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Viability of the Happy Factor^{TM} Targeted Selective Treatment approach on several sheep farms in Scotland.

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Highlights

Happy Factor^{TM} Targeted Selective Treatment (TST) method applied on 4 different farms

TST group showed no loss of lamb productivity compared with routine treatment (RT)

Lambs in TST group used up to 52% less anthelmintic compared with RT group

TST is a viable control method for worm infection on commercial farms

Abstract

The aim of this study was to examine the use of Happy Factor^{TM} weight based targeted selective treatment (TST) on several commercial farms in Scotland in combination with findings from a long term trial on a research farm to assess the potential for TST use in varying farming operations as an alternative to the current regimen of whole flock treatment. Lambs on each farm were regularly weighed and climatic conditions and pasture availability measured for inclusion into the Happy Factor^{TM} model to calculate weight targets. Half of the lambs were allocated to TST treatment and any failing to reach the weight target was treated with the anthelmintic of choice on that farm, while the remaining half of each flock was treated with anthelmintic as per normal practice on that farm (routine treatment, RT). The research farm (farm 1) hosted a long term trial using four anthelmintic treatment regimes over 6 years, and data from two regimes are presented here, alongside findings from three further farms: two commercial enterprises (farms 2 and 3) and a research farm operating as a commercial analogue with two breeds (farms 4a and 4b). The effect of TST strategy on lamb productivity and the number of anthelmintic treatments was investigated. There was no evidence ($p>0.300$) that mean bodyweight or growth rate was different between TST and RT groups on any of the farms and 95% confidence intervals of TST and RT groups generally suggested that TST had negligible unfavourable effects on the average growth of lambs for most of the farms. Growth rates ranged from 97.39 to 189.16 g/day reflecting the varied nature of the farms. All commercial farms used significantly less (1.34 RT versus 1.14 TST treatments per animal, $p<0.05$) anthelmintic in lambs following TST, with a reduction from 1, 1, 1.03 and 1.14 to 0.77, 0.57, 0.82 and 0.81 in the number of treatments per animal for farms 2,3 4a and 4b respectively. This study suggests that

TST is a viable means of controlling parasitic disease without incurring production losses.

Introduction:

Infection with ovine gastrointestinal nematodes leads to a significant threat to efficient sheep production due to considerable welfare and productivity issues coupled with the growing global problem of resistance to many of the currently used anthelmintic drug classes (Waller 1999, Papadopoulos 2012, Torres-Acosta *et al*, 2012). To meet global demand for ever increasing food supplies, increased animal productivity and sustainability are key issues, and hence there is a pressing need to slow the development of anthelmintic resistance (Fitzpatrick, 2013). The current method of controlling such infections through use of anthelmintic drugs, conventionally administered in a whole flock suppressive treatment strategy, contributes strong selection pressures for the development of resistant strains of parasites (Sargison 2012, Taylor 2012); so alternative means of controlling production losses while maintaining drug efficacy are required.

The concept of leaving parasites unexposed to treatment (“in refugia”) and thus maintaining susceptible alleles within the population is considered to be of critical importance in slowing the evolution of resistant parasite strains (Van Wyk, 2001). Recently research has focussed on maintaining parasites in refugia through Targeted Selective Treatment (TST) strategies using disease indicators such as anaemia (FAMACHA©, Van Wyk and Bath, 2002), faecal egg count (FEC, Leathwick *et al.* 2006, Gallidis *et al.* 2009) or production traits such as liveweight (Happy Factor^{TM}) (Greer et al, 2009, Kenyon, 2013a), body condition score (BCS, Gallidis *et al.* 2009) or milk production (Hoste et al 2002, Cringoli *et al*. 2009, Gallidis *et al.* 2009) to identify individuals at risk of parasitic disease and treating only those animals, thus leaving reproductive parasites in untreated hosts.

This study used the Happy Factor^{TM} method (Greer *et al.* 2009) which involves predicting an individual weight target for growing lambs and only treating each animal which fails to achieve this level of productivity. Identification of the most suitable indicator is critical for acceptance by farmers (Kenyon *et al*, 2009), with clear evidence of the benefits of maintenance of efficacy and minimised production losses necessary for uptake of any TST strategy (Van Wyk *et* al, 2006, Kenyon *et al.* 2009). TST implementation also depends on the decision support method being easily introduced and cost effective for use on farm (Kenyon *et al.* 2009). BCS, FAMACHA© and liveweight gain indicators such as Happy Factor^{TM} fall into this category. BCS has been found to be effective at identifying individual ewes which would benefit the most from anthelmintic treatment (Cornelius *et al.* 2014) however it may be less suitable for a lamb production system as these animals are still growing, with associated natural changes in body shape and fat coverage unassociated with worm infection. FAMACHA$^{©}$ is unsuitable in assessing pathological effects of temperate species such as *Teladorsagia circumcincta* which are not haematophageous and has been found to be of low value in identifying early infection with *Haemonchus contortus* (Chylinski *et al,* 2015) in a study where weight reduction was found to be the most effective of several indicators of infection examined. In the UK, Happy Factor^{TM} based liveweight gain has been shown to be an effective indicator of animals requiring treatment under a TST strategy (Greer *et* *al.* 2009, Kenyon *et al.* 2013a), maintaining productivity while reducing anthelmintic use. That study also proved that the development of resistance can be dramatically slowed using this approach. Studies on one farm in Scotland (Busin *et al.* 2014) further demonstrated that lambs treated under this TST regime received 50% of the anthelmintic treatments of lambs treated routinely every 6 weeks, without significant penalty to productivity compared with RT lambs in terms of daily weight gain or time to reach slaughter weight.

The present study aimed to extend the study of Kenyon *et al.* (2013a) for a further two grazing seasons as well as to apply the TST approach on three other commercial farms in Scotland to compare the productivity and anthelmintic usage of the TST groups with a routine treatment strategy. The individual farm trials were designed to compare weight gain of fat lamb production systems using either the Happy Factor^{TM} TST protocol or the farms' own routine anthelmintic treatment protocol.

