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

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**Highlights**

Happy Factor™ 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

## 22 **Abstract**

23           The aim of this study was to examine the use of Happy Factor™ weight based  
24 targeted selective treatment (TST) on several commercial farms in Scotland in  
25 combination with findings from a long term trial on a research farm to assess the  
26 potential for TST use in varying farming operations as an alternative to the current  
27 regimen of whole flock treatment. Lambs on each farm were regularly weighed and  
28 climatic conditions and pasture availability measured for inclusion into the Happy  
29 Factor™ model to calculate weight targets. Half of the lambs were allocated to TST  
30 treatment and any failing to reach the weight target was treated with the anthelmintic  
31 of choice on that farm, while the remaining half of each flock was treated with  
32 anthelmintic as per normal practice on that farm (routine treatment, RT). The  
33 research farm (farm 1) hosted a long term trial using four anthelmintic treatment  
34 regimes over 6 years, and data from two regimes are presented here, alongside  
35 findings from three further farms: two commercial enterprises (farms 2 and 3) and a  
36 research farm operating as a commercial analogue with two breeds (farms 4a and  
37 4b). The effect of TST strategy on lamb productivity and the number of anthelmintic  
38 treatments was investigated. There was no evidence ( $p>0.300$ ) that mean  
39 bodyweight or growth rate was different between TST and RT groups on any of the  
40 farms and 95% confidence intervals of TST and RT groups generally suggested that  
41 TST had negligible unfavourable effects on the average growth of lambs for most of  
42 the farms. Growth rates ranged from 97.39 to 189.16 g/day reflecting the varied  
43 nature of the farms. All commercial farms used significantly less (1.34 RT versus  
44 1.14 TST treatments per animal,  $p<0.05$ ) anthelmintic in lambs following TST, with a  
45 reduction from 1, 1, 1.03 and 1.14 to 0.77, 0.57, 0.82 and 0.81 in the number of  
46 treatments per animal for farms 2,3 4a and 4b respectively. This study suggests that

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

49

50

## 51 **Introduction:**

52 Infection with ovine gastrointestinal nematodes leads to a significant threat to  
53 efficient sheep production due to considerable welfare and productivity issues  
54 coupled with the growing global problem of resistance to many of the currently used  
55 anthelmintic drug classes (Waller 1999, Papadopoulos 2012, Torres-Acosta *et al*,  
56 2012). To meet global demand for ever increasing food supplies, increased animal  
57 productivity and sustainability are key issues, and hence there is a pressing need to  
58 slow the development of anthelmintic resistance (Fitzpatrick, 2013). The current  
59 method of controlling such infections through use of anthelmintic drugs,  
60 conventionally administered in a whole flock suppressive treatment strategy,  
61 contributes strong selection pressures for the development of resistant strains of  
62 parasites (Sargison 2012, Taylor 2012); so alternative means of controlling  
63 production losses while maintaining drug efficacy are required.

64 The concept of leaving parasites unexposed to treatment (“in refugia”) and  
65 thus maintaining susceptible alleles within the population is considered to be of  
66 critical importance in slowing the evolution of resistant parasite strains (Van Wyk,  
67 2001). Recently research has focussed on maintaining parasites in refugia through  
68 Targeted Selective Treatment (TST) strategies using disease indicators such as  
69 anaemia (FAMACHA©, Van Wyk and Bath, 2002), faecal egg count (FEC, Leathwick

70 *et al.* 2006, Gallidis *et al.* 2009) or production traits such as liveweight (Happy  
71 Factor<sup>TM</sup>) (Greer *et al.*, 2009, Kenyon, 2013a), body condition score (BCS, Gallidis *et*  
72 *al.* 2009) or milk production (Hoste *et al.* 2002, Cringoli *et al.* 2009, Gallidis *et al.*  
73 2009) to identify individuals at risk of parasitic disease and treating only those  
74 animals, thus leaving reproductive parasites in untreated hosts.

75 This study used the Happy Factor<sup>TM</sup> method (Greer *et al.* 2009) which involves  
76 predicting an individual weight target for growing lambs and only treating each  
77 animal which fails to achieve this level of productivity. Identification of the most  
78 suitable indicator is critical for acceptance by farmers (Kenyon *et al.*, 2009), with clear  
79 evidence of the benefits of maintenance of efficacy and minimised production losses  
80 necessary for uptake of any TST strategy (Van Wyk *et al.*, 2006, Kenyon *et al.* 2009).  
81 TST implementation also depends on the decision support method being easily  
82 introduced and cost effective for use on farm (Kenyon *et al.* 2009). BCS,  
83 FAMACHA<sup>©</sup> and liveweight gain indicators such as Happy Factor<sup>TM</sup> fall into this  
84 category. BCS has been found to be effective at identifying individual ewes which  
85 would benefit the most from anthelmintic treatment (Cornelius *et al.* 2014) however it  
86 may be less suitable for a lamb production system as these animals are still growing,  
87 with associated natural changes in body shape and fat coverage unassociated with  
88 worm infection. FAMACHA<sup>©</sup> is unsuitable in assessing pathological effects of  
89 temperate species such as *Teladorsagia circumcincta* which are not  
90 haematophageous and has been found to be of low value in identifying early  
91 infection with *Haemonchus contortus* (Chylinski *et al.*, 2015) in a study where weight  
92 reduction was found to be the most effective of several indicators of infection  
93 examined. In the UK, Happy Factor<sup>TM</sup> based liveweight gain has been shown to be  
94 an effective indicator of animals requiring treatment under a TST strategy (Greer *et*

