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1 Targeted anthelmintic treatment of parasitic gastroenteritis in first
2 grazing season dairy calves using daily live weight gain as an indicator

3
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20
21 **ABSTRACT**

22
23 Control of parasitic gastroenteritis in cattle is typically based on group
24 treatments with ~~appropriate~~ anthelmintics, complemented by grazing
25 management, where feasible. However, the almost inevitable evolution of

26 resistance in parasitic nematodes to anthelmintics over time necessitates a
27 reappraisal of their use in order to reduce selection pressure. One such
28 approach is targeted selective treatment (TST), in which only individual
29 animals that will most benefit are treated, rather than whole groups of at-
30 risk cattle. This study was designed to assess the feasibility of implementing
31 TST on three commercial farms, two of which were organic. A total of 104
32 first-grazing season (FGS), weaned dairy calves were enrolled in the study;
33 ~~each was. All animals were~~ weighed at monthly intervals from the start of
34 the grazing season using scales or weigh-bands. ~~A;~~ at the same time dung
35 and blood samples were collected in order to measure faecal egg counts
36 (FEC) and plasma pepsinogen, respectively. A pre-determined threshold
37 weight gain of ~~less than~~ 0.75 kg/day was used to determine those animals
38 that would be treated; ~~t.~~ The anthelmintic used was eprinomectin, ~~which~~
39 ~~has persistent efficacy of 3 weeks against *Cooperia oncophora* and 4 weeks~~
40 ~~against *Ostertagia ostertagi*.~~ No individual animal received more than one
41 treatment during the grazing season and all treatments were given in July
42 or August; five animals were not treated at all because their growth rates
43 consistently exceeded the threshold. Mean daily live weight gain over the
44 entire grazing season ranged between 0.69 and 0.82 kg/day on the three
45 farms. ~~On the two organic farms, these growth rates exceeded those~~
46 ~~recorded during the preceding grazing season.~~ Neither FEC nor pepsinogen
47 values were significantly associated with live weight gain ~~and therefore are~~
48 ~~unsuitable markers for performance-based TST.~~ Implementation of TST at
49 farm level requires regular (monthly) handling of the animals and the use of
50 weigh scales or tape, but can be integrated into farm management

51 practices. This study has shown that acceptable growth rates can be
52 achieved in ~~young~~ FGS cattle with modest levels of treatment and
53 correspondingly less exposure of their nematode populations to
54 anthelmintics, which should mitigate selection pressure for resistance by
55 increasing the size of the refugia in ~~the~~ both hosts and ~~on~~ pasture.

56

57 Key words: Targeted selective treatment, TST, parasitic gastroenteritis,
58 PGE, cattle, eprinomectin, ~~organic~~

59

60 1. INTRODUCTION

61 ~~The spectre of a~~ Anthelmintic resistance (AR) ~~hangs like a malevolent cloud~~
62 ~~over many popular methods of parasite control and consequently resistance~~
63 has become a major driver for parasitology research and in tailoring advice
64 on parasite control ~~to farmers~~. In northern temperate Europe there are
65 currently only three classes of anthelmintic that are licensed for the control
66 of parasitic gastroenteritis (PGE) in cattle: benzimidazoles,
67 tetrahydropyrimidines (levamisole)s and macrocyclic lactones (MLs), none of
68 which are available in combination with each other. The most commonly
69 reported cases of resistance in bovine nematode parasites in Europe have
70 been in *Cooperia* species, in which the efficacy of MLs has been shown to be
71 sub-optimal (Geurden et al., 2015). Given that *Cooperia* spp. are ~~commonly~~
72 dose-limiting in for the several MLs (Vercruysse and Rew, 2002), accurate
73 weighing of animals and ~~dose~~ administration of the correct dose is essential
74 for efficacy and reports of resistance in which these basic criteria have not
75 be fulfilled should be treated circumspectly. In addition there is some

76 evidence for ML-resistant *Ostertagia ostertagi* in Europe, which has also
77 been observed in other regions of the world (Sutherland and Leathwick,
78 2011; Waghorn et al., 2016). For these reasons it is paramount that
79 practices that reduce selection pressure for resistance and conserve the
80 longevity of the current array of cattle anthelmintics are adopted.

81

82 In New Zealand, the emergence of ML-resistant *Cooperia* was associated
83 with high frequency (every 3-4 weeks) administration over periods of six
84 months or longer each year in young cattle grazed intensively (Jackson et
85 al., 2006). There is little evidence for similar use patterns in Europe, where
86 specific risk factors for AR in cattle have not been determined. Early season
87 strategic anthelmintic treatments have been well established in Europe and
88 shown to provide effective control of parasitic gastroenteritis (PGE)
89 particularly in set-stocked, weaned first grazing season (FGS) cattle (Shaw
90 et al., 1998), but also in the second year at grass (Taylor et al., 1995). The
91 primary objective of strategic approaches is to limit concentrations of
92 infective larvae in the herbage throughout the grazing season by minimising
93 worm egg output and ~~autore~~-infection, so strategic treatments create low
94 challenge pastures with correspondingly low refugia; this has the potential
95 to increase the speed of selection for anthelmintic resistance (Martin et al.,
96 1981).

97

98 Irrespective of the possible risk factors for AR in cattle nematodes,
99 practices that reduce anthelmintic usage are likely to limit selection
100 pressure on parasite populations. One such approach is targeted selective

101 treatment (TST) in which, rather than the more typical, synchronous group
102 anthelmintic treatments, individual animals are treated on the basis of a
103 marker or markers that indicate that they will benefit from removal of their
104 parasite burdens. Targeted selective anthelmintic treatments (TST) were
105 initially studied in small ruminants (Kenyon et al., 2009), in which proof of
106 concept was demonstrated insofar as disease control and animal
107 performance could be maintained with TST at a level comparable to that
108 seen in animals that were treated more intensively. Equally important was
109 the demonstration that TST applied over successive years led to lower
110 selection for resistance compared to that in lambs treated at 4-week
111 intervals over the grazing season (Kenyon et al., 2013).

112

113 There is limited published literature regarding the use of performance-
114 based TST approaches in cattle in the field (Charlier et al., 2014; Kenyon
115 and Jackson, 2012). Analysis of published trial data using reporter operating
116 curve (ROC) analysis suggested that an appropriate threshold for daily live
117 weight gain (DLWG) in a TST regime in young cattle would be 0.75 kg/day
118 (Hoglund et al., 2009). This figure coincides with growth rates that are
119 required for replacement dairy heifers to reach minimal breeding weight at
120 15 months in order to calve at two years of age (Froidmont et al., 2013;
121 Zanton and Heinrichs, 2005), ~~thus, DLWGs of ~0.75kg are consistent with~~
122 ~~commercial targets and farmer aspirations~~. Weight-gain based TST
123 approaches have provided similar results to those reported in sheep, that is
124 to say acceptable weight gains have been maintained and the number of
125 anthelmintic treatments has been reduced compared to routine, whole

126 group treatments (Greer et al., 2010; Hoglund et al., 2013; McAnulty et al.,
127 2011). It should be noted that to date, TST has only been shown to be
128 effective in the management of PGE, furthermore, if, for example,
129 lungworm (*Dictyoacaulus viviparus*) is present and has not been controlled
130 through vaccination, then parasitic bronchitis can thwart efforts to control
131 PGE through TST (O'Shaughnessy et al., 2015).