Materials and methods:

Experimental design:

On each farm, lambs were grouped according to weight and sex and each group allocated randomly into Routine Treatment (RT) or Targeted Selective Treatment (TST) groups, with RT animals following a simulation of common farming practice. Lambs were monitored for body weight during the trial period which lasted from approximately end July/beginning August until the lambs were either sold for slaughter or housed for winter on each farm. Anthelmintic treatment was given individually based on target growth rates (TST) or following the farms' normal treatment policy. TST animals were treated immediately when they failed to reach weight targets generated by the Happy Factor^{TM} model described by Greer *et al.* (2009). Specific anthelmintic products used were also in line with normal farm practice and administered at manufacturers recommended dose rate according to weight.

Farms:

Summary data for the four farms used in the study are shown in Table 1.

Farm 1: Data from this experimental trial was drawn from the TST (Targeted Selective Treatment) and SPT (here described as RT or Routine Treatment) groups previously described in Kenyon *et al.* (2013a) with the addition of two further years of study (a total of six years: 2007 to 2012). This farm used twin lambs grazing with their dams.. Replicated groups (2 paddocks per treatment group) of 16-20 lambs were grazed on separate paddocks in close proximity, with the same 2 paddocks per treatment group used every year. RT animals received whole flock treatment at pre-determined times on the basis of prior knowledge of the epidemiology of parasite infection on these premises, namely at weaning and at six weeks post weaning.

Farms 2 and 3: These two farms were purely commercial enterprises in nature and consisted of lowland pasture. Trials on these farms were conducted within a single grazing season and both RT and TST groups grazed the same pasture throughout the trial. Animals were chosen from a single mob on each farm and groups were balanced for sex and initial bodyweight and randomly assigned to treatments. Both farms also treated RT lambs at pre-determined times with whole flock treatments, while TST lambs were treated as required at fortnightly weighing times. On farm 2, TST was used in two groups of lambs, receiving either Zolvix (Novartis Animal Health, UK) or Oramec (Merial Animal Health Ltd, UK) with RT lambs receiving Zolvix.

Farm 4: A research farm operating a commercial fat lamb production system covering a mixture of upland and rough hill grazing. Two breeds of lambs, Scottish Blackface (farm 4a) and Lleyn (farm 4b) were used on this farm and these were analysed separately. Lambs were grazed on a number of pastures in mobs over the course of a single grazing season. Each mob comprised approximately 50% RT and 50% TST lambs from both breeds, balanced for sex and initial bodyweight. Lambs were weighed approximately monthly, which is normal practice for such a farm. RT treatments were reactive on this farm, with pooled faecal egg counts being taken and treatments being administered to all RT animals in each mob when the mean FEC was over 500 eggs per gram (epg).

Happy Factor^{TM}:

The Happy Factor model (Greer *et al.* 2009) was used to determine individual weight targets. In brief, the maximum possible growth rate achievable was calculated from each lambs' previous weight in conjunction with mean temperature, estimated pasture quality and actual pasture mass. In previous studies, the optimum threshold for treatment was calculated to be 0.66 of the theoretical maximum (Greer et al. 2009) and had been used successfully in the studies by Kenyon *et al.* (2013) and Busin *et al.* (2014). In the absence of historical data for farms 2 to 4, the same treatment threshold was applied. The available pasture mass was measured using a Grassmaster II pasture probe (Novel Ways, New Zealand) by taking measurements in a z-pattern approximately 5 paces apart from each field with a minimum of 50 measurements taken each time. This was measured approximately mid way between each treatment giving a median value of mass to allow for changes during the time period between treatments. These data were incorporated into the Happy Factor model along with previous body weight data.

Weight measurement:

Animals were weighed regularly on each farm (and TST treatments applied at these timepoints) using the farms' own weighing equipment. Each lamb on farm 1 had body weight measurements at 9 times from day 42 to day 154 post turnout onto grazing of the experiment with an interval of approximately 14 days. Farms 2 and 3 weighed every 14 days, and farm 4 approximately monthly. Farms 1, 2 and 3 used a simple checklist method of identifying animals for treatment and their own calibrated weighing equipment while farm 4 used an automatic sorting crate to isolate animals requiring treatment.

Parasitology measurements:

The study on farm 1 measured faecal egg counts (Christie and Jackson 1982), and 2 tracer lambs per paddock were co-grazed twice annually for a period of 1 month prior to worm burden estimation. This method was also used on farms 2 and 3 faecal egg counts where counts were performed at each treatment point. Farm 4 performed pooled faecal egg counts using the McMaster method (MAFF, 1986) for each mob at regular intervals.

Statistical analyses

The data from farms 1, 2, and 3, and for the two breeds on farm 4, were analysed separately.

Body weight and daily liveweight gain:

The body weight data at different time points (days) were analysed by a linear mixed model (LMM). For farms 2, 3 and 4, the final LMM included initial body weight (included as a deviation from the farm mean), treatment group (RT or TST), time point (as a factor with appropriate levels for each farm) and sex (male or female) as fixed effects. For farm 1, fixed effects of the final LMM included: initial body weight, treatment group, sex, time (as a continuous variable measured in days included as a deviation from themean day of the farm), and year (six levels 2007 to 2012). All models included a random effect for lamb. For farm 1, random effects also included: paddocks, years within the paddock, sampling times (as a factor), and sampling times within each year and paddock.

The daily live weight gain of lambs attained between the start and end time points for each farm was modelled using a linear model (LM) with treatment group and sex as categorical variables , and in addition, year effect for farm 1. The 95% confidence intervals of the difference between mean weight and daily live weight gain of the TST and RT groups were generated in order to investigate whether TST treatments on average had any appreciable effect on production when compared with RT lambs.