95 *al.* 2009, Kenyon *et al.* 2013a), maintaining productivity while reducing anthelmintic  
96 use. That study also proved that the development of resistance can be dramatically  
97 slowed using this approach. Studies on one farm in Scotland (Busin *et al.* 2014)  
98 further demonstrated that lambs treated under this TST regime received 50% of the  
99 anthelmintic treatments of lambs treated routinely every 6 weeks, without significant  
100 penalty to productivity compared with RT lambs in terms of daily weight gain or time  
101 to reach slaughter weight.

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

## 109 **Materials and methods:**

### 110 *Experimental design:*

111         On each farm, lambs were grouped according to weight and sex and each  
112 group allocated randomly into Routine Treatment (RT) or Targeted Selective  
113 Treatment (TST) groups, with RT animals following a simulation of common farming  
114 practice. Lambs were monitored for body weight during the trial period which lasted  
115 from approximately end July/beginning August until the lambs were either sold for  
116 slaughter or housed for winter on each farm. Anthelmintic treatment was given  
117 individually based on target growth rates (TST) or following the farms' normal  
118 treatment policy. TST animals were treated immediately when they failed to reach

119 weight targets generated by the Happy Factor™ model described by Greer *et al.*  
120 (2009). Specific anthelmintic products used were also in line with normal farm  
121 practice and administered at manufacturers recommended dose rate according to  
122 weight.

123 *Farms:*

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

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

134

135 *Farms 2 and 3:* These two farms were purely commercial enterprises in nature and  
136 consisted of lowland pasture. Trials on these farms were conducted within a single  
137 grazing season and both RT and TST groups grazed the same pasture throughout  
138 the trial. Animals were chosen from a single mob on each farm and groups were  
139 balanced for sex and initial bodyweight and randomly assigned to treatments. Both  
140 farms also treated RT lambs at pre-determined times with whole flock treatments,  
141 while TST lambs were treated as required at fortnightly weighing times. On farm 2,

142 TST was used in two groups of lambs, receiving either Zolvix (Novartis Animal  
143 Health, UK) or Oramec (Merial Animal Health Ltd, UK) with RT lambs receiving  
144 Zolvix.

145

146 *Farm 4:* A research farm operating a commercial fat lamb production system  
147 covering a mixture of upland and rough hill grazing. Two breeds of lambs, Scottish  
148 Blackface (farm 4a) and Lleyn (farm 4b) were used on this farm and these were  
149 analysed separately. Lambs were grazed on a number of pastures in mobs over the  
150 course of a single grazing season. Each mob comprised approximately 50% RT and  
151 50% TST lambs from both breeds, balanced for sex and initial bodyweight. Lambs  
152 were weighed approximately monthly, which is normal practice for such a farm. RT  
153 treatments were reactive on this farm, with pooled faecal egg counts being taken and  
154 treatments being administered to all RT animals in each mob when the mean FEC  
155 was over 500 eggs per gram (epg).

156 *Happy Factor<sup>TM</sup>:*

157 The Happy Factor model (Greer *et al.* 2009) was used to determine individual  
158 weight targets. In brief, the maximum possible growth rate achievable was calculated  
159 from each lambs' previous weight in conjunction with mean temperature, estimated  
160 pasture quality and actual pasture mass. In previous studies, the optimum threshold  
161 for treatment was calculated to be 0.66 of the theoretical maximum (Greer *et al.*  
162 2009) and had been used successfully in the studies by Kenyon *et al.* (2013) and  
163 Busin *et al.* (2014). In the absence of historical data for farms 2 to 4, the same  
164 treatment threshold was applied. The available pasture mass was measured using a  
165 Grassmaster II pasture probe (Novel Ways, New Zealand) by taking measurements



166 in a z-pattern approximately 5 paces apart from each field with a minimum of 50  
167 measurements taken each time. This was measured approximately mid way  
168 between each treatment giving a median value of mass to allow for changes during  
169 the time period between treatments. These data were incorporated into the Happy  
170 Factor model along with previous body weight data.

171 *Weight measurement:*

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

180

181 *Parasitology measurements:*

182         The study on farm 1 measured faecal egg counts (Christie and Jackson  
183 1982), and 2 tracer lambs per paddock were co-grazed twice annually for a period of  
184 1 month prior to worm burden estimation. This method was also used on farms 2 and  
185 3 faecal egg counts where counts were performed at each treatment point. Farm 4  
186 performed pooled faecal egg counts using the McMaster method (MAFF, 1986) for  
187 each mob at regular intervals.