132

133 A series of studies were conducted to extend the scientific evidence base
134 for TST in cattle and to determine its on-farm feasibility (Jackson, 2012).
135 Included in this work was an assessment of various biomarkers as potential
136 indicators for TST, an evaluation of the accuracy and utility of weigh bands
137 for farms that do not have access to weigh scales and implementation of a
138 weight gain-based TST. The objective of the study described in this paper
139 was to determine the feasibility of a weight-gain based TST in first season
140 dairy-bred calves on three livestock farms, two of which were organic.

141

142 2. MATERIALS AND METHODS

143

144 This TST study was approved by the Ethics and Welfare Committee of the
145 School of Veterinary Medicine, University of Glasgow.

146

147 2.1. Participating Farms

148 Three dairy farms located in central and south-west Scotland were recruited
149 into the study: two organic and one conventional (Farm O1, Farm O2 and
150 Farm C3). The three farms were a sub-set of the six farms that were

151 involved in a monitoring study of gastrointestinal parasitism the previous
152 year (Jackson, 2012).

153

154 2.1.1 Organic Farm 1 (O1)

155 Organic dairy farm 1 comprised a mixed breed milking herd, predominantly
156 of Friesians and Ayrshires, with some Brown Swiss and Jersey crosses,
157 calving all-year-round and grazing over 93 hectares (ha) of semi-improved
158 grassland from April to October. All FGS cattle in the study were vaccinated
159 against lungworm prior to turnout in late April, when the calves grazed a
160 small paddock near the farm and were given supplementary feed. Two
161 weeks later the calves were moved onto another pasture and subsequently
162 were rotated every two weeks around seven different paddocks in an
163 extensive grazing system. The previous year these fields were grazed by
164 FGS, second season grazers (SGS) or adult dairy cattle.

165

166 In the year prior to the TST study, faecal egg counts (FEC) were taken in
167 June and September and only calves with a FEC of ≥ 200 eggs per gram (epg)
168 were treated with fenbendazole (Panacur[®] 10% oral suspension, MSD). The
169 farmer had used this method of anthelmintic treatment over the previous
170 two grazing seasons. The average DLWG in FGS calves during the year that
171 preceded the TST study was 0.46 kg/day.

172

173 2.1.2. Organic Farm 2 (O2)

174 Organic dairy farm 2 covered 344 ha which supported a milking herd of 135
175 Ayrshire and Ayrshire cross cows; some Aberdeen Angus suckler cows and

176 sheep were also kept on the farm. Approximately forty per cent of the dairy
177 herd calved between November and December, the rest calved year-round;
178 heifers calved between February and April. The FGS were turned out in
179 early May as a group of sixty calves, which were rotationally grazed over
180 three fields, each of ~20 ha. The year before the TST study, based on faecal
181 egg counts, all FGS were treated with fenbendazole drench in mid-July; the
182 treatment was repeated again at housing in late November. The average
183 DLWG in FGS calves during the year that preceded the TST study was 0.57
184 kg/day.

185

186 2.1.3. Conventional Farm 3 (C3)

187 The conventional dairy farm milked a herd of eighty five Holstein-Friesian
188 cows and there were also beef and sheep enterprises on the farm. Calving in
189 the dairy herd was year round and both heifer replacements and beef x
190 dairy calves were grazed together. The previous year, the FGS animals were
191 not turned out until mid-July because herbage regrowth after early sheep
192 grazing was insufficient; they were set-stocked on four hectares of land and
193 treated with moxidectin injection (Cydectintm 10%, Zoetis) at turnout. The
194 average DLWG in FGS calves during the year that preceded the TST study
195 was 0.93 kg/day.

196

197 2.2 Experimental Animals

198

199 All first season grazers (FGS) on-farm were included in the study (Farm O1 n
200 = 20, Farm O2 n = 41, Farm C3 n = 43). All animals on Farms O1 and C3 were

201 vaccinated against *D. viviparus* (Bovilis Huskvac™, MSD) before turnout to
202 control lungworm disease.

203

204 2.3. Experimental Design

205

206 Farms were visited in late April and early May 2010, just prior to turnout
207 from housing onto pasture and then at 28-day intervals until housing in the
208 autumn, except for September, when two of the farmers were unable to
209 gather the cattle because of other farming activities. At visit 1 on all farms,
210 each FGS animal had its live weight calculated by weigh-band (Coburn®
211 weigh tape). On Farm C3, all FGS were also weighed on Ritchie® mechanical
212 weigh-scales. At visit 3 in July, eight to ten weeks post-turnout, the girth of
213 all FGS calves were measured using the weigh-band and their live weight
214 gain from turnout calculated. If the live weight gain of an individual animal
215 was < 0.75 kg/day they were treated with eprinomectin (Eprinex™ pour-on,
216 Merial). At visit 4 in August, the live weight gain of the FGS over the
217 previous four weeks was calculated. Animals that had not been treated
218 previously and were growing < 0.75 kg/day were treated with eprinomectin.

219

220 Because eEprinomectin has persistent activity of twenty-eight days against
221 *O. ostertagi* and 21 days against *C. oncophora* (Cramer et al., 2000), ~~the~~
222 ~~two most common species contributing to PGE in FGS in northern Europe.~~
223 ~~Thus, following treatment, FECs would be expected to be minimal for 6-7~~
224 ~~weeks, this being the sum of persistent activity and a typical pre-patent~~
225 ~~period of ~3 weeks for *O. ostertagi* and *C. oncophora*. For this reason,~~

226 animals previously treated at visit 3 were not treated again at visit 4,
227 irrespective of their DLWG in the interim, as this would have meant treating
228 within the effective pre-patent period and this can potentially exert a high
229 selection pressure for AR. As farmers had requested a month off from
230 sampling in September on farms O1 and O2, no treatments were given on
231 this visit (5) on Farm C3. No treatment was planned for visit 6 at housing.

232

233 2.3.1. Laboratory Analysis

234

235 Each calf had a blood sample taken by jugular or coccygeal venepuncture
236 into an EDTA tube for serum pepsinogen analysis (all visits) and a faecal
237 sample taken *per rectum* obtained at visits 2, 3, 4, 5 and 6 for faecal egg
238 count, lungworm and liver fluke monitoring. Larval culture was performed
239 on faeces collected during visit 3. Further details of the standard laboratory
240 techniques used can be found in a ~~companion~~previously published paper
241 (Ellis et al., 2011).

242

243 2.3.2. Statistical Analysis

244

245 The Spearman's rank correlation test was used on non-normally distributed
246 data to investigate any associations with live weight gain. Statistical analysis
247 of the data was performed using Excel, Minitab 16 for Windows and SAS
248 University edition (SAS Institute, Cary, N. Carolina). The association of
249 bodyweight or growth rate with faecal egg count (FEC) or pepsinogenaemia
250 (Pep) was assessed by repeated measures variance analysis. The proc mixed

251 procedure in SAS was used and the model fitted the effects of farm, sample
252 date, test variable (FEC or Pep) and the interaction between sample date
253 and test variable. Several variance structures were tested including
254 unstructured, compound symmetry and heterogeneous autoregressive of
255 order 1. The best fitting model was chosen using four criteria: residual log
256 likelihood, Akaike's information criterion (AIC), the finite-population
257 corrected AIC and Bayes Information criterion (BIC). For both faecal egg
258 count and plasma pepsinogen concentration, a heterogeneous
259 autoregressive structure provided the best fit.