Finishing weight:

Each lamb was scored by a binary variable as 1 or 0 to indicate the success or failure of the lamb to attain the target body weight of 40kg at the end of the experiment. For farm 1, a generalised linear mixed model (GLMM) was fitted to the binary data: the model additionally included year as a categorical variable and paddock as a random effect. For farms 2 to 4, a generalised linear model (GLM) was fitted to the binary data using a Bernoulli distribution and logit link function with categorical variables treatment group and sex, continuous variable initial body weight (included as a deviation from the farm mean).

Number of anthelmintic treatments:

The number of lambs that received no, or at least one anthelmintic treatment, and the number of lambs that received 0, 1, 2, 3 or 4 treatments, were each tabulated by RT and TST treatment groups. Fisher’s exact non-parametric test was used to investigate the effect of treatment group on the proportion of treated lambs and the proportion of lambs with different numbers of anthelmintic treatments.

All parametric models included only statistically significant ($p<0.05$) interaction terms. Parameters of the LMM were estimated using the residual maximum likelihood (REML) method, and the overall statistical significance of a factor (or covariate) was assessed from the *F*-statistic with denominator degrees of freedom estimated using the method suggested by Kenward and Roger (1997). The overall statistical significance of the treatment group in the linear model was assessed by *F*-statistic and GLM by the *Chi-square* statistic.

All statistical analyses were carried out using R software version 3.1.0 with appropriate R packages (stats, lme4, ggplot) (R Core Team, 2014).

Results:

Body weight:

Farm 1:

Final bodyweights on farm 1 are shown in Figure 1. Initial mean bodyweight (standard deviation) for farm 1 was 25.52Kg (3.97). There was a statistically significant interaction between year (factor) and time (covariate) on the mean body weight with 2011 and 2012 showing a decline on final bodyweight. Male lambs were significantly heavier than females ($p<0.05$). There was no evidence of differences in initial or final bodyweight between the RT and TST groups ($p>0.500$) in any of the years of the study. The estimate of 95% confidence intervals for the differences between TST and RT mean body weights (kg) was -1.59 to 1.68. Liveweight gain is shown in Figure 3. Mean gain (standard deviation) for all lambs was 97.39g/day (33.03). Again no differences were found between RT and TST groups ($p>0.300$) in any of the study years (95% CI: -27.31 to 26.16g/day)

Farm 2:

Initial mean body weight of the lambs (standard deviation) (in kg) was 24.47 (3.57). Data for the observed body weights of male and female lambs for all years recorded at the end of the experiment for final mean bodyweight is shown in Figure 2 along with estimated mean body weights and corresponding 95% confidence intervals for farms 2 to 4. Liveweight gain through the study period is similarly shown in Figure 4. As expected, the initial body weight had a positive association with the body weight at all time points for all farms ($p<0.001$), and on average, the body weight increased with time as indicated by increased mean body weights at succeeding time points. As with farm 1 there was no evidence of differences between RT and TST lambs in initial bodyweight or final bodyweight ($p>0.500$). The estimate of 95% confidence intervals for the differences between TST and RT mean body weights (kg) was -0.58 to 0.61. Mean liveweight gain is shown in Figure 4. The mean liveweight gain (standard deviation) for all lambs was 182.41g/day (32.84). There was no evidence for any difference between RT and TST groups ($p>0.300$) (95% CI: -16.85 to 4.20g/day).

Farm 3:

Initial mean body weight of the lambs (standard deviation) (in kg) was 26.41 (4.56). As with farm 2 the data for final bodyweight and liveweight gain is shown in Figures 2 and 4 respectively. Similarly to farm 2 the bodyweight increased with time and was positively associated with higher initial bodyweight ($p<0.001$). Again there was no difference in initial bodyweight, liveweight gain or final weight between RT and TST lambs ($p>0.500$). Estimated 95% confidence interval was -0.92 to 0.67Kg. As for farm 2, liveweight gain is shown in Figure 4. Mean liveweight gain (standard deviation) was 189.16/day (57.31). Again, there was no evidence for any difference between RT and TST groups ($p>0.300$) (95% CI: -21.12 to 12.75g/day).

Farm 4:

Farm 4 lambs were analysed separately with the Scottish Blackface lambs (4a) having an initial mean bodyweight (standard deviation) of 17.63Kg (3.65) and the Lleyn lambs 17.69Kg (3.66). Data for final bodyweight and liveweight gain are shown in Figures 2 and 4. Again bodyweight increased with time ($p<0.001$). Male lambs were also significantly heavier than female lambs ($p<0.009$). There was no difference between RT and TST groups for initial mean bodyweight, liveweight gain or final mean bodyweight ($p>0.500$) for either farm 4a or 4b. Estimated 95% confidence interval was -0.59 to 0.29Kg for 4a and -0.54 to 0.49Kg for 4b. Mean liveweight gain is again shown in Figure 4. Daily gain (standard deviation) was 136.14g/day (54.60) for farm 4a and 139.05g/day (45.09) for 4b. As with farms 2 and 3 there was no evidence for any difference between RT and TST groups for either breed ($p>0.300$) (95% CI: -10.02 to 8.83 (4a) and -9.11 to 10.65g/day (4b)).

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Finishing weight:

Farm 1:

The proportions of lambs reaching the finishing weight of 40kg on farm 1 for RT and TST groups was: 0.25, 0.17 (year 2007); 0.13, 0.19 (year 2008); 0.25, 0.33 (year 2009); 0.65, 0.70 (year 2010); 0.25, 0.30 (year 2011); 0.10, 0.05 (year 2012), respectively. Mean proportions of finishing lambs were not significantly different between RT and TST groups ($p=0.959$). Significantly more males than females reached finishing weight ($p<0.05$).

Farm 2:

The proportion of RT lambs reaching the finishing weight was 0.82, with the ivermectin-treated TST lambs at 0.68 and monepantel treated TST at 0.70. There was no significant difference between the two drug treatments in TST lambs (p>0.900), and the difference in proportions between RT and all TST lambs was not significant (p=0.143).