188

189

190 **Statistical analyses**

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

193 *Body weight and daily liveweight gain:*

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

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

211 *Finishing weight:*

212 Each lamb was scored by a binary variable as 1 or 0 to indicate the success  
213 or failure of the lamb to attain the target body weight of 40kg at the end of the  
214 experiment. For farm 1, a generalised linear mixed model (GLMM) was fitted to the

215 binary data: the model additionally included year as a categorical variable and  
216 paddock as a random effect. For farms 2 to 4, a generalised linear model (GLM) was  
217 fitted to the binary data using a Bernoulli distribution and logit link function with  
218 categorical variables treatment group and sex, continuous variable initial body weight  
219 (included as a deviation from the farm mean).

220 *Number of anthelmintic treatments:*

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

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

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

235

236 **Results:**

237

238 *Body weight:*

239 *Farm 1:*

240 Final bodyweights on farm 1 are shown in Figure 1. Initial mean bodyweight  
241 (standard deviation) for farm 1 was 25.52Kg (3.97). There was a statistically  
242 significant interaction between year (factor) and time (covariate) on the mean body  
243 weight with 2011 and 2012 showing a decline on final bodyweight. Male lambs were  
244 significantly heavier than females ( $p < 0.05$ ). There was no evidence of differences in  
245 initial or final bodyweight between the RT and TST groups ( $p > 0.500$ ) in any of the  
246 years of the study. The estimate of 95% confidence intervals for the differences  
247 between TST and RT mean body weights (kg) was -1.59 to 1.68. Liveweight gain is  
248 shown in Figure 3. Mean gain (standard deviation) for all lambs was 97.39g/day  
249 (33.03). Again no differences were found between RT and TST groups ( $p > 0.300$ ) in  
250 any of the study years (95% CI: -27.31 to 26.16g/day)

251 *Farm 2:*

252 Initial mean body weight of the lambs (standard deviation) (in kg) was 24.47 (3.57).  
253 Data for the observed body weights of male and female lambs for all years recorded  
254 at the end of the experiment for final mean bodyweight is shown in Figure 2 along  
255 with estimated mean body weights and corresponding 95% confidence intervals for  
256 farms 2 to 4. Liveweight gain through the study period is similarly shown in Figure 4.  
257 As expected, the initial body weight had a positive association with the body weight  
258 at all time points for all farms ( $p < 0.001$ ), and on average, the body weight increased  
259 with time as indicated by increased mean body weights at succeeding time points.  
260 As with farm 1 there was no evidence of differences between RT and TST lambs in  
261 initial bodyweight or final bodyweight ( $p > 0.500$ ). The estimate of 95% confidence

262 intervals for the differences between TST and RT mean body weights (kg) was -0.58  
263 to 0.61. Mean liveweight gain is shown in Figure 4. The mean liveweight gain  
264 (standard deviation) for all lambs was 182.41g/day (32.84). There was no evidence  
265 for any difference between RT and TST groups ( $p>0.300$ ) (95% CI: -16.85 to  
266 4.20g/day).

267

268 *Farm 3:*

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

278

279 *Farm 4:*

280 Farm 4 lambs were analysed separately with the Scottish Blackface lambs (4a)  
281 having an initial mean bodyweight (standard deviation) of 17.63Kg (3.65) and the  
282 Lleyn lambs 17.69Kg (3.66). Data for final bodyweight and liveweight gain are shown  
283 in Figures 2 and 4. Again bodyweight increased with time ( $p<0.001$ ). Male lambs  
284 were also significantly heavier than female lambs ( $p<0.009$ ). There was no difference

285 between RT and TST groups for initial mean bodyweight, liveweight gain or final  
286 mean bodyweight ( $p>0.500$ ) for either farm 4a or 4b. Estimated 95% confidence  
287 interval was -0.59 to 0.29Kg for 4a and -0.54 to 0.49Kg for 4b. Mean liveweight gain  
288 is again shown in Figure 4. Daily gain (standard deviation) was 136.14g/day (54.60)  
289 for farm 4a and 139.05g/day (45.09) for 4b. As with farms 2 and 3 there was no  
290 evidence for any difference between RT and TST groups for either breed ( $p>0.300$ )  
291 (95% CI: -10.02 to 8.83 (4a) and -9.11 to 10.65g/day (4b)).

292

293 .

294 *Finishing weight:*

295 *Farm 1:*

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

302

303 *Farm 2:*

304 The proportion of RT lambs reaching the finishing weight was 0.82, with the  
305 ivermectin-treated TST lambs at 0.68 and monepantel treated TST at 0.70. There  
306 was no significant difference between the two drug treatments in TST lambs

307 (p>0.900), and the difference in proportions between RT and all TST lambs was not  
308 significant (p=0.143).