260

261 3. RESULTS

262

263 3.1. Live weight Gain

264 Mean live weight gains (\pm Standard Deviation) over the grazing season for all
265 FGS animals in the study were:

- 266 • Farm O1 0.69 ± 0.28 kg/day (weighband)
- 267 • Farm O2 0.82 ± 0.13 kg/day (weighband)
- 268 • Farm C3 0.75 ± 0.23 kg/day (weigh scale)

269 The cattle on the conventional farm were heavier (277 kg) at turnout than
270 those on the organic farms (190 and 167 kg), but the growth curves of cattle
271 on all three farms were similar and DLWG was distributed normally amongst
272 all the animals (Figure 1).

273

274 3.2. Faecal Egg Count

275 ~~No results are available from t~~The faecal samples taken from the cattle on
276 the organic farms on visit 6 ~~as they were stored incorrectly~~poiled after
277 ~~collection in the laboratory~~. The majority of faecal egg counts on all farms
278 over the grazing season were less than 200 epg (Figure 2), though at the
279 July sampling a peak individual count of 1200 epg was observed on one of
280 the organic farms (O1). There were significant differences among the farms
281 ($p=0.007$). Consistent with results on the same farms sampled the previous
282 year, faecal egg counts showed no significant association with growth rate
283 ($p=0.605$) and there was no interaction between FEC and sample date
284 ($p=0.177$).

285

286 3.3 Larval Culture

287 ~~Using standard techniques and keys~~ (MAFF, 1986; van Wyk et al., 2004),
288 ~~Larval culture and speciation identification~~ was undertaken on dung
289 samples collected at visit 3 in July, corresponding to the middle of the
290 grazing season before anthelmintic treatment. The results are tabulated in
291 Table 1. The majority of larvae cultured were *C. oncophora*, the remainder
292 were *O. ostertagi*.

293

294 3.4. Pepsinogen

295 Plasma pepsinogen concentrations were at baseline on visit 1 prior to
296 turnout; thereafter concentrations increased on all farms over the grazing
297 season, though the majority of values remained at ≤ 2 IU (Figure 3). The
298 differences among farms in the mean pepsinogen response were not
299 significant ($p=0.051$), although cattle farm O1 had high plasma pepsinogen

300 concentrations at housing (3.2 ± 1.7 iu/l). Consistent with results on the
301 same farms sampled the previous year, plasma pepsinogen concentrations
302 showed no association with growth rate ($p=0.409$) and there was no
303 interaction between pepsinogen and sample date ($p=0.131$).

304

305 3.5. Targeted Selective Anthelmintic Treatment

306 None of the animals on any farm were treated more than once over the
307 grazing season; all the treatments were administered in either July or
308 August according to individual DLWG over the preceding 28 days.

- 309 • Farm O1 18 in July; 1 in August; 1 animal not treated at all
- 310 • Farm O2 29 in July; 8 in August; 4 animals not treated at all
- 311 • Farm C3 18 in July; 25 in August

312

313 ~~5.4.~~ DISCUSSION

314

315 The basic premise for DLWG-based TST is that, providing nutrition is not
316 limiting and that no other identifiable causes of ill-health are present, then
317 the individual growth rate of weaned calves (or lambs) at pasture is linearly
318 and consistently related to the impact of gastrointestinal parasitism (Greer
319 et al., 2009) through its effect on appetite, feed intake, protein metabolism
320 and nutrient partitioning (Forbes et al., 2000; Fox, 1997). In ~~order to~~
321 ~~incorporate the quality and quantity of the herbage available into the~~
322 ~~implementation of TST, in~~ sheep systems an algorithm named the Happy
323 FactorTM has been developed (Greer et al., 2009), ~~which. This~~ adjusts the
324 target DLWG to the availability and quality of the herbage. This approach

325 has not yet been used in cattle TST, where the assessment of pasture is
326 typically undertaken either subjectively by observation, or quantitatively
327 through the use of standard techniques to measurements of herbage mass
328 and/or sward height (Lambert et al., 2004). Individual DLWG alone was used
329 as the determinant for treatment in this study, though samples were also
330 taken for parasitological examination in order to gain further knowledge of
331 their interrelationships.

332

333 ~~5.1. Biomarkers~~

334

~~335 Faecal egg counts and plasma pepsinogen concentrations were analysed
336 throughout the grazing season and an evaluation of their correlation with
337 live weight gain was undertaken as both have been advocated for use in
338 targeted selective anthelmintic regimes (Charlier et al., 2014).~~

339

340 ~~5.1.1. Faecal Egg Counts~~

341 As in the preceding year (Jackson, 2012), there were no significant
342 associations between FEC and DLWG. This result is not surprising, given that
343 FECs in young cattle in temperate regions with an *Ostertagia/Cooperia*
344 dominant nematode fauna, whether in experimental infections or under
345 field conditions, have shown no consistent or linear relationship with worm
346 burdens or animal performance (Brunsdon, 1969, 1971; Michel, 1969).

347

348 An analysis was performed of the number of calves that would have been
349 treated with anthelmintic at visit 3 if FECs were used as an indicator using

350 an arbitrary threshold of ≥ 250 epg. The results show only ten FGS had FEC of
351 ≥ 250 epg, all on Farm O1. Overall, 54 calves, growing < 0.75 kg/day would
352 not have been treated with anthelmintic had FEC been used as an indicator.

353

354 | ~~5.1.2 Larval culture~~

355 | *Cooperia* spp. larvae predominated in the faecal cultures conducted in July,
356 | but these results do not necessarily reflect the worm burdens in the animals
357 | at the time (Brunsdon, 1968, 1971). The results of the pepsinogen assays
358 | suggest that *O. ostertagi* ~~nematodes-waswere~~ having a greater impact over
359 | the second half of the grazing season.

360

361 | ~~5.1.3 Pepsinogen~~

362 | Consistent with results from the preceding year (Jackson, 2012), there were
363 | no significant correlations between plasma pepsinogen concentrations and
364 | DLWG. Pepsinogen provides a direct measure of abomasal dysfunction and is
365 | closely associated with abomasal pathology and intra-luminal *O. ostertagi*
366 | populations (Michel et al., 1978). It is perhaps surprising that it is not more
367 | closely correlated with growth rate, but this ~~h~~was also been observed in
368 | other field studies in temperate regions (Brunsdon, 1969, 1971, 1972) and
369 | may be due to co-infection with the intestinal species of *Cooperia* in FGS
370 | calves, which can also impact growth rate, singly (Armour et al., 1987) or in
371 | combination with *O. ostertagi* (Parkins et al., 1990), but *Cooperia* spp. do
372 | not typically provoke an increase in pepsinogen.