Farm 3:

The proportion of farm 3 reaching 40kg was 0.28 and 0.24 for RT and TST, respectively. There was no significant difference between groups (p=0.299).

Farm 4:

The proportion of lambs reaching finishing weight on farm 4 was considerably lower than other farms due to its hill system, where lambs are generally overwintered indoors and finished the following year, often on lowland pastures. Here it was 0.026 and 0.019 for RT (farm 4a and 4b respectively), and 0.042 and 0.030 for TST (4a and 4b). However, the difference in mean proportions of finishing lambs was not significantly different between TST and RT for both farm 4a (p=0.233) and farm 4b (p=0.869).

Number of anthelmintic treatments:

Farm 1:

Farm 1 used more anthelmintic in TST than RT animals (506 vs. 476 total treatments), although this was due to much higher levels of treatment in TST lambs in 2010, 2011 and 2012 (TST treatments per animal: 1.56, 1.91, 1.67 in 2007, 2008, 2009 followed by 2.20, 2.57, 2.80 in 2010, 2011 and 2012 respectively), compared with 2 per animal in the RT group in every year of the study. Numbers of treatments (proportion of TST group) ranged from one (0.19) to four (0.05) with the highest proportion of lambs receiving two treatments (0.48).

Farm2:

Farm 2 used one treatment per animal in the RT group and significantly fewer ($p<0.05$) in the TST group at 0.77 per animal with 0.64 of TST lambs requiring at least one treatment. Of the TST lambs 0.14 required more than one treatment, the highest number given on this farm.

Farm 3:

Farm 3 gave significantly fewer treatments to TST lambs with one treatment per animal to RT lambs and 0.57 to TST lambs ($p<0.05$). Just over half of TST lambs required treatment (0.52) with 0.47 receiving one treatment and the remainder two treatments.

Farm 4:

Both farms 4a and 4b gave fewer treatments to TST lambs at 0.82 and 0.81 compared with 1.02 and 1.14 per lamb, although this was only significant on farm 4b ($p<0.05$). Some RT mobs received no treatment, most one treatment and some two treatments as a result of the fec based treatment decision system in place where mobs were treated if pooled fec samples were in excess of 500 epg. The proportion of TST lambs receiving one treatment was 0.63 and 0.61 for 4a and 4b respectively, the remainder received two treatments.

Parasitology:

Farm 1:

Mean faecal egg counts for the RT and TST groups (epg) were ; 2007: 160.8, 135.4, 2008: 143.3, 212.3, 2009: 65.3, 106.9, 2010: 164.7, 135.6, 2011: 44.0, 44.1, 2012:, 13.08, 121.0. No comparison was made due to differences in anthelmintic treatments given to each group. Ivermectin efficacies ranged from 73.5 to 97.7%, in general showing a decline over time. No differences in efficacy between RT and TST groups were observed ($p>0.500$).

Farm 2:

Mean faecal egg counts were 15.7 and 49.6 epg for the RT and TST groups respectively. Prior to the study a faecal egg count reduction test (FECRT) was carried out according to WAAVP guidelines and ivermectin efficacy was found to be 77.8%. This drug was selected due to its importance to the farm in controlling ectoparasites as well as endoparasites. During the trial efficacy was found to be 72.1% for ivermectin and monepantel efficacy was 98.9%.

Farm 3:

Mean faecal egg counts were 112.1 (RT) and 129.8 epg (TST), and levamisole efficacy during the trial was 96.5%.

Farm 4:

Pooled mean faecal egg counts for both farm 4a and 4b were 310 epg with a range of 50-900 epg. No data was available for levamisole efficacy, however the farm regarded this class as being efficacious.

Pasture Mass:

On farm 1 mean pasture mass for the study periods (min,max) was; RT, 1845 (1077,2775), TST, 1767 (1071, 2692). There was no relationship between year of study and pasture mass and there was no significant difference in pasture mass between the RT and TST paddocks ($p>0.300$).

For the other farms, mean pasture mass (min,max) was; farm 2, 1476 (1001, 3158), farm 3, 1948 (1624, 2913) and farm 4a and b, 1683 (1139, 2513). Both treatment groups grazed the same paddocks on these farms.

Discussion:

As global anthelmintic resistance increasingly threatens sheep production (Waller 1999, Papadopoulos 2012, Torres-Acosta *et al*, 2012), the need to conserve efficacy in existing anthelmintics through introduction of alternatives to the currently standard suppressive treatment regimes is paramount (Sargison 2012). Maintaining susceptible parasites in refugia by treating only a proportion of a flock slows the development of anthelmintic resistance dramatically (Waghorn *et al.* 2008*,* Kenyon *et al*. 2013a). The use of Happy Factor^{TM} reduces anthelmintic use in an experimental situation (Kenyon *et al.* 2013a), and the same also been reported in one commercial fat lamb production system (Busin *et al*. 2014), but further evidence of its viability in a range of farming situations is required. This study explored the viability of Happy Factor^{TM} based TST across a number of farming systems and sheep breeds. By using the Happy Factor^{TM} system to predict optimum growth rate, we targeted anthelmintic to those individual animals most affected by disease, and left a considerable proportion of the animals untreated.