309

310 *Farm 3:*

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

313

314 *Farm 4:*

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

322

323 *Number of anthelmintic treatments:*

324 *Farm 1:*

325 Farm 1 used more anthelmintic in TST than RT animals (506 vs. 476 total  
326 treatments), although this was due to much higher levels of treatment in TST lambs  
327 in 2010, 2011 and 2012 (TST treatments per animal: 1.56, 1.91, 1.67 in 2007, 2008,  
328 2009 followed by 2.20, 2.57, 2.80 in 2010, 2011 and 2012 respectively), compared

329 with 2 per animal in the RT group in every year of the study. Numbers of treatments  
330 (proportion of TST group) ranged from one (0.19) to four (0.05) with the highest  
331 proportion of lambs receiving two treatments (0.48).

332

333

334 *Farm2:*

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

339

340 *Farm 3:*

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

345

346 *Farm 4:*

347 Both farms 4a and 4b gave fewer treatments to TST lambs at 0.82 and 0.81  
348 compared with 1.02 and 1.14 per lamb, although this was only significant on farm 4b  
349 ( $p < 0.05$ ). Some RT mobs received no treatment, most one treatment and some two  
350 treatments as a result of the fec based treatment decision system in place where



351 mobs were treated if pooled fec samples were in excess of 500 epg. The proportion  
352 of TST lambs receiving one treatment was 0.63 and 0.61 for 4a and 4b respectively,  
353 the remainder received two treatments.

354

355 *Parasitology:*

356 *Farm 1:*

357 Mean faecal egg counts for the RT and TST groups (epg) were ; 2007: 160.8,  
358 135.4, 2008: 143.3, 212.3, 2009: 65.3, 106.9, 2010: 164.7, 135.6, 2011: 44.0, 44.1,  
359 2012:, 13.08, 121.0. No comparison was made due to differences in anthelmintic  
360 treatments given to each group. Ivermectin efficacies ranged from 73.5 to 97.7%, in  
361 general showing a decline over time. No differences in efficacy between RT and TST  
362 groups were observed ( $p>0.500$ ).

363 *Farm 2:*

364 Mean faecal egg counts were 15.7 and 49.6 epg for the RT and TST groups  
365 respectively. Prior to the study a faecal egg count reduction test (FECRT) was  
366 carried out according to WAAVP guidelines and ivermectin efficacy was found to be  
367 77.8%. This drug was selected due to its importance to the farm in controlling  
368 ectoparasites as well as endoparasites. During the trial efficacy was found to be  
369 72.1% for ivermectin and monepantel efficacy was 98.9%.

370 *Farm 3:*

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

373 *Farm 4:*

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

377

378 *Pasture Mass:*

379 On farm 1 mean pasture mass for the study periods (min,max) was; RT, 1845  
380 (1077,2775), TST, 1767 (1071, 2692). There was no relationship between year of  
381 study and pasture mass and there was no significant difference in pasture mass  
382 between the RT and TST paddocks ( $p>0.300$ ).

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

386

387 **Discussion:**

388 As global anthelmintic resistance increasingly threatens sheep production  
389 (Waller 1999, Papadopoulos 2012, Torres-Acosta *et al*, 2012), the need to conserve  
390 efficacy in existing anthelmintics through introduction of alternatives to the currently  
391 standard suppressive treatment regimes is paramount (Sargison 2012). Maintaining  
392 susceptible parasites in refugia by treating only a proportion of a flock slows the  
393 development of anthelmintic resistance dramatically (Waghorn *et al*. 2008, Kenyon *et*  
394 *al*. 2013a). The use of Happy Factor™ reduces anthelmintic use in an experimental

395 situation (Kenyon *et al.* 2013a), and the same also been reported in one commercial  
396 fat lamb production system (Busin *et al.* 2014), but further evidence of its viability in a  
397 range of farming situations is required. This study explored the viability of Happy  
398 Factor™ based TST across a number of farming systems and sheep breeds. By  
399 using the Happy Factor™ system to predict optimum growth rate, we targeted  
400 anthelmintic to those individual animals most affected by disease, and left a  
401 considerable proportion of the animals untreated.

402         Production losses associated with reduced anthelmintic use is likely to be a  
403 key concern affecting uptake of TST by farmers. In this study, the 95% confidence  
404 intervals of mean daily live weight gain of TST and RT groups were close and  
405 centred around 0, suggesting that TST had negligible unfavourable effects on  
406 average growth traits on the commercial farms. The slightly larger confidence  
407 interval for the experimental farm was an artefact of using a different model of  
408 random variation. Thus this study generally suggested that the study farms had  
409 similar productivity in TST lambs compared with the routine treatments used in the  
410 RT groups despite differences in local environment, animal breeds and anthelmintic  
411 drugs in use. These findings support and extend those of Kenyon *et al.* (2013a) who  
412 found that weight-based TST did not reduce productivity when compared with other  
413 non-suppressive treatment regimes in an experimental situation. While this finding is  
414 important evidence that TST is suitable in terms of maintaining productivity, further  
415 research is required, particularly into whether the 66% of maximum gain used here  
416 can be considered as a 'one size fits all' weight gain threshold. There may be many  
417 farm-specific factors affecting productivity, so the question of whether these factors  
418 will lead to higher or lower optimum treatment thresholds than that used here is  
419 critical for further implementation of TST on farm. Most farms saw a reduction in the