373

374 | ~~4.5.2. Performance-based Targeted Selective Anthelmintic Treatment~~

375 | ~~5.2.1. Growth rate~~

376 | The current trial was primarily a feasibility study for TST on commercial
377 | farms, so ~~there are~~ no contemporary comparisons were possible, however
378 | cattle growth rates from the previous year are available for each farm and
379 | these provide a basis on which to assess the impact of TST. Despite some
380 | concurrent (non-parasitic) respiratory disease, the mean growth rate of the
381 | FGS cattle on the conventional farm C3 was ≥ 0.75 kg/day over the grazing
382 | season, which was the target, though less than the previous year when,
383 | using a long-acting anthelmintic and over a shortened grazing season, the
384 | growth rate was 0.93 kg/day. On the organic farm O2 the average growth
385 | rate under the TST regimen exceeded 0.75 kg/day and this was considerably
386 | higher than in the previous year (0.57 kg/day). Although the growth rate on
387 | organic farm O1 was less than target, at 0.69 kg/day it was again higher
388 | than that of the previous grazing season when it was 0.46 kg/day. On
389 | neither of the organic farms were there any major changes in nutritional or
390 | grazing management between years.

391

392 | ~~5.2.2. Anthelmintic use~~

393 | The number of animals treated (all) on the conventional farm was the same
394 | using TST as it was the previous year, but the potential exposure to
395 | discriminating doses of anthelmintic was reduced with TST through the
396 | asynchronous, mid/late season administration of eprinomectin, which has
397 | persistent activity of 28 days against *O. ostertagi*, compared to moxidectin
398 | 10%, which has 120 days of persistent activity against this species. On
399 | organic farm O2, all FGS calves were treated once in July the previous year

400 with fenbendazole, which has no persistent activity, whereas under the TST
401 regimen, all bar four animals were treated in July or August, with
402 eprinomectin, so arguably ~~the anthelmintic~~ selection pressure could have
403 increased under TST. Similarly, on organic farm O1, only two calves were
404 treated the previous year with fenbendazole, while 19/20 animals were
405 treated with eprinomectin under TST, however, on both organic farms, the
406 FGS growth rates were higher under the TST regime.

407

408 In order to assess the effect of TST in satisfying the joint objectives of
409 achieving satisfactory growth rates while limiting selection pressure for
410 anthelmintic resistance, modellers have introduced a factor named ‘benefit
411 per R’, abbreviated to BPR (Laurenson et al., 2016). This is calculated from
412 a ratio between the average weight gain benefit (AWGB) arising from
413 whatever control measures have been used and the increase in anthelmintic
414 resistance allele frequency (IRAF) under that system; both are calculated
415 over the duration of the grazing season. This approach was used initially in
416 sheep and has subsequently extrapolated to cattle (Berk et al., 2016), in
417 which it was shown that the use of a DLWG threshold as an indicator for
418 anthelmintic treatments in TST was the approach that optimised BPR.

419

420 4.5.3. Concluding remarks

421

422 Applying a performance-based TST in the field was shown to be feasible
423 through the use of weigh bands, albeit this measurement requires adequate
424 restraint of animals. Gathering and handling young stock can be a critical

425 factor in commercial dairy herds, where replacement heifers are often
426 grazed on pastures away from the main farm and where handling facilities
427 may be rudimentary and inadequate for monthly individual animal
428 assessments. Wider adoption of some of the technologies that are already
429 used by some sheep farmers, such as electronic identification (EID), weigh-
430 scales with integrated software and automatic shedding gates (McBean et
431 al., 2016) would all facilitate the adoption of TST in cattle. Faecal egg
432 count and plasma pepsinogen concentration were found to have no
433 significant association with live weight gain and showed high levels of
434 variability amongst individuals within the management groups, so cannot be
435 recommended if one of the primary objectives for parasite control in
436 youngstock is to maintain growth rates that are commensurate with farm
437 objectives and industry standards.

438

439 On the organic farms, where anthelmintic treatment was already minimal,
440 DLWG was increased compared to the previous grazing season to rates that
441 are considered to be more compatible with optimum life-time performance
442 in heifer replacements (Wathes et al., 2014). Although organic principles
443 eschew the priority of performance in medication decisions, poor growth is
444 virtually a universal indicator of illness in young animals, commonly through
445 mechanisms that include anorexia (Exton, 1997; Hart, 1990), then it seems
446 that monitoring DLWG should be compatible with the organic ethos in
447 promoting animal welfare.

448

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454

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611 **Tables**

612

613 Table 1. Percentage of *O. ostertagi* and *C. oncophora* larvae cultured from
614 faecal samples collected pre-treatment in July (visit 3) on each farm.

615

616 **Figures**

617

618 • Figure 1. Normal distribution (Kolmogorov-Smirnov test $p > 0.150$) of
619 live weights of animals throughout study.

620 • Figure 2. Skewed distribution (Kolmogorov-Smirnov test $p < 0.01$) of
621 individual faecal egg counts (FEC) throughout study.

622 • Figure 3. Skewed distribution (Kolmogorov-Smirnov test $p < 0.01$) of
623 individual plasma pepsinogen (PEP) throughout study.

624

1 **Targeted anthelmintic treatment of parasitic gastroenteritis in first**
2 **grazing season dairy calves using daily live weight gain as an indicator**

3

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20

21 **ABSTRACT**

22

23 Control of parasitic gastroenteritis in cattle is typically based on group
24 treatments with anthelmintics, complemented by grazing management,
25 where feasible. However, the almost inevitable evolution of resistance in

26 parasitic nematodes to anthelmintics over time necessitates a reappraisal of
27 their use in order to reduce selection pressure. One such approach is
28 targeted selective treatment (TST), in which only individual animals that
29 will most benefit are treated, rather than whole groups of at-risk cattle.
30 This study was designed to assess the feasibility of implementing TST on
31 three commercial farms, two of which were organic. A total of 104 first-
32 grazing season (FGS), weaned dairy calves were enrolled in the study; each
33 was weighed at monthly intervals from the start of the grazing season using
34 scales or weigh-bands. At the same time dung and blood samples were
35 collected in order to measure faecal egg counts (FEC) and plasma
36 pepsinogen, respectively. A pre-determined threshold weight gain of 0.75
37 kg/day was used to determine those animals that would be treated; the
38 anthelmintic used was eprinomectin. No individual animal received more
39 than one treatment during the grazing season and all treatments were
40 given in July or August; five animals were not treated at all because their
41 growth rates consistently exceeded the threshold. Mean daily live weight
42 gain over the entire grazing season ranged between 0.69 and 0.82 kg/day on
43 the three farms. Neither FEC nor pepsinogen values were significantly
44 associated with live weight gain. Implementation of TST at farm level
45 requires regular (monthly) handling of the animals and the use of weigh
46 scales or tape, but can be integrated into farm management practices. This
47 study has shown that acceptable growth rates can be achieved in FGS cattle
48 with modest levels of treatment and correspondingly less exposure of their
49 nematode populations to anthelmintics, which should mitigate selection

50 pressure for resistance by increasing the size of the refugia in both hosts
51 and pasture.

52

53 Key words: Targeted selective treatment, TST, parasitic gastroenteritis,
54 PGE, cattle, eprinomectin,

55

56 1. INTRODUCTION

57 Anthelmintic resistance (AR) has become a major driver for parasitology
58 research and in tailoring advice on parasite control. In northern temperate
59 Europe there are currently only three classes of anthelmintic that are
60 licensed for the control of parasitic gastroenteritis (PGE) in cattle:
61 benzimidazoles, tetrahydropyrimidines (levamisole) and macrocyclic
62 lactones (MLs), none of which are available in combination with each other.
63 The most commonly reported cases of resistance in bovine nematode
64 parasites in Europe have been in *Cooperia* species, in which the efficacy of
65 MLs has been shown to be sub-optimal (Geurden et al., 2015). Given that
66 *Cooperia* spp. are dose-limiting for several MLs (Vercruyssen and Rew, 2002),
67 accurate weighing of animals and administration of the correct dose is
68 essential for efficacy and reports of resistance in which these basic criteria
69 have not been fulfilled should be treated circumspectly. In addition there is
70 some evidence for ML-resistant *Ostertagia ostertagi* in Europe, which has
71 also been observed in other regions of the world (Sutherland and Leathwick,
72 2011; Waghorn et al., 2016). For these reasons it is paramount that
73 practices that reduce selection pressure for resistance and conserve the
74 longevity of the current array of cattle anthelmintics are adopted.

