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SID 5 Research Project Final Report

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Project identification

1. Defra Project code: ODO550
2. Project title: Validation of Current SCOPS Recommendations and Supporting Tools: Effective Worm Control and the Delayed Development of Anthelmintic Resistance in Sheep.
3. Contractor organisation(s): Food and Environment Research Agency (Fera)
   Sand Hutton
   York
   YO41 1LZ
4. Total Defra project costs (agreed fixed price): £ 603,485
5. Project: start date..... 02 January 2007
   end date..... 16 October 2009

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Executive Summary

7. The executive summary must not exceed 2 sides in total of A4 and should be understandable to the intelligent non-scientist. It should cover the main objectives, methods and findings of the research, together with any other significant events and options for new work.

Nematode infections cause significant disease and death in cattle, sheep and goats, and have led to a heavy reliance on anthelmintic drugs for their control. As a consequence, there have been increasing reports of anthelmintic resistance in nematode populations globally. This is a major issue for the long-term sustainability of livestock industries and in the UK has been addressed by the formation of a steering committee for the Sustainable Control of Parasites in Sheep (SCOPS). In 2003, UK specific guidelines for worm control, which aim at delaying the development of anthelmintic resistance, were published in a technical manual under the auspices of SCOPS. The major objective of this study was to promote these guidelines to sheep farmers and the wider industry. The study also aimed to provide a subjective evaluation of the practicality and effectiveness of the guidelines by deploying them across a network of representative farms. Study farms were divided into two comparative groups, one of which employed the SCOPS control recommendations and a second (Control-1) that continued their usual practice. A third group (Control-2) was included to measure uptake of SCOPS principles without direct intervention during the study period. There were 10 farms in each study group. The SCOPS guidelines advocate a 'toolbox' of resistance delaying control methods, with their deployment dependent on individual farm requirements. Hence, evolving strategies were devised for each farm based on veterinary advice. A network of veterinarians was, therefore, established at the start of the project, with each vet visiting and monitoring their assigned farms eight times across a two-year period. Worm infection levels on each farm were quantified by collecting faecal samples from a designated flock at each of the farm visits and measuring faecal egg counts in the laboratory and the number of treatments carried out. Individual feedback was collected from the farmers during phone interviews and questions were based around a questionnaire that allowed evaluation of the efficacy and practicality of the SCOPS control methods.

Mean faecal egg counts across the study period were calculated for all the lamb samples and results were found to be consistently, but not significantly, lower for the SCOPS group compared to the Control-1's. The mean number of treatments carried out on SCOPS farms was also lower, though again, not significantly so. This data is supported by the qualitative assessment at the end of the study, which showed that all SCOPS farmers had as good or better worm control during 2-year period of the study. Furthermore, the majority of SCOPS farmers found animal performance improved during the trial and that most SCOPS control methods were easy to implement. These results suggest a reduction in selection pressure for drug resistance is possible without negative effects on productivity.

Faecal samples were also used to collect worm eggs for use in an *in vitro* assay to determine resistance levels to the benzimidazole (BZ) and levamisole (LEV) classes of anthelmintics in the key pathogenic genera, *Teladorsagia, Trichostrongylus* and *Haemonchus* on all of the farms.

Field data collected was also used to validate a farm specific epidemiological computer model and further development of this Fera model was carried out to allow evaluation of SCOPS control methods and their potential