420 number of treatments given to lambs in the TST groups of between 8.7% and  
421 52.3% less than that given to RT groups. Farm 1 was the only farm to administer  
422 more anthelmintic to TST than RT animals. This may be attributed to later years  
423 when the number of treatments increased dramatically (treatments per animal were  
424 2.20 in 2010; 2.57 in 2011 and 2.80 in 2012) while RT treatments remained at two  
425 per animal. The reason for this increase in demand for treatment and decline in  
426 productivity amongst all groups on farm 1 is unclear at present and may have been  
427 affected by a number of factors such as breed differences between years,  
428 environmental differences or poorer pasture quality.

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

441         Due to the differing anthelmintic treatment schedules, it is not possible to  
442 directly compare the faecal egg counts, however counts were taken to ensure that  
443 sufficient parasite challenge was present, and to establish the efficacy of the  
444 anthelmintic treatments. The mean faecal egg counts on all the farms were found to

445 be representative of normal exposure to the parasite populations in Scotland. The  
446 efficacy of the anthelmintics used was reduced and resistance was found on farm 1  
447 and in ivermectin on farm 2, however this was felt to be within acceptable levels and  
448 representative of drug efficacy on most farms in the region. The pasture mass on all  
449 farms was representative of normal grazing pasture in the region and sufficient for  
450 growth at all times during the studies, and there was no difference between pastures  
451 to account for differences between treatment groups on farm 1. All other farms  
452 grazed both groups on the same pasture.

453         On farm 1 there was the possibility that the different treatment regimes would  
454 lead to differences in pasture parasite contamination over time and hence differing  
455 levels of infection between groups, however previous analysis of data from this farm  
456 showed no difference in tracer lamb worm burdens between the RT (there known as  
457 SPT) and TST groups from 2007 to 2010 (Kenyon *et al.* 2013a). Similarly tracer lamb  
458 worm burdens for the continuation of this study into 2011 and 2012 (unpublished  
459 data) showed no significant differences between RT and TST groups. As increased  
460 pasture contamination is a key drawback to reducing the number of anthelmintic  
461 treatments, this is an important finding as it suggests that there is little danger of  
462 increased pasture infectivity resulting from the use of this system on other farms. The  
463 main advantage of implementing TST on farm is the ability to slow the development  
464 of anthelmintic resistance, without affecting animal performance. Kenyon *et al.*  
465 (2013a) demonstrated that reducing anthelmintic treatment by 50% in TST animals,  
466 compared with a suppressive treatment regime, slowed the development of  
467 resistance to ivermectin, and we observed that all the commercial and commercial  
468 analogue farms (farms 2-4) achieved similar levels of treatment reduction. Modelling  
469 data (Gaba *et al.*, 2010) has shown that the effect of long term reduction in

470 treatments on the frequency of resistant alleles depends greatly on the level of  
471 treatment reduction possible. That model suggested that more than 70% of animals  
472 must be left untreated treated to maintain low levels of resistance alleles where  
473 lambs flocks are treated twice yearly, but also that even a small reduction in  
474 treatments (leaving 10% of animals untreated) will have an effect in reducing the  
475 prevalence of resistance alleles in the parasite population. In this study, TST  
476 assessments were given either bi-weekly or monthly, and up to 31.53% of animals  
477 were left untreated at any given time, suggesting this approach is not likely to halt  
478 development of resistance entirely, but will dramatically slow it. This is the best that  
479 may be hoped for, as any application of anthelmintic drug will create selection  
480 pressure for resistance. With further modelling studies showing that even leaving 2%  
481 of the animals in a flock untreated can have significant delaying effects on the  
482 development of resistance in an 98% effective drug (Pech *et al.*, 2009), the value of  
483 reducing treatments cannot be underestimated. Although these studies used only a  
484 single anthelmintic compound, combining TST with rotation of drug classes, which is  
485 already well established as a means of slowing resistance and as best practice, is  
486 likely to slow the development of resistance through reducing exposure of parasites  
487 to any given anthelmintic compound and increasing the dilution of those alleles  
488 responsible for resistance. Drug efficacy was found to be lower on farm 1 in latter  
489 years and on farm 2 for ivermectin, however all the other farms which checked for  
490 efficacy used drugs that were efficacious (>95% by faecal egg count reduction).  
491 While reduced efficacy on farms 1 and 2 is an issue as the initial efficacy will have  
492 consequent effects on the ability of TST to reduce increased prevalence of resistant  
493 alleles in the parasite population, there will still be an effect of slowing the  
494 development of a resistant population of parasites.