75

76 In New Zealand, the emergence of ML-resistant *Cooperia* was associated
77 with high frequency (every 3-4 weeks) administration over periods of six
78 months or longer each year in young cattle grazed intensively (Jackson et
79 al., 2006). There is little evidence for similar use patterns in Europe, where
80 specific risk factors for AR in cattle have not been determined. Early season
81 strategic anthelmintic treatments have been well established in Europe and
82 shown to provide effective control of parasitic gastroenteritis (PGE)
83 particularly in set-stocked, weaned first grazing season (FGS) cattle (Shaw
84 et al., 1998), but also in the second year at grass (Taylor et al., 1995). The
85 primary objective of strategic approaches is to limit concentrations of
86 infective larvae in the herbage throughout the grazing season by minimising
87 worm egg output and re-infection, so strategic treatments create low
88 challenge pastures with correspondingly low refugia; this has the potential
89 to increase the speed of selection for anthelmintic resistance (Martin et al.,
90 1981).

91

92 Irrespective of the possible risk factors for AR in cattle nematodes,
93 practices that reduce anthelmintic usage are likely to limit selection
94 pressure on parasite populations. One such approach is targeted selective
95 treatment (TST) in which, rather than the more typical, synchronous group
96 anthelmintic treatments, individual animals are treated on the basis of a
97 marker or markers that indicate that they will benefit from removal of their
98 parasite burdens. Targeted selective anthelmintic treatments (TST) were
99 initially studied in small ruminants (Kenyon et al., 2009), in which proof of

100 concept was demonstrated insofar as disease control and animal
101 performance could be maintained with TST at a level comparable to that
102 seen in animals that were treated more intensively. Equally important was
103 the demonstration that TST applied over successive years led to lower
104 selection for resistance compared to that in lambs treated at 4-week
105 intervals over the grazing season (Kenyon et al., 2013).

106

107 There is limited published literature regarding the use of performance-
108 based TST approaches in cattle in the field (Charlier et al., 2014; Kenyon
109 and Jackson, 2012). Analysis of published trial data using receiver operating
110 curve (ROC) analysis suggested that an appropriate threshold for daily live
111 weight gain (DLWG) in a TST regime in young cattle would be 0.75 kg/day
112 (Hoglund et al., 2009). This figure coincides with growth rates that are
113 required for replacement dairy heifers to reach minimal breeding weight at
114 15 months in order to calve at two years of age (Froidmont et al., 2013;
115 Zanton and Heinrichs, 2005). Weight-gain based TST approaches have
116 provided similar results to those reported in sheep, that is to say acceptable
117 weight gains have been maintained and the number of anthelmintic
118 treatments has been reduced compared to routine, whole group treatments
119 (Greer et al., 2010; Hoglund et al., 2013; McNulty et al., 2011). It should
120 be noted that to date, TST has only been shown to be effective in the
121 management of PGE, furthermore, if, for example, lungworm (*Dictyocaulus*
122 *viviparus*) is present and has not been controlled through vaccination, then
123 parasitic bronchitis can thwart efforts to control PGE through TST
124 (O'Shaughnessy et al., 2015).

125

126 A series of studies were conducted to extend the scientific evidence base
127 for TST in cattle and to determine its on-farm feasibility (Jackson, 2012).
128 Included in this work was an assessment of various biomarkers as potential
129 indicators for TST, an evaluation of the accuracy and utility of weigh bands
130 for farms that do not have access to weigh scales and implementation of a
131 weight gain-based TST. The objective of the study described in this paper
132 was to determine the feasibility of a weight-gain based TST in first season
133 dairy-bred calves on three livestock farms, two of which were organic.

134

135 2. MATERIALS AND METHODS

136

137 This TST study was approved by the Ethics and Welfare Committee of the
138 School of Veterinary Medicine, University of Glasgow.

139

140 2.1. Participating Farms

141 Three dairy farms located in central and south-west Scotland were recruited
142 into the study: two organic and one conventional (Farm O1, Farm O2 and
143 Farm C3). The three farms were a sub-set of the six farms that were
144 involved in a monitoring study of gastrointestinal parasitism the previous
145 year (Jackson, 2012).

146

147 2.1.1 Organic Farm 1 (O1)

148 Organic dairy farm 1 comprised a mixed breed milking herd, predominantly
149 of Friesians and Ayrshires, with some Brown Swiss and Jersey crosses,

150 calving all-year-round and grazing over 93 hectares (ha) of semi-improved
151 grassland from April to October. All FGS cattle in the study were vaccinated
152 against lungworm prior to turnout in late April, when the calves grazed a
153 small paddock near the farm and were given supplementary feed. Two
154 weeks later the calves were moved onto another pasture and subsequently
155 were rotated every two weeks around seven different paddocks in an
156 extensive grazing system. The previous year these fields were grazed by
157 FGS, second season grazers (SGS) or adult dairy cattle.

158

159 In the year prior to the TST study, faecal egg counts (FEC) were taken in
160 June and September and only calves with a FEC of ≥ 200 eggs per gram (epg)
161 were treated with fenbendazole (Panacur[®] 10% oral suspension, MSD). The
162 farmer had used this method of anthelmintic treatment over the previous
163 two grazing seasons. The average DLWG in FGS calves during the year that
164 preceded the TST study was 0.46 kg/day.

165

166 2.1.2. Organic Farm 2 (O2)

167 Organic dairy farm 2 covered 344 ha which supported a milking herd of 135
168 Ayrshire and Ayrshire cross cows; some Aberdeen Angus suckler cows and
169 sheep were also kept on the farm. Approximately forty per cent of the dairy
170 herd calved between November and December, the rest calved year-round;
171 heifers calved between February and April. The FGS were turned out in
172 early May as a group of sixty calves, which were rotationally grazed over
173 three fields, each of ~20 ha. The year before the TST study, based on faecal
174 egg counts, all FGS were treated with fenbendazole drench in mid-July; the

175 treatment was repeated again at housing in late November. The average
176 DLWG in FGS calves during the year that preceded the TST study was 0.57
177 kg/day.

178

179 2.1.3. Conventional Farm 3 (C3)

180 The conventional dairy farm milked a herd of eighty five Holstein-Friesian
181 cows and there were also beef and sheep enterprises on the farm. Calving in
182 the dairy herd was year round and both heifer replacements and beef x
183 dairy calves were grazed together. The previous year, the FGS animals were
184 not turned out until mid-July because herbage regrowth after early sheep
185 grazing was insufficient; they were set-stocked on four hectares of land and
186 treated with moxidectin injection (Cydectintm 10%, Zoetis) at turnout. The
187 average DLWG in FGS calves during the year that preceded the TST study
188 was 0.93 kg/day.

