbathing with any product was associated with significantly higher OR for shelly hoof in
- 559 2013; footbathing product data not collected in 2004 and 2014

Table 4
 The number and percentage of flocks by management protocols for lameness in England in
 2004, 2013, 2014 and 2015^a.

Variable	2004 (n=7:	52)	2013 (n=901)		2014 (n=603)		2015 (n=158)	
	n	%	n	%	n	%	n	%
Trimmed feet as footrot to	Trimmed feet as footrot treatment							
No	35	5					62	39
Yes	705	94					88	56
Never			38	4	28	5		
Always			345	38	110	18		
Sometimes			161	18	257	43		
Usually			292	32	174	29		
Routine foot trimming pra	actised							
No	173	23	395	44	295	49	131	83
Yes	572	76	487	54	303	50	27	17
Never								
Bled during routine								
trimming								
No trimming			395	44	295	49		
No bleeding			60	7	53	9		
Bleeding			408	45	244	40		
Used footbaths								
No	261	35	341	38	248	41	68	43
Yes	486	65			355	59	90	57
Yes: Used formalin			411	46				

Yes: Did not use formalin			145	16				
Used Footvax								
No	649	86	693	77	470	78	98	62
Yes	97	13	194	22	132	22	55	35
Checked feet of sheep pre-purc	hase							
Always			254	28	130	22		
Usually			182	20	126	21		
Sometimes			125	14	75	12		
Never			135	15	97	16		
Did not purchase			192	21	167	27		
Isolated new sheep								
Never			102	11	50	8		
Sometimes			73	8	39	6		
Usually			133	15	93	15		
Always			393	44	266	44		
No new arrivals			176	20	138	23		
Sheep left the flock then return	ed							
No			548	61				
Yes			339	38				
Flock mixed with other flocks								
No			838	93				
Yes			35	4				
Don't know			5	1				
Farm type								
Lowland			766	85			140	87

Hill			25	3				
Upland			94	10				
Hill/Upland							16	10
Organic farm								
No			849	94				
Yes			41	5				
Stocking rate								
<4 ewes/acre	361	48	385	43	266	44	69	44
4-8 ewes/acre	241	32	451	50	296	49	84	53
>8 ewes/acre	102	14	36	4	28	5		

^a Blank cells,

565 Figure legend

566

569

Fig. 1. Example photograph and description of granuloma (A), and shelly hoof (B), also known as white line separation or degeneration, provided to farmers in questionnaires to

investigate their ability to identify common foot lesions.