Production losses associated with reduced anthelmintic use is likely to be a key concern affecting uptake of TST by farmers. In this study, the 95% confidence intervals of mean daily live weight gain of TST and RT groups were close and centred around 0, suggesting that TST had negligible unfavourable effects on average growth traits on the commercial farms. The slightly larger confidence interval for the experimental farm was an artefact of using a different model of random variation. Thus this study generally suggested that the study farms had similar productivity in TST lambs compared with the routine treatments used in the RT groups despite differences in local environment, animal breeds and anthelmintic drugs in use. These findings support and extend those of Kenyon *et al.* (2013a) who found that weight-based TST did not reduce productivity when compared with other non-suppressive treatment regimes in an experimental situation. While this finding is important evidence that TST is suitable in terms of maintaining productivity, further research is required, particularly into whether the 66% of maximum gain used here can be considered as a ‘one size fits all’ weight gain threshold. There may be many farm-specific factors affecting productivity, so the question of whether these factors will lead to higher or lower optimum treatment thresholds than that used here is critical for further implementation of TST on farm. Most farms saw a reduction in the number of treatments given to lambs in the TST groups of between 8.7% and 52.3% less than that given to RT groups. Farm 1 was the only farm to administer more anthelmintic to TST than RT animals. This may be attributed to later years when the number of treatments increased dramatically (treatments per animal were 2.20 in 2010; 2.57 in 2011 and 2.80 in 2012) while RT treatments remained at two per animal. The reason for this increase in demand for treatment and decline in productivity amongst all groups on farm 1 is unclear at present and may have been affected by a number of factors such as breed differences between years, environmental differences or poorer pasture quality.

While lamb growth is a key indicator of farm productivity, a more important measure to the farms' profitability, and hence interest to the farmer, is in the time to reach slaughter weight. An enterprise becomes more profitable as the lambs take shorter time to reach the slaughter weight as well as reduced costs incurred due to housing and feeding over winter for lambs that fail to reach the marketable weight. While this is standard practice on farm 4, where the hill growing conditions mean that lambs are unlikely to achieve the 40kg weight during the first growing season, the other farms in the study would aim to sell the majority of the lambs before winter. This study demonstrated no statistically significant decrease in the systems tested in the number of lambs achieving the slaughter weight by the end of the trials between TST and RT groups, thus TST could be a suitable alternative to blanket drenching of lamb flocks.

Due to the differing anthelmintic treatment schedules, it is not possible to directly compare the faecal egg counts, however counts were taken to ensure that sufficient parasite challenge was present, and to establish the efficacy of the anthelmintic treatments. The mean faecal egg counts on all the farms were found to be representative of normal exposure to the parasite populations in Scotland. The efficacy of the anthelmintics used was reduced and resistance was found on farm 1 and in ivermectin on farm 2, however this was felt to be within acceptable levels and representative of drug efficacy on most farms in the region. The pasture mass on all farms was representative of normal grazing pasture in the region and sufficient for growth at all times during the studies, and there was no difference between pastures to account for differences between treatment groups on farm 1. All other farms grazed both groups on the same pasture.

On farm 1 there was the possibility that the different treatment regimes would lead to differences in pasture parasite contamination over time and hence differing levels of infection between groups, however previous analysis of data from this farm showed no difference in tracer lamb worm burdens between the RT (there known as SPT) and TST groups from 2007 to 2010 (Kenyon *et al.* 2013a). Similarly tracer lamb worm burdens for the continuation of this study into 2011 and 2012 (unpublished data) showed no significant differences between RT and TST groups. As increased pasture contamination is a key drawback to reducing the number of anthelmintic treatments, this is an important finding as it suggests that there is little danger of increased pasture infectivity resulting from the use of this system on other farms.The main advantage of implementing TST on farm is the ability to slow the development of anthelmintic resistance, without affecting animal performance. Kenyon *et al.* (2013a) demonstrated that reducing anthelmintic treatment by 50% in TST animals, compared with a suppressive treatment regime, slowed the development of resistance to ivermectin, and we observed that all the commercial and commercial analogue farms (farms 2-4) achieved similar levels of treatment reduction. Modelling data (Gaba *et* al., 2010) has shown that the effect of long term reduction in treatments on the frequency of resistant alleles depends greatly on the level of treatment reduction possible. That model suggested that more than 70% of animals must be left untreated treated to maintain low levels of resistance alleles where lambs flocks are treated twice yearly, but also that even a small reduction in treatments (leaving 10% of animals untreated) will have an effect in reducing the prevalence of resistance alleles in the parasite population. In this study, TST assessments were given either bi-weekly or monthly, and up to 31.53% of animals were left untreated at any given time, suggesting this approach is not likely to halt development of resistance entirely, but will dramatically slow it. This is the best that may be hoped for, as any application of anthelmintic drug will create selection pressure for resistance. With further modelling studies showing that even leaving 2% of the animals in a flock untreated can have significant delaying effects on the development of resistance in an 98% effective drug (Pech *et al*., 2009), the value of reducing treatments cannot be underestimated. Although these studies used only a single anthelmintic compound, combining TST with rotation of drug classes, which is already well established as a means of slowing resistance and as best practice, is likely to slow the development of resistance through reducing exposure of parasites to any given anthelmintic compound and increasing the dilution of those alleles responsible for resistance. Drug efficacy was found to be lower on farm 1 in latter years and on farm 2 for ivermectin, however all the other farms which checked for efficacy used drugs that were efficacious (>95% by faecal egg count reduction). While reduced efficacy on farms 1 and 2 is an issue as the initial efficacy will have consequent effects on the ability of TST to reduce increased prevalence of resistant alleles in the parasite population, there will still be an effect of slowing the development of a resistant population of parasites.

Research into treatment regimes showed that reactive practices, where animals are treated following emergence of clinical signs, demonstrated reduced productivity and increased CO_2 emissions (Kenyon *et al.* 2013b), and hence there is a pressing need for the sheep farming industry to implement more pro-active and targeted approaches to parasite control. In this study, we have confirmed the previous findings and shown that weight-based TST is indeed a viable means of controlling parasite infections in Scottish sheep flocks, with no evidence of loss of productivity and with the potential to slow the development of anthelmintic resistance as demonstrated by previous studies.Despite a large reduction in anthelmintic use on the commercial farms it was possible to maintain the normal levels of productivity in a commercial environment. None of the farms used in the study showed any adverse productivity in terms of growth rate resulting from the use of TST. This has also been shown to be the case in other TST studies, where other production parameters were used, according to the requirements of the farming system in question. Studies using Body Condition Score (BCS) in ewes (Cornelius *et al*. 2014) and dairy goats (Gallidis *et al.* 2009) and milk production in dairy goats (Hoste *at al.* 2002) all showed that the productivity markers used could be maintained under a reduced treatment TST regime. Taken together these findings suggest that treatment of underperforming animals, based on the locally appropriate marker, is of potential benefit in terms of slowing resistance development.