effects on resistance. Farm husbandry, management, grazing patterns, treatment data and faecal and pasture samples were collected by the vets during the visits. These data were used as model inputs to allow simulation of infection levels over a lambing season. Regression analysis was used to compare values for observed and predicted infection. Results suggest adequate fit for the computer model using both the lamb and the ewe data. The model allows resistance development to be examined under a range of alternative farm management strategies and could crucially focus future UK research that might otherwise require costly long-term field studies. Further development of the model would enable, for example, assessment of the value of vaccines. Approaches have been made by industry to use the model to identify resistance delaying strategies and best practice for new mode of action anthelmintic drugs. A recent Europe wide study (PARASOL) has explored aspects of worm control and a major focus of the study was to investigate targeted selective treatments (TST's). Results demonstrated the potential of this strategy using small experimental farm data, but the project did not address major issues of field application, (e.g. evaluation of optimal time of application and selectivity of treatment for maximum effect on resistance delay), essential to ensuring the full benefit of such strategies in the field. The Fera model is able to do this and is an effective tool for focussing research to answer such questions, particularly as the type and range of UK sheep farms, and therefore husbandry, is broad. A model assessment of the economic benefit of such strategies would also be feasible and equally critical to the further development of such guidelines. Issues such as TST's have been discussed at length for the SCOPS toolbox, but current guidelines are limited for the same reasons cited above. The Fera model is climate driven and could potentially be used to evaluate possible effects of climate change on infection on UK farms and subsequent development of anthelmintic resistance. Alongside the study reported here, the model has been used as part of an international collaborative project with the University of Geulph to evaluate its use in predicting infection in Canadian sheep flocks and this work has been presented at the WAAVP meeting (2009) in Calgary, Canada giving additional value to the commissioned research.

The cohort of commercial farms and data collected was used for widespread knowledge transfer to farmers and vets to demonstrate the SCOPS recommendations and their application. In 2007, this process began with four meetings in association with EBLEX on the project's SCOPS farms as part of a wider extension programme for the SCOPS principles. The project team demonstrated techniques, SCOPS principles and the computer model at Sheep 2008 held in Malvern in July 2008, and in September 2007 ran a CPD course for Vets at the Sheep Veterinary Society Meeting. In 2008 a further seven meetings were carried out in conjunction with EBLEX and HCC, based on a farm walk concept on some of the SCOPS project farms. The project was steered by the SCOPS committee and this platform was used to engage additional experts active in the industry. Farm case studies were used to provide publications for both the scientific and farming press. The results have been presented at conferences in Norway and Canada, and at further farmer meetings etc. Headline messages have been taken to the farming press. Feedback has also been used to help the SCOPS steering group decide on priorities for the future. This has been carried out during regular SCOPS committee meetings throughout the project period, which, given its membership, has provided good debate and peer review of the ongoing study.

The project has also allowed collaboration with other teams carrying out related research in the UK and overseas giving additional value to the commissioned research. Particularly, molecular probes for speciation of *Teladorsagia* and *Haemonchus* have been developed and validated alongside the project to give additional value. The faecal sample data collected for this project was used in the molecular work with additional funding from Seedcorn funds and the Yorkshire Agricultural Society. Diagnostics were developed in collaboration with researchers at the University of Veterinary Medicine, Institute of Parasitology, Hanover, Germany and the Moredun Research Institute (Learmount *et al*, 2009).

Additional funding was also provided by EBLEX to compare *in vivo* and *in vitro* resistance detection methods and to provide case studies on a further 5 farms using the network and diagnostic facilities and systems established for this study to give additional value. The work has been presented at conference and published to provide critical data to further inform SCOPS recommendations (Taylor *et al*., 2009). The parasitology facilities at Fera were also used to collaborate with and support the PARASOL project, providing diagnostics and *in vivo* resistance data for the PARASOL project.

All the data sets collected for the study and the additional projects that it has underpinned, have been used to provide a further update of the SCOPS Technical Manual, which sets out the UK guidelines for worm control for vets and farmers (Abbott *et al* 2009).

Project Report to Defra

8. As a guide this report should be no longer than 20 sides of A4. This report is to provide Defra with details of the outputs of the research project for internal purposes; to meet the terms of the contract; and to allow Defra to publish details of the outputs to meet Environmental Information Regulation or Freedom of Information obligations. This short report to Defra does not preclude contractors from also seeking to publish a full, formal scientific report/paper in an appropriate scientific or other journal/publication. Indeed, Defra actively encourages such publications as part of the contract terms.

The report to Defra should include:

- the scientific objectives as set out in the contract;
- the extent to which the objectives set out in the contract have been met;
- details of methods used and the results obtained, including statistical analysis (if appropriate);
- a discussion of the results and their reliability;
- the main implications of the findings;
- possible future work; and
- any action resulting from the research (e.g. IP, Knowledge Transfer).