495           Research into treatment regimes showed that reactive practices, where  
496 animals are treated following emergence of clinical signs, demonstrated reduced  
497 productivity and increased CO<sub>2</sub> emissions (Kenyon *et al.* 2013b), and hence there is  
498 a pressing need for the sheep farming industry to implement more pro-active and  
499 targeted approaches to parasite control. In this study, we have confirmed the  
500 previous findings and shown that weight-based TST is indeed a viable means of  
501 controlling parasite infections in Scottish sheep flocks, with no evidence of loss of  
502 productivity and with the potential to slow the development of anthelmintic resistance  
503 as demonstrated by previous studies. Despite a large reduction in anthelmintic use  
504 on the commercial farms it was possible to maintain the normal levels of productivity  
505 in a commercial environment. None of the farms used in the study showed any  
506 adverse productivity in terms of growth rate resulting from the use of TST. This has  
507 also been shown to be the case in other TST studies, where other production  
508 parameters were used, according to the requirements of the farming system in  
509 question. Studies using Body Condition Score (BCS) in ewes (Cornelius *et al.* 2014)  
510 and dairy goats (Gallidis *et al.* 2009) and milk production in dairy goats (Hoste *at al.*  
511 2002) all showed that the productivity markers used could be maintained under a  
512 reduced treatment TST regime. Taken together these findings suggest that treatment  
513 of underperforming animals, based on the locally appropriate marker, is of potential  
514 benefit in terms of slowing resistance development.

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

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

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



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

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

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

685 n: Number of lambs within each treatment group

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687 *Table 1: Farms used in the study.*

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<b>Farm</b>	<b>RT regime</b>	<b>Number of weighings</b>	<b>Number of TST treatments per lamb</b>	<b>Number of RT treatments per lamb</b>
<b>1</b>	Planned At weaning and +6weeks	9	2007: 1.56 2008: 1.91 2009: 1.67 2010: 2.20 2011: 2.57 2012: 2.80 Mean: 2.10	2
<b>2</b>	Planned At weaning	6	0.77	1
<b>3</b>	Planned Planned 6 weekly	3	0.57	1
<b>4a</b>	Reactive FEC>500epg	4	0.81	1.02
<b>4b</b>	Reactive FEC>500epg	4	0.81	1.14

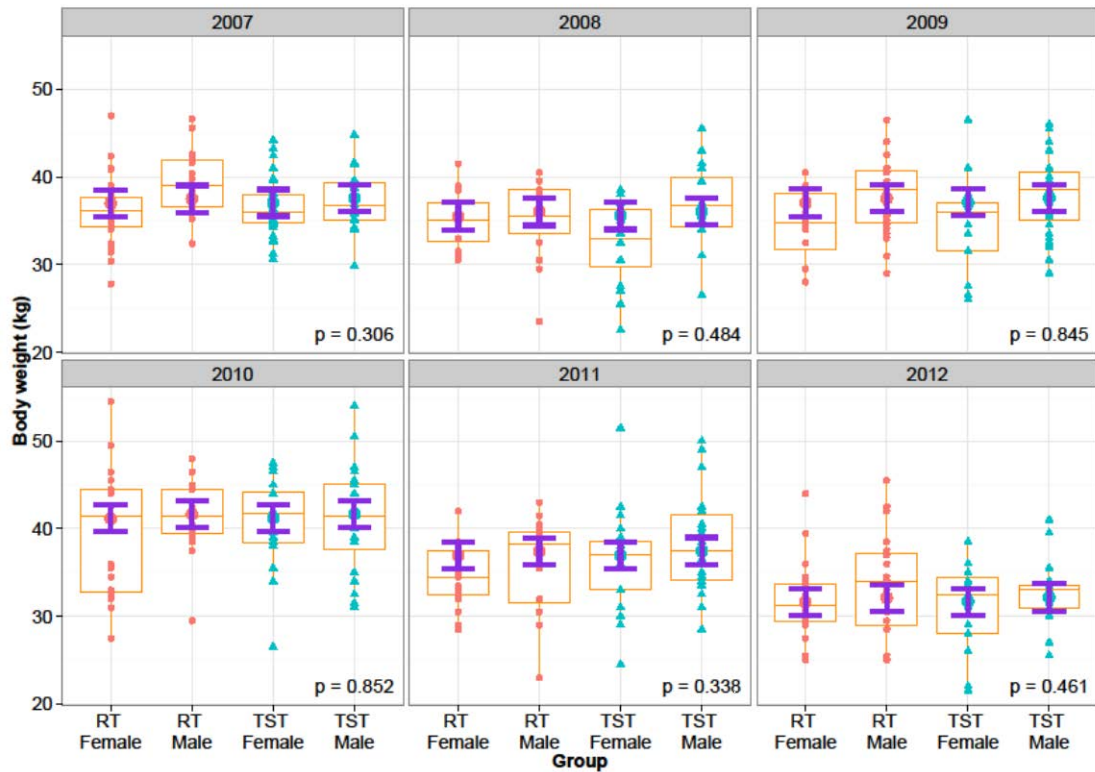
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698 *Table 2: Treatment regimes and number of anthelmintic treatments administered per*  
699 *lamb.*