While TST may prove beneficial to farmers by lengthening the useful lifespan of current anthelmintic products, this will depend entirely on communicating the benefits to farmers in a way that will lead to uptake of the method. Previous schemes aimed at increasing parasites in refugia (Morgan and Coles, 2010) in the UK have had mixed results. Farmers exposed to the guidelines introduced by SCOPS

(Sustainable Control Of Parasites in Sheep, www.scops.org.uk) did largely make changes to their parasite management practice and were increasingly aware of the concept of refugia. While some improvements in parasite control practice were being made, others, particularly the continuance of dose and move strategies and poor practice in quarantine dosing, were continuing (Morgan and Coles 2010). Furthermore, the study found that only 50% of farmers were worried about the problem of anthelmintic resistance, with many of the remainder content that anthelmintics were effective on their farm, and that alternatives exist should resistance to a drug class appear. Other surveys of parasite control practice have shown an impact on parasite control practice on farm. Bartley *et al.* (2008) showed a reduction in the use of dose and move strategies, but this was amongst farmers who had actively solicited information, and were more likely to be actively concerned with acting to prevent anthelmintic resistance.

One key factor in the uptake of any new control practice is the ease of understanding and implementation by the end user. In these studies, much of the on farm work was carried out by research staff and farm workers under supervision by researchers. Some of the research groups were unfamiliar with TST however, and implemented the system with ease. Further unpublished pilot studies involved work on a farm using automated weighing and drafting equipment, where a method was developed such that the lambs were automatically drafted into treatment and non-treatment groups. Once this was implemented the farm staff were able to perform the TST method during routine weight monitoring of lambs with little extra effort. That these farms were able to implement the system easily is a major selling point in convincing users to implement TST on farms.

In addition to slowing the development of resistance, there is the potential for this method of TST to act as a general indicator of flock health in situations of poor lamb productivity. This will manifest as the repeated appearance of high levels of anthelmintic requirement. It may be the case that high levels of anthelmintic use can be utilised as a trigger for further veterinary investigation. This was highlighted during a TST pilot study on a farm in Scotland (data not published) where over 85% of TST group animals appeared to require treatment at any given weighing. This was initially assumed to be a breed or farm difference, and that treatment thresholds would vary according to farm or breed. Subsequent carcass reports at slaughter revealed widespread subclinical pasteurellosis in the flock, which was the likely cause of the poor performance. While TST performed well on all the farms in this study, further research into the question of individual farm specificity of treatment thresholds is required, with the aim of not only investigating the potential of TST to act as a flock health indicator, but also to identify any farm specific factors that may influence treatment thresholds.

In conclusion, we demonstrated that the lamb productivity of the TST group was similar to the RT group in most instances of experimental and commercial farming scenarios, and additionally, the lambs in the TST group used up to 52% less anthelmintics compared with the RT group. This study has shown that TST is a viable means of controlling parasitic disease without incurring production losses.

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Farm	Farm type	Breed	n (RT)	n (TST)
1	Lowland	Blackface/Texel	239	240
2	Lowland	Suffolk Crossbred	60	60 (monepantel) 80 (ivermectin)
3	Lowland	Suffolk Crossbred	82	41
4a	Upland and Hill	Scottish Blackface	234	234
4b	Upland and Hill	Lleyn	153	163

n:Number of lambs within each treatment group

Table 1: Farms used in the study.

Farm	RT regime	Number ofweighings	Number of TST treatments per lamb	Number of RT treatments per lamb
1	Planned At weaning and +6weeks	9	2007: 1.56 2008: 1.91 2009: 1.67 2010: 220 2011: 2.57 2012: 2.80 Mean: 2.10	2
2	Planned At weaning	6	0.77	1
3	Planned Planned 6 weekly	3	0.57	1
4a	Reactive FEC>500epg	4	0.81	1.02
4b	Reactive FEC>500epg	4	0.81	1.14

Table 2: Treatment regimes and number of anthelmintic treatments administered per lamb.