189

190 2.2 Experimental Animals

191

192 All first season grazers (FGS) on-farm were included in the study (Farm O1 n
193 = 20, Farm O2 n = 41, Farm C3 n = 43). All animals on Farms O1 and C3 were
194 vaccinated against *D. viviparus* (Bovilis HuskvacTM, MSD) before turnout to
195 control lungworm disease.

196

197 2.3. Experimental Design

198

199 Farms were visited in late April and early May 2010, just prior to turnout
200 from housing onto pasture and then at 28-day intervals until housing in the
201 autumn, except for September, when two of the farmers were unable to
202 gather the cattle because of other farming activities. At visit 1 on all farms,
203 each FGS animal had its live weight calculated by weigh-band (Coburn®
204 weigh tape). On Farm C3, all FGS were also weighed on Ritchie® mechanical
205 weigh-scales. At visit 3 in July, eight to ten weeks post-turnout, the girth of
206 all FGS calves were measured using the weigh-band and their live weight
207 gain from turnout calculated. If the live weight gain of an individual animal
208 was < 0.75 kg/day they were treated with eprinomectin (Eprinex™ pour-on,
209 Merial). At visit 4 in August, the live weight gain of the FGS over the
210 previous four weeks was calculated. Animals that had not been treated
211 previously and were growing < 0.75 kg/day were treated with eprinomectin.

212

213 Because eprinomectin has persistent activity of twenty-eight days against *O.*
214 *ostertagi* and 21 days against *C. oncophora* (Cramer et al., 2000), animals
215 previously treated at visit 3 were not treated again at visit 4, irrespective of
216 their DLWG in the interim, as this would have meant treating within the
217 effective pre-patent period and this can potentially exert a high selection
218 pressure for AR. As farmers had requested a month off from sampling in
219 September on farms O1 and O2, no treatments were given on this visit (5)
220 on Farm C3. No treatment was planned for visit 6 at housing.

221

222 2.3.1. Laboratory Analysis

223

224 Each calf had a blood sample taken by jugular or coccygeal venepuncture
225 into an EDTA tube for serum pepsinogen analysis (all visits) and a faecal
226 sample taken *per rectum* obtained at visits 2, 3, 4, 5 and 6 for faecal egg
227 count, lungworm and liver fluke monitoring. Larval culture was performed
228 on faeces collected during visit 3. Further details of the standard laboratory
229 techniques used can be found in a previously published paper (Ellis et al.,
230 2011).

231

232 2.3.2. Statistical Analysis

233

234 The Spearman's rank correlation test was used on non-normally distributed
235 data to investigate any associations with live weight gain. Statistical analysis
236 of the data was performed using Excel, Minitab 16 for Windows and SAS
237 University edition (SAS Institute, Cary, N. Carolina). The association of
238 bodyweight or growth rate with faecal egg count (FEC) or pepsinogaemia
239 (Pep) was assessed by repeated measures variance analysis. The proc mixed
240 procedure in SAS was used and the model fitted the effects of farm, sample
241 date, test variable (FEC or Pep) and the interaction between sample date
242 and test variable. Several variance structures were tested including
243 unstructured, compound symmetry and heterogeneous autoregressive of
244 order 1. The best fitting model was chosen using four criteria: residual log
245 likelihood, Akaike's information criterion (AIC), the finite-population
246 corrected AIC and Bayes Information criterion (BIC). For both faecal egg
247 count and plasma pepsinogen concentration, a heterogeneous
248 autoregressive structure provided the best fit.

249

250 3. RESULTS

251

252 3.1. Live weight Gain

253 Mean live weight gains (\pm Standard Deviation) over the grazing season for all
254 FGS animals in the study were:

- 255 • Farm O1 0.69 \pm 0.28 kg/day (weighband)
- 256 • Farm O2 0.82 \pm 0.13 kg/day (weighband)
- 257 • Farm C3 0.75 \pm 0.23 kg/day (weigh scale)

258 The cattle on the conventional farm were heavier (277 kg) at turnout than
259 those on the organic farms (190 and 167 kg), but the growth curves of cattle
260 on all three farms were similar and DLWG was distributed normally amongst
261 all the animals (Figure 1).

262

263 3.2. Faecal Egg Count

264 No results are available from the faecal samples taken from the cattle on
265 the organic farms on visit 6 as they were stored incorrectly after collection.

266 The majority of faecal egg counts on all farms over the grazing season were
267 less than 200 epg (Figure 2), though at the July sampling a peak individual
268 count of 1200 epg was observed on one of the organic farms (O1). There
269 were significant differences among the farms ($p=0.007$). Consistent with
270 results on the same farms sampled the previous year, faecal egg counts
271 showed no significant association with growth rate ($p=0.605$) and there was
272 no interaction between FEC and sample date ($p=0.177$).

273

274 3.3 Larval Culture

275 Using standard techniques and keys (MAFF, 1986; van Wyk et al., 2004),
276 larval culture and identification was undertaken on dung samples collected
277 at visit 3 in July, corresponding to the middle of the grazing season before
278 anthelmintic treatment. The results are tabulated in Table 1. The majority
279 of larvae cultured were *C. oncophora*, the remainder were *O. ostertagi*.

280

281 3.4. Pepsinogen

282 Plasma pepsinogen concentrations were at baseline on visit 1 prior to
283 turnout; thereafter concentrations increased on all farms over the grazing
284 season, though the majority of values remained at ≤ 2 IU (Figure 3). The
285 differences among farms in the mean pepsinogen response were not
286 significant ($p=0.051$), although cattle farm O1 had high plasma pepsinogen
287 concentrations at housing (3.2 ± 1.7 iu/l). Consistent with results on the
288 same farms sampled the previous year, plasma pepsinogen concentrations
289 showed no association with growth rate ($p=0.409$) and there was no
290 interaction between pepsinogen and sample date ($p=0.131$).

291

292 3.5. Targeted Selective Anthelmintic Treatment

293 None of the animals on any farm were treated more than once over the
294 grazing season; all the treatments were administered in either July or
295 August according to individual DLWG over the preceding 28 days.

- 296 • Farm O1 18 in July; 1 in August; 1 animal not treated at all
- 297 • Farm O2 29 in July; 8 in August; 4 animals not treated at all
- 298 • Farm C3 18 in July; 25 in August

299

300 4. DISCUSSION

301

302 The basic premise for DLWG-based TST is that, providing nutrition is not
303 limiting and that no other identifiable causes of ill-health are present, then
304 the individual growth rate of weaned calves (or lambs) at pasture is linearly
305 and consistently related to the impact of gastrointestinal parasitism (Greer
306 et al., 2009) through its effect on appetite, feed intake, protein metabolism
307 and nutrient partitioning (Forbes et al., 2000; Fox, 1997). In sheep systems
308 an algorithm named the Happy FactorTM has been developed (Greer et al.,
309 2009), which adjusts the target DLWG to the availability and quality of the
310 herbage. This approach has not yet been used in cattle TST, where the
311 assessment of pasture is typically undertaken either subjectively by
312 observation, or quantitatively through the use of standard techniques to
313 measure herbage mass and/or sward height (Lambert et al., 2004).
314 Individual DLWG alone was used as the determinant for treatment in this
315 study, though samples were also taken for parasitological examination in
316 order to gain further knowledge of their interrelationships.