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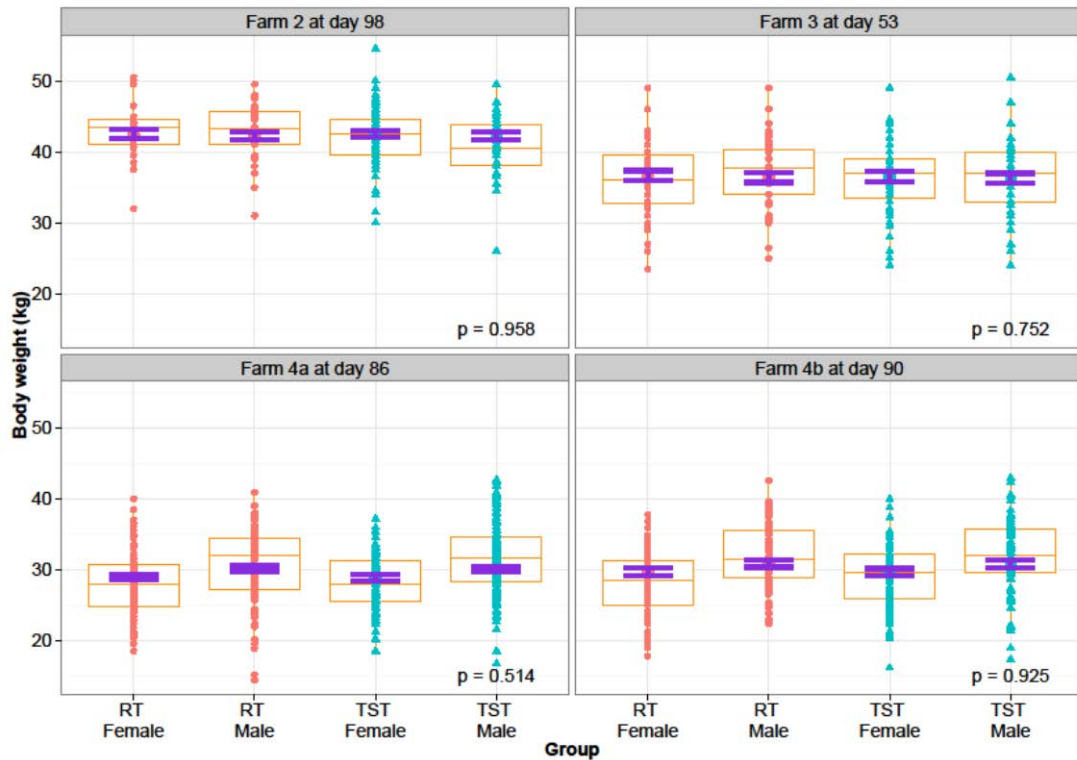
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705 Figure 1: Observed body weights of female and male lambs of Routine Treatment  
 706 (RT; in circle) and Targeted Selective Treatment (TST; in triangle) groups recorded  
 707 at the end of the trial in an experimental farm (farm 1 in the text)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