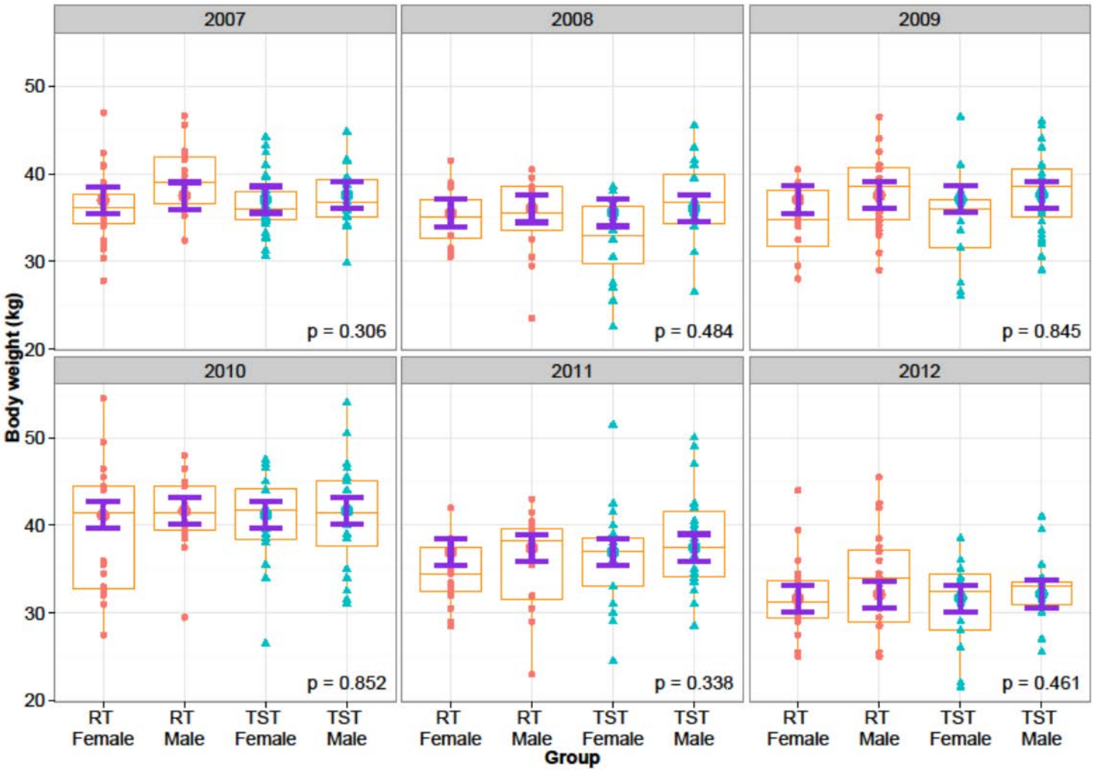

Figure 1: Observed body weights of female and male lambs of Routine Treatment (RT; in circle) and Targeted Selective Treatment (TST; in triangle) groups recorded at the end of the trial in an experimental farm (farm 1 in the text) for six years (2007 to 2012) along with the mean body weights (large circle) and corresponding 95% confidence intervals (error bar) estimated from LMM. Boxplots with summary statistics (median, lower and upper quartiles) of the observed data for each year are also included. The mean initial body weight for male and female lambs in each year was used to obtain the estimated mean body weights.

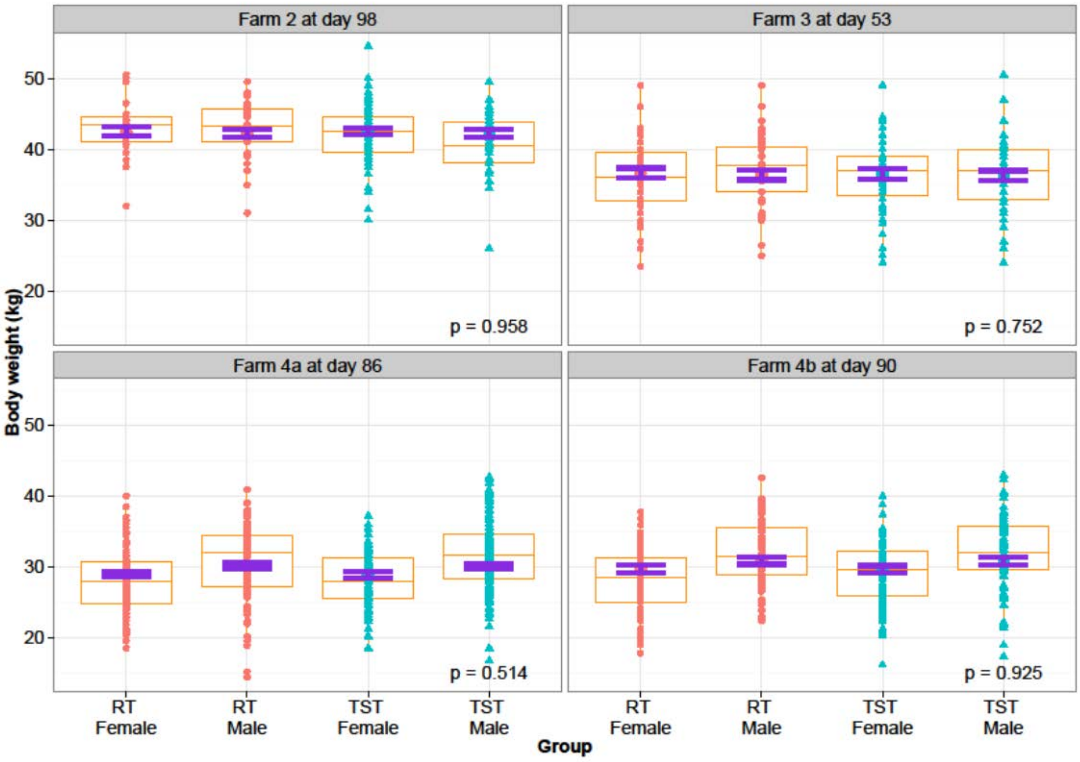

Figure 2: Observed body weights of female and male lambs of Routine Treatment (RT; in circle) and Targeted Selective Treatment (TST; in triangle) groups recorded at the end of the trial in three commercial farms (farms 2, 3, 4a, 4b), along with the mean body weights (large circle) and corresponding 95% confidence intervals (error bar) estimated from LMM. Boxplots with summary statistics (median, lower and upper quartiles) of the observed data for each farm are also included. We used the mean initial body weight of males and females on each farm to obtain the estimated mean body weights.