Scientific Approaches

Objective 1. To evaluate the practicality and effectiveness of the new guidelines for worm control strategies in sheep published by SCOPS in 2004.

Milestones 1,2,3, 5, 6, 8, 9, 10, 11, 12, 16, 17

Selection of farms for field study
Seventeen private veterinarians located across England and Wales were recruited to the study and full training in the scope and requirements for this two-year project were provided via a workshop session and subsequent one-to-one ad hoc training. An initial sift form was completed by farmers from 70 candidate farms identified by the vets. The data was collated and farms were sorted into the study groups depending on their current worm management practices. The groups were designated:

- SCOPS: the SCOPS control guidelines were actively promoted on these farms.
- Control-1: farms in this group were resistant to advice and continued with their usual worm control.
- Control-2. This group was used to allow a qualitative estimate of general uptake of SCOPS recommendations when not actively promoted via the trial

The study aimed to collect data for 10 study farms in each of the groups over a two-year period and so, initially, 49 farms were selected for farm visits, to allow for natural dropouts as field data was collected.

The SCOPS and Control-1 groups were match paired to minimise the effect of external confounding factors using the following criteria:

- Organic/Non organic status
- Farm type (Upland/Lowland/Hill)
- Geographic and climatic location
- No breeding ewes
- Proportion of permanent grass
- Lambing period
- Scope for cattle alternation

A range of farms was selected to represent different husbandry systems operating in the UK. So, for example, the largest farm had approx. 1400 breeding ewes and the smallest had approx. 100. Of the farms selected, 60% were upland or hill farms and 40% were lowland. Peak lambing times ranged from early February to early April. All the data on which the farms were selected and paired for SCOPS and Control-1 groups is presented in Table 1.

Application of SCOPS guidelines
SCOPS provide a toolbox of worm control guidelines with decisions for treatment being responsive and so all control strategies were determined on farm in discussions between vet and farmer, and were dependant on the particular husbandry systems, infection and drug resistance status for each farm, the data for which, was collected during the course of the study. Laboratory-based services were freely available to all of the SCOPS farms and a brief synopsis of the different guidelines is given:

(Please note that this report refers to the 1st edition of the SCOPS Technical Manual (Abott *et al*. 2004)).

1. Work out a control strategy with your advisor (SCOPS guideline 1)

Throughout the study SCOPS group farmers were actively encouraged to engage with their veterinarian to develop worm control programmes based on SCOPS principles. Farmers in the Control-1 group were given general advice on request in order to maintain animal welfare, but were not given SCOPS advice. The Control-2 group were given SCOPS advice only if they sought it and this information was recorded so that the extent of SCOPS uptake could be monitored in this group.

2. Use effective quarantine strategies for introduced sheep (SCOPS guideline 2)

SCOPS farmers were asked to follow SCOPS quarantine procedures for all sheep introduced on to the farm during the course of the study.

3. Test for AR on your farm (SCOPS guideline 3)

In vitro resistance tests

Larval Development Tests (LDTs) were carried out, where possible, on faecal samples collected from ewes at the start of the season and from lambs at the end. Tests were carried out at the Veterinary Laboratories Agency (VLA) or Fera using standard protocols originally described by Taylor 1990. For each sample, larvae were exposed to five dilutions of thiabendizole (TBZ) or levamisole (LEV) as well as untreated control wells and the number of survivors for each genus recorded. For farms in the SCOPS treatment group, sample results were communicated as "indicating resistance" if more than 10% of control numbers survived at the lowest dose for either drug, as these doses are minimum inhibitory concentrations (MIC's) for susceptible *Teladorsagia*, *Trichostrongylus*, *Cooperia* and *Haemonchus* worms (Hong *et al* 1992, VLA pers. comm., Taylor, 1989) except for *Haemonchus* and LEV where 2.5 µg/ml was used as the MIC for susceptible individuals (Taylor, 1989). Details for the compound and species implicated were reported and results were communicated to the vets within 24h of receipt at Fera to allow strategic selection of drug classes for treatment on the SCOPS farms. There is no current reliable and validated laboratory method for assessing resistance to the ML class of anthelmintics and so *in vitro* resistance tests for this class of compound were not undertaken.