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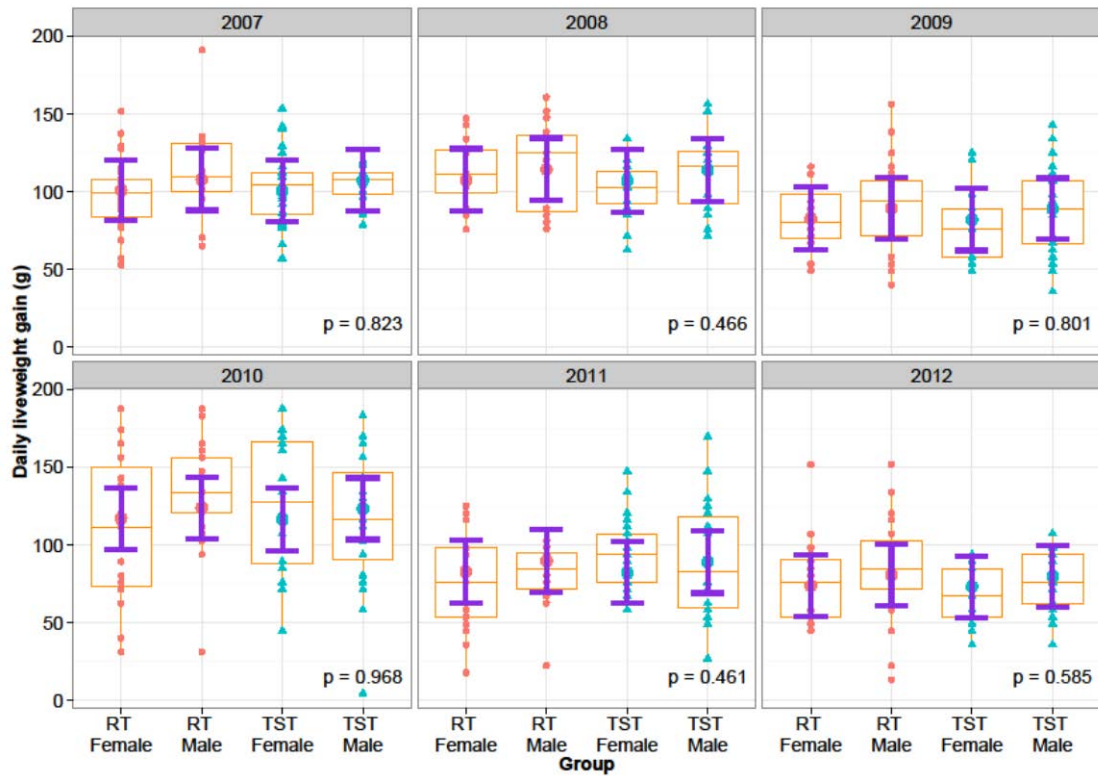
718 Figure 2: Observed body weights of female and male lambs of Routine Treatment  
 719 (RT; in circle) and Targeted Selective Treatment (TST; in triangle) groups recorded  
 720 at the end of the trial in three commercial farms (farms 2, 3, 4a, 4b), along with the  
 721 mean body weights (large circle)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

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

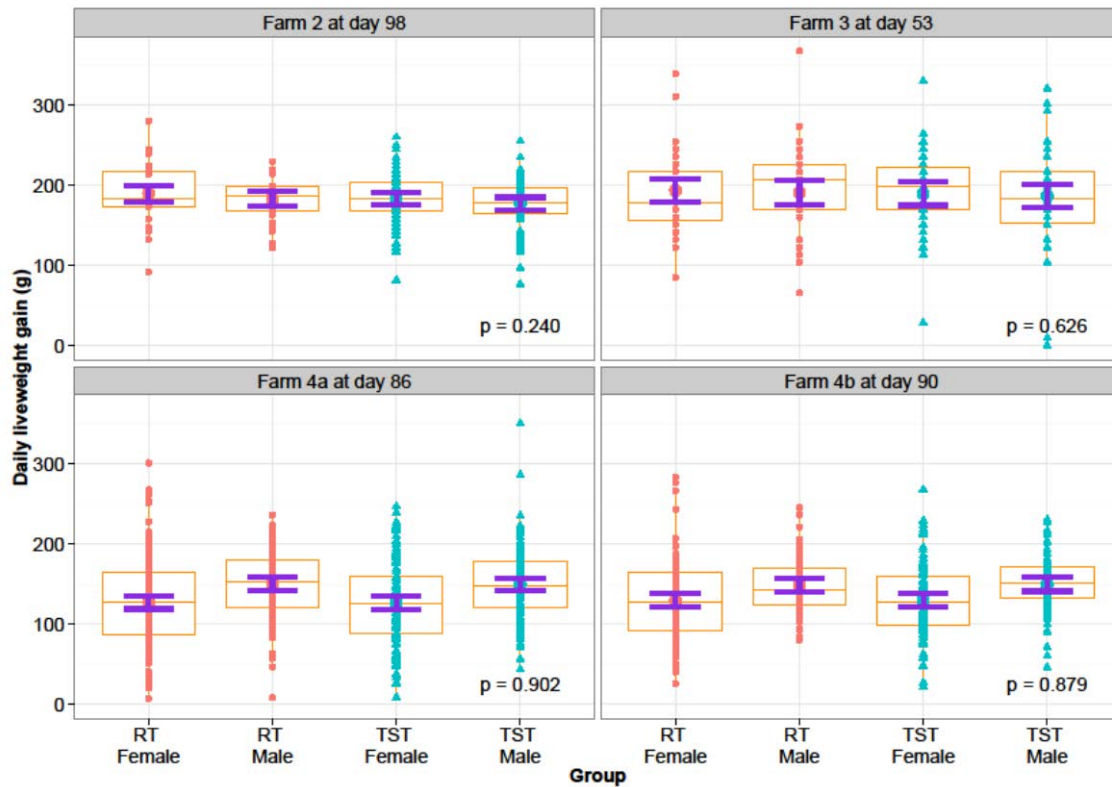
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743 Figure 4: Observed daily liveweight gain of female and male lambs of Routine  
 744 Treatment (RT; in circle) and Targeted Selective Treatment (TST; in triangle) groups  
 745 during the period of the trial in three commercial farms (Farms 2, 3,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

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751 Conflict of interest:

752 All authors declare to have no conflicts of interest regarding the information provided  
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754

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