317 As in the preceding year (Jackson, 2012), there were no significant
318 associations between FEC and DLWG. This result is not surprising, given that
319 FECs in young cattle in temperate regions with an *Ostertagia/Cooperia*
320 dominant nematode fauna, whether in experimental infections or under
321 field conditions, have shown no consistent or linear relationship with worm
322 burdens or animal performance (Brunsdon, 1969, 1971; Michel, 1969).

323

324 An analysis was performed of the number of calves that would have been
325 treated with anthelmintic at visit 3 if FECs were used as an indicator using
326 an arbitrary threshold of ≥ 250 epg. The results show only ten FGS had FEC of
327 ≥ 250 epg, all on Farm O1. Overall, 54 calves, growing < 0.75 kg/day would
328 not have been treated with anthelmintic had FEC been used as an indicator.

329

330 *Cooperia* spp. larvae predominated in the faecal cultures conducted in July,
331 but these results do not necessarily reflect the worm burdens in the animals
332 at the time (Brunsdon, 1968, 1971). The results of the pepsinogen assays
333 suggest that *O. ostertagi* was having a greater impact over the second half
334 of the grazing season.

335

336 Consistent with results from the preceding year (Jackson, 2012), there were
337 no significant correlations between plasma pepsinogen concentrations and
338 DLWG. Pepsinogen provides a direct measure of abomasal dysfunction and is
339 closely associated with abomasal pathology and intra-luminal *O. ostertagi*
340 populations (Michel et al., 1978). It is perhaps surprising that it is not more
341 closely correlated with growth rate, but this has also been observed in other
342 field studies in temperate regions (Brunsdon, 1969, 1971, 1972) and may be
343 due to co-infection with the intestinal species of *Cooperia* in FGS calves,
344 which can also impact growth rate, singly (Armour et al., 1987) or in
345 combination with *O. ostertagi* (Parkins et al., 1990), but *Cooperia* spp. do
346 not typically provoke an increase in pepsinogen.

347

348 4

349 The current trial was primarily a feasibility study for TST on commercial
350 farms, so no contemporary comparisons were possible, however cattle
351 growth rates from the previous year are available for each farm and these
352 provide a basis on which to assess the impact of TST. Despite some
353 concurrent (non-parasitic) respiratory disease, the mean growth rate of the
354 FGS cattle on the conventional farm C3 was ≥ 0.75 kg/day over the grazing
355 season, which was the target, though less than the previous year when,
356 using a long-acting anthelmintic and over a shortened grazing season, the
357 growth rate was 0.93 kg/day. On the organic farm O2 the average growth
358 rate under the TST regimen exceeded 0.75 kg/day and this was considerably
359 higher than in the previous year (0.57 kg/day). Although the growth rate on
360 organic farm O1 was less than target, at 0.69 kg/day it was again higher
361 than that of the previous grazing season when it was 0.46 kg/day. On
362 neither of the organic farms were there any major changes in nutritional or
363 grazing management between years.

364

365 The number of animals treated (all) on the conventional farm was the same
366 using TST as it was the previous year, but the potential exposure to
367 discriminating doses of anthelmintic was reduced with TST through the
368 asynchronous, mid/late season administration of eprinomectin, which has
369 persistent activity of 28 days against *O. ostertagi*, compared to moxidectin
370 10%, which has 120 days of persistent activity against this species. On
371 organic farm O2, all FGS calves were treated once in July the previous year
372 with fenbendazole, which has no persistent activity, whereas under the TST
373 regimen, all bar four animals were treated in July or August, with

374 eprinomectin, so arguably anthelmintic selection pressure could have
375 increased under TST. Similarly, on organic farm O1, only two calves were
376 treated the previous year with fenbendazole, while 19/20 animals were
377 treated with eprinomectin under TST, however on both organic farms the
378 FGS growth rates were higher under the TST regime.

379

380 In order to assess the effect of TST in satisfying the joint objectives of
381 achieving satisfactory growth rates while limiting selection pressure for
382 anthelmintic resistance, modellers have introduced a factor named 'benefit
383 per R', abbreviated to BPR (Laurenson et al., 2016). This is calculated from
384 a ratio between the average weight gain benefit (AWGB) arising from
385 whatever control measures have been used and the increase in anthelmintic
386 resistance allele frequency (IRAF) under that system; both are calculated
387 over the duration of the grazing season. This approach was used initially in
388 sheep and has subsequently extrapolated to cattle (Berk et al., 2016), in
389 which it was shown that the use of a DLWG threshold as an indicator for
390 anthelmintic treatments in TST was the approach that optimised BPR.

391

392 4.3. Concluding remarks

393

394 Applying a performance-based TST in the field was shown to be feasible
395 through the use of weigh bands, albeit this measurement requires adequate
396 restraint of animals. Gathering and handling young stock can be a critical
397 factor in commercial dairy herds, where replacement heifers are often
398 grazed on pastures away from the main farm and where handling facilities

399 may be rudimentary and inadequate for monthly individual animal
400 assessments. Wider adoption of some of the technologies that are already
401 used by some sheep farmers, such as electronic identification (EID), weigh-
402 scales with integrated software and automatic shedding gates (McBean et
403 al., 2016) would all facilitate the adoption of TST in cattle. Faecal egg
404 count and plasma pepsinogen concentration were found to have no
405 significant association with live weight gain and showed high levels of
406 variability amongst individuals within the management groups, so cannot be
407 recommended if one of the primary objectives for parasite control in
408 youngstock is to maintain growth rates that are commensurate with farm
409 objectives and industry standards.

410

411 On the organic farms, where anthelmintic treatment was already minimal,
412 DLWG was increased compared to the previous grazing season to rates that
413 are considered to be more compatible with optimum life-time performance
414 in heifer replacements (Wathes et al., 2014). Although organic principles
415 eschew the priority of performance in medication decisions, poor growth is
416 virtually a universal indicator of illness in young animals, commonly through
417 mechanisms that include anorexia (Exton, 1997; Hart, 1990), then it seems
418 that monitoring DLWG should be compatible with the organic ethos in
419 promoting animal welfare.

420

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426

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583 **Tables**

584

585 Table 1. Percentage of *O. ostertagi* and *C. oncophora* larvae cultured from
586 faecal samples collected pre-treatment in July (visit 3) on each farm.

587

588 **Figures**

589

590 • Figure 1. Normal distribution (Kolmogorov-Smirnov test $p > 0.150$) of
591 live weights of animals throughout study.

592 • Figure 2. Skewed distribution (Kolmogorov-Smirnov test $p < 0.01$) of
593 individual faecal egg counts (FEC) throughout study.