In vivo resistance tests

Farmers were also encouraged to carry out Drench Tests (DT) to determine anthelmintic efficacy. This requires collecting faecal samples post-anthelmintic treatment and carrying out a laboratory faecal egg count (FEC), which was offered as a free service to farms in the SCOPS group. This allowed an assessment of the efficacy of all drug classes including macrocyclic lactone (ML) anthelmintics, prior to a more rigorous Faecal Egg Count Reduction Test (FECRT) (Abbott *et al*. 2004, 2007) which was also offered if required. This test was carried out on at least 3 groups of sheep using a representative drug from each of the 3 classes as well as a control group as described in the SCOPS Technical Manual. Results from the *in vivo* resistance tests were also rapidly communicated to vets and farmers in the SCOPS treatment group to inform the worm control strategy. FECRT results were communicated as % reduction in efficacy calculated using the formula:

FECRT% = 1–[(Treatment2/Treatment1) x (Control-1/Control-2)] x 100

Results that showed <90% reduction were reported as indicative of resistance. Any post treatment samples with egg counts >100 eggs per gram (epg) were cultured and larval differentiation tests carried out to determine the surviving genera (M.A.F.F., 1986) and used to inform the treatments carried out on the SCOPS farms.

4. Administer anthelmintics effectively (SCOPS guideline 4)

Farmers on the SCOPS farms were asked to adhere to the SCOPS recommendations for effective drug administration, so that for all treatments carried out on the farm they used the following procedures:

a. Dose to heaviest animal
b. Calibrate dosing gun
c. Restrict feed before treatments

5. Use anthelmintics only when necessary (SCOPS guideline 5)

Regular monitoring of parasite infection levels was carried out on all the farms and on SCOPS farms this information was used to allow targeted treatments. For each farm, 4 visits were carried out each year to coincide lambing, marking, weaning and drafting. The samples were taken from the same group of sheep each season, designated the monitored flock (MF) and samples from ewes and lambs were analysed separately. Faecal egg counts (FEC) were determined in the laboratory, using a modified McMaster technique (MAFF 1986) on bulked samples (Morgan *et al*., 2005) with larval culture and differentiation to determine genera (Taylor et al. 2007). This gave the temporal pattern of infection for the MF on each farm. This data was collected for all farms in the study and results communicated to the vets within 24hrs of receipt of each sample. For the SCOPS groups, however, these results were then communicated via the vets to the farmers to allow targeted treatments.
Furthermore, farms in the SCOPS group were also given 10 faecal sample kits and encouraged to submit further samples (designated FreeSCOPS) at regular intervals and to discuss these results with their study vet.

6. Select the appropriate anthelmintic (SCOPS guideline 6)

On the SCOPS farms, farmers were encouraged to:

- Use narrow spectrum anthelmintics where appropriate
- Rotate anthelmintics where appropriate

All farms had *Nematodirus* at some stage during the trial and some had *Haemonchus* and so the use of narrow spectrum drugs was appropriate to all.

7. Preserve susceptible worms on the farm (SCOPS guideline 7)

SCOPS farmers were encouraged to carry out targeted selective treatments wherever possible, to part treat flock before moving and always to delay flock movements after dosing.

8. ***Reduce dependence on anthelmintics (SCOPS guideline 8)***

Vets were encouraged to discuss and plan a grazing strategy with each SCOPS farmer at the start of the season, to allow optimal use of clean pasture, mixed grazing or alternated grazing with cattle.

Measured effects

1. Lamb productivity

Infection levels on farms in the SCOPS and Control 1 groups were assessed by calculating mean FEC for the lamb samples collected at each farm visit and compared using a paired t test.

2. Comparison of number of anthelmintic treatments carried out across groups

Implementation of SCOPS principles as a whole should result in a reduction in the number of drug treatments and so the number of treatments carried out across the study period was determined and compared for SCOPS and Control-1 groups using a paired t-test.