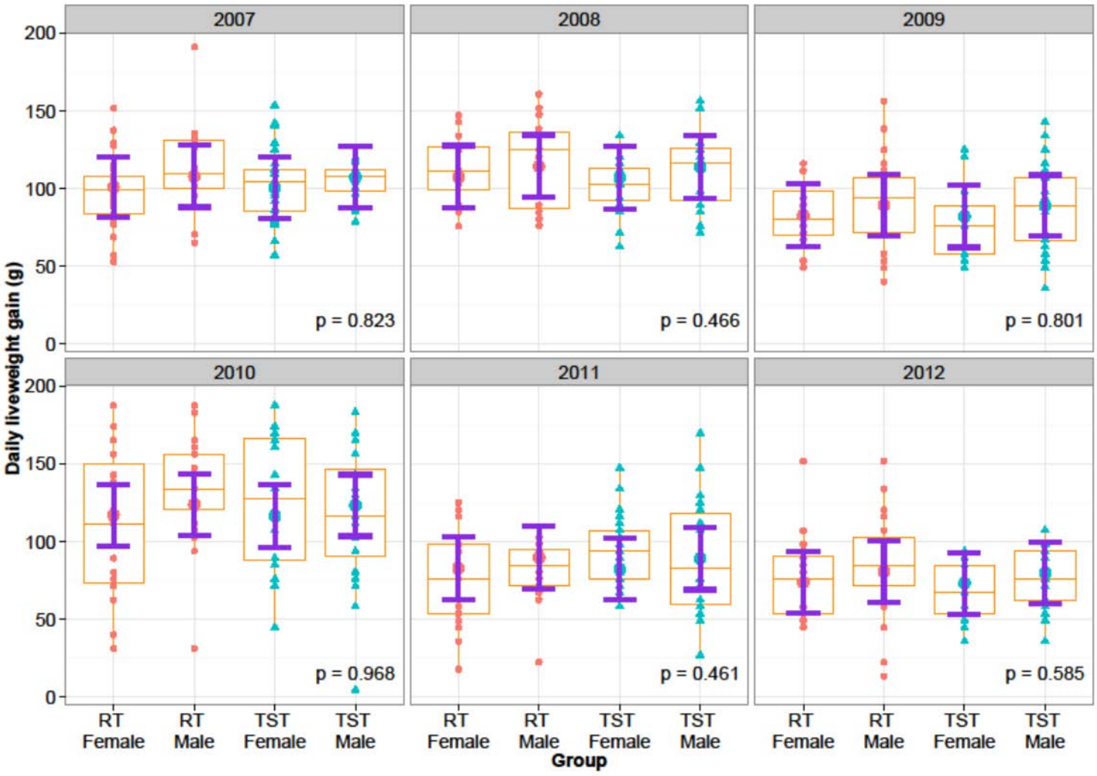

Figure 3: Observed liveweight gain of female and male lambs of Routine Treatment (RT; in circle) and Targeted Selective Treatment (TST; in triangle) groups recorded at the end of the trial in Farm 1 for six years (2007 to 2012) along with the mean liveweight gain (large circle) and corresponding 95% confidence intervals (error bar) estimated from LM. Boxplots with summary statistics (median, lower and upper quartiles) of the observed data for each year are also included.

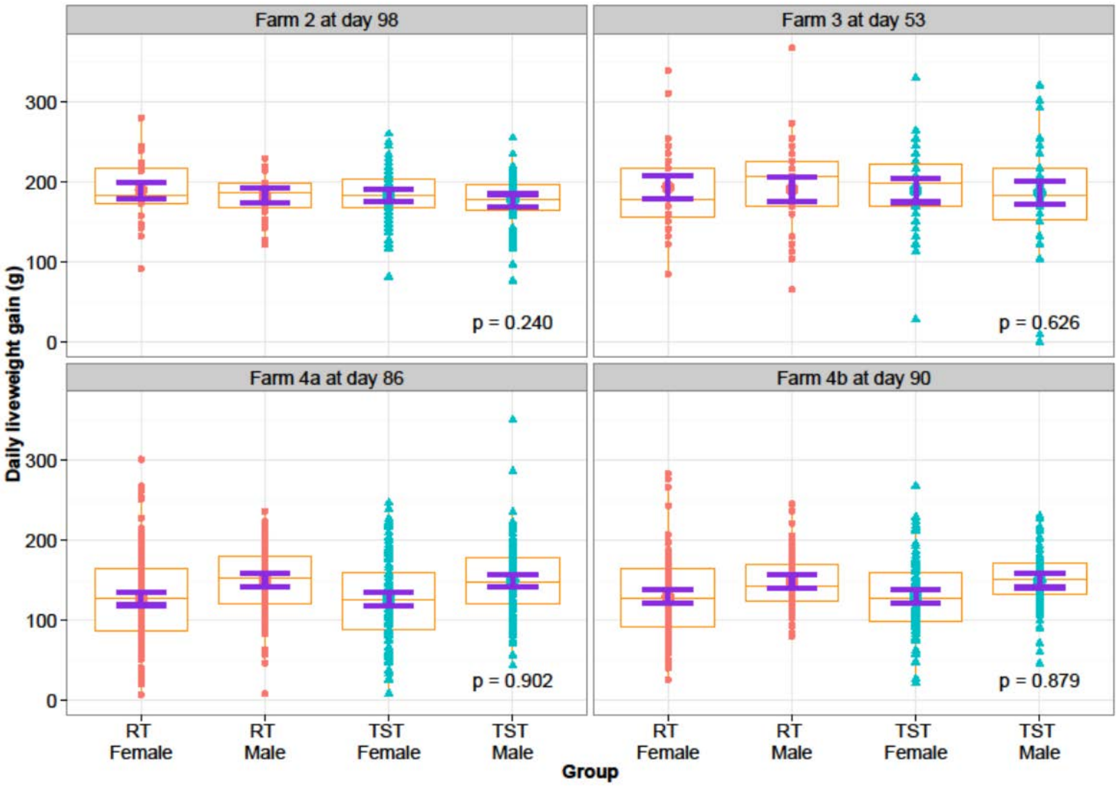

Figure 4: Observed daily liveweight gain of female and male lambs of Routine Treatment (RT; in circle) and Targeted Selective Treatment (TST; in triangle) groups during the period of the trial in three commercial farms (Farms 2, 3, 4a and 4b), along with the mean body weights (large circle) and corresponding 95% confidence intervals (error bar) estimated from LM. Boxplots with summary statistics (median, lower and upper quartiles) of the observed data for each farm are also included.

Conflict of interest:

All authors declare to have no conflicts of interest regarding the information provided in this manuscript.

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