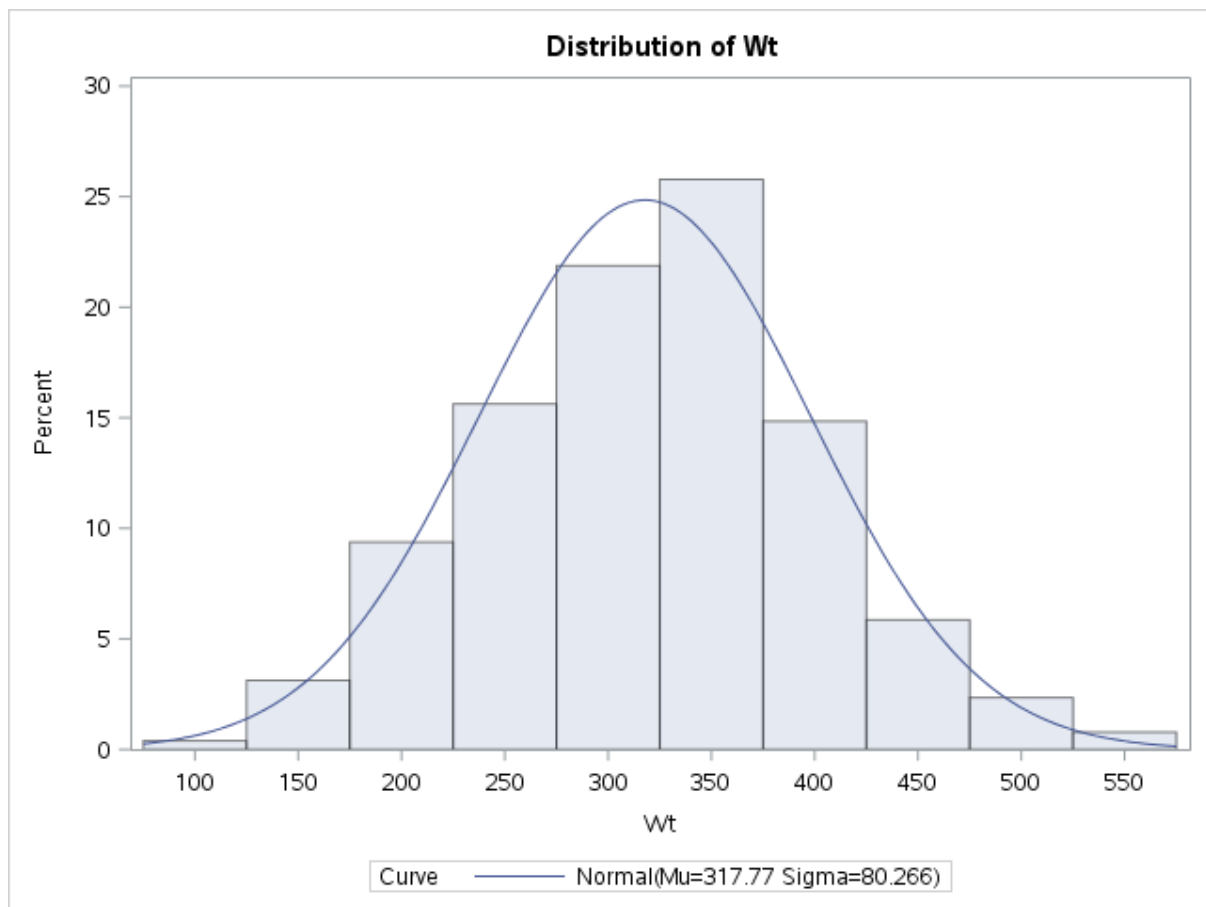
594 • Figure 3. Skewed distribution (Kolmogorov-Smirnov test $p < 0.01$) of
595 individual plasma pepsinogen (PEP) throughout study.

596

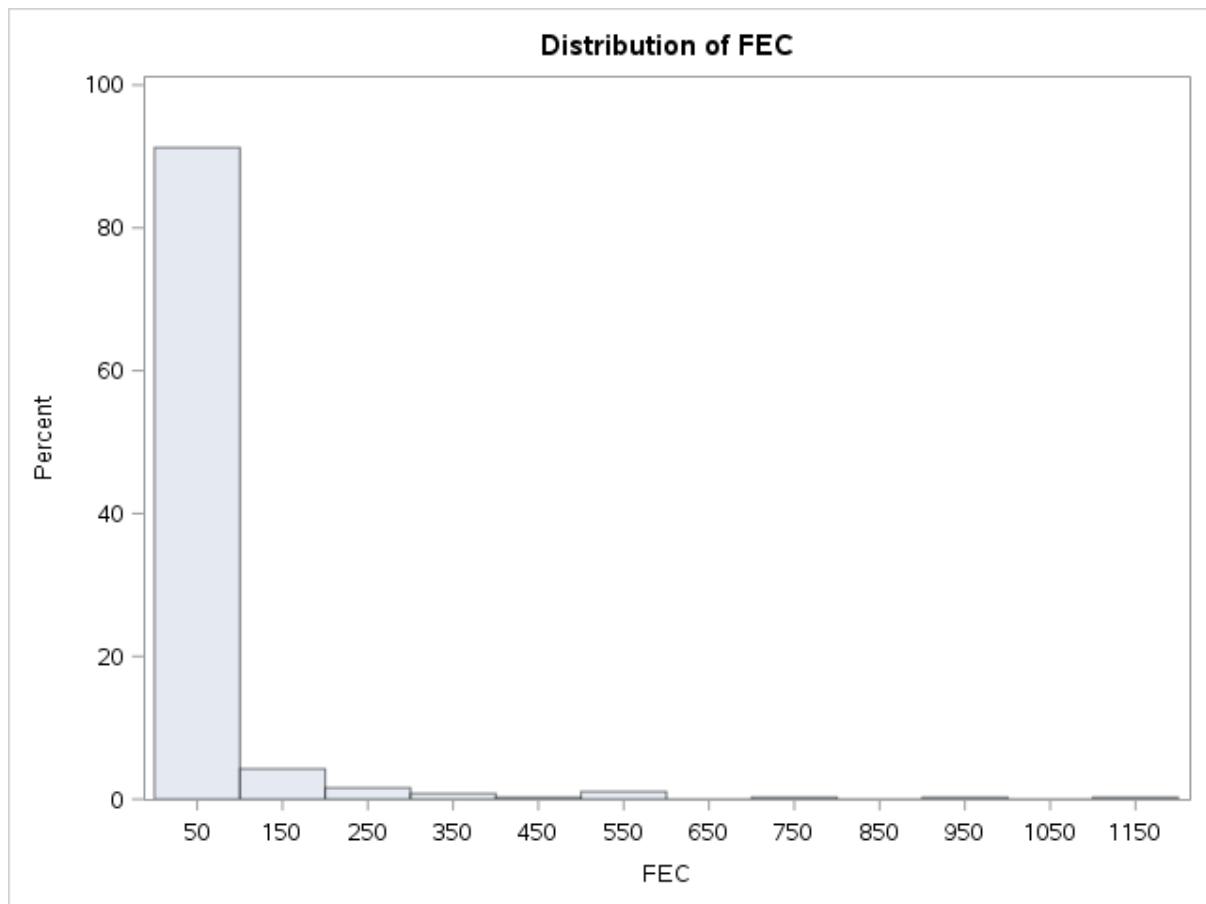
Table 1. Percentage of *O. ostertagi* and *C. oncophora* larvae cultured from faecal samples collected pre-treatment in July (visit 3) on each farm.

Farm	<i>O. ostertagi</i>	<i>C. oncophora</i>
C3	18%	82%
O1	21%	79%
O2	4%	96%

Figure 1. Normal distribution (Kolmogorov-Smirnov test $p > 0.150$) of live weights of animals throughout study



- Figure 2. Skewed distribution (Kolmogorov-Smirnov test $p < 0.01$) of individual faecal egg counts (FEC) throughout study.



- Figure 3. Skewed distribution (Kolmogorov-Smirnov test $p < 0.01$) of individual plasma pepsinogen (PEP) throughout study.