3. Anthelmintic resistance

The main aim of the SCOPS principles for worm control is to minimise selection for anthelmintic resistance. However, it was not possible to measure shifts in resistance levels on individual farms, due to the short trial duration and insensitivity of current established test protocols for measuring resistance. The resistance data collected on the farms is, however, summarised and presented to measure temporal trends and further inform SCOPS recommendations. At the start of 2009, LDT data was collected from all farms in each of the test groups using a modified protocol at Fera to allow evaluation of BZ and LEV resistant populations of *Teladorsagia*, *Trichostrongylus* and *Haemonchus* to provide a baseline for future research and to inform the SCOPS recommendations.

4. Farmer's perception of the SCOPS strategy

At the end of the study each farmer completed a questionnaire. This allowed a qualitative assessment of the farmer's perception of the worm control strategy. The farmers were asked to assess their worm control and animal performance before and then during the trial. A qualitative assessment of ease of implementation of some of the key SCOPS guidelines was also carried out for all farms in the SCOPS group.

Objective 2. Use the data generated by the samples taken on participating farms to validate the computer model developed under ODO542 and evaluate it's use to vets and advisors as a decision support tool for applying SCOPS principles in the field.

Milestones 4, 14

Model overview

The model was written using STELLA software (Costanza *et al.*, 1998). Difference equations are resolved daily ($\Delta T=1$), based on algorithms devised by Euler. For the purposes of this study the model was set to run for each year of the study, as the lambing cycle on farms is seasonal. The model includes three main sectors and the first of these describes the free living and host dependant stages of the parasite. The increase in parasite numbers is a product of fecundity of the adult worms in the host and development rates of the free-living stages are dependant on the weather which is entered separately for each of the UK meteorological office regions. Parasites can leave the population at all stages via outflows for mortality. The second sector describes the flock dynamics and the rise and fall in host immunity. The flock is made up of ewes and lambs and these may be immune or infected with worms depending on

their exposure to infection or, in the case of ewes, their reproductive state. The third sector describes the chemistry of the three major anthelmintic classes available in the UK as treatments for sheep, and the response of different resistant and susceptible worm genotypes to those treatments. The values for model parameters were taken from published data and, where possible, from UK data. Where unavailable New Zealand data was used as a next best alternative as this has the most similar climate and vegetation pattern to the UK using the Köppen classification system (Kao *et al.*, 2000). Finite daily rates were used unless otherwise stated and published data were converted if necessary. Where more than one value was determined for a parameter, the mean was used in the model. Further model details as well as all parameter values are published (Learmount *et al* 2006).
Sample data for ewe egg counts, resistance, infection levels for the pasture on which the ewes and lambs were turned out to, as well as all the flock information collected at the first visit and treatment and movement data collected at subsequent visits was used to initiate a model run for each of the farms for both of the study years and this data is shown in Table 2 and 3. Data for animal movements into and out of the monitored flock were also included so that the calculated stocking densities were precise throughout each simulation. The model used climatic data derived from UK meteorological office 30-year regional averages (1970-2000) to drive the epidemiological parameters for each model simulation, depending on the location of the farm. The simulated nematode infection generated as egg counts from each model run was compared to the actual faecal egg count data collected from each farm during the visits. Regression analysis and Pearson correlation coefficients were calculated using the pooled data for ewes and lambs.

Model sensitivity assessment
For the sensitivity experiments it was assumed that no management control measures were undertaken, i.e. there were no inputs for drug treatment or pasture moves for any of the model runs and the initial ewe worm burdens and pasture contamination were set at the middle of the possible range of input possibilities. Analysis was performed for each of the three model species (*Teladorsagia* spp, *Trichostrongylus* spp. and *Haemonchus* spp.) and for four key management possibilities, which were early and late lambing and high and low stocking rates, giving a total of twelve different input scenarios for each sensitivity run. The maximum and minimum value for each lifecycle parameter used in the model was determined from the literature and used as the limits for the range of values used as inputs for the sensitivity runs (Table 4). Where this data was not available, ± 10% of the value used in the model was calculated and used for the parameter limits. Uniform distributions were assumed for all the data as the values considered were all means and as such it was impossible to make inferences about their distribution.
For each of the twelve input scenarios, model outputs for faecal egg counts were recorded at three time points corresponding to (i) a time in the middle of the time period before immunity is accounted for; (ii) the peak value for the output (i.e. just before immunity develops) and (iii) a time point halfway down the immunity drop curve. Zero values were substituted with 0.01 (the smallest non-zero value in the data set) and then all output data was log transformed. Outputs for each time-point were assumed to be independent although this is unlikely, in reality, to be so. Outputs for each scenario were designated *i*HE*t*, *i*HL*t*, *i*LE*t*, *i*LL*t* for species *i*, and time-point *t* where H=high stocking rate, L=low stocking rate, E=early lambing and L=late lambing.
Model sensitivity was measured using a Gaussian Emulation Machine for Sensitivity Analysis (GEM-SA), which is a stand-alone software system for Bayesian uncertainty, prediction and sensitivity analysis of deterministic computer models and is freely available (http://www.tonyohagan.co.uk/academic/GEM/). This is a quantitative sensitivity analysis

method that gives information about the contribution of first and higher order effects. Histograms were plotted to show the percentage contribution of each lifecycle parameter to the total output variance.

Objective 3. To use the cohort of commercial farms and data collected for widespread knowledge transfer
Milestones 13, 15

Objective 3 was included to allow further promotion of the SCOPS principles across the wider farming community and sheep industry in the UK.

Objective 4. To update the SCOPS recommendations firstly on the basis of knowledge gained since 2003 and secondly to incorporate the findings of this project

Milestones 7, 13, 15

Data collected during the course of the study was used to update the SCOPS technical manual, which is available on line to the vet and farming community.

Results

Objective 1. Evaluation of practicality and effectiveness of SCOPS

Infection levels on farms

There was seasonal variation in nematode genera on all the farms. In general, *Teladorsagia* was the predominant genus although both *Teladorsagia* and *Trichostrongylus* were present year round on the majority of farms with other genera being detected more sporadically over the two years. *Haemonchus* were detected on 15 of the study farms and for 9 of these farms, *Haemonchus* was only found in samples collected in 2007. *Nematodirus* was found in the majority of pasture samples taken at the start of each year and *Nematodirus* eggs were subsequently detected in early lamb samples. Results for FEC and larval differentiation data collected for the study highlights the importance of being able to differentiate worm species present, and the need for expert interpretation to allow judicious selection of treatments. Graphs of FEC with the proportions of genera present, estimated using larval differentiation results, are shown in Figures 1 and 2.

Table 5 presents the results for the mean FEC data for the lambs across the 2-year period for each of the farms in the SCOPS and Control-1 groups. Overall means for the two comparative groups were calculated and the mean for the SCOPS group was lower than for the Control-1 group (482 and 522 epg. respectively). This lower mean was consistent across the two years of the study (357 and 445 epg for 2007, 580 and 621epg for 2008 for the SCOPS and Control-1 groups respectively). There was no significant difference between results for the 2 groups compared with a paired t-test.

Comparison of number of anthelmintic treatments carried out across groups
The number of treatments carried out on the farms and drug classes used are presented in Table 6. Treatments were adjusted proportionately to account for the number of sheep treated so that 1 equated to a treatment of all sheep in the MF. The mean number of treatments carried out on the SCOPS farms was lower than on the Control-1 group (5.7 compared to 8.7

respectively) and for seven of the ten pairs the number of treatments was lower for the SCOPS farm. The number of treatments carried out on ewes was significantly lower for the SCOPS group compared to Control-1s (p=0.008), but there was no significant difference between the 2 groups when comparing results for treatments to lambs and overall. BZ and ML compounds were used more often than LEV type compounds when comparing percentages for all the treatments carried out on all farms in the study regardless of experimental group (44 and 37% compared to 19% respectively).

Anthelmintic Resistance

Results of the BZ LDT resistance tests carried out during 2007 and 2008 for all the study farms are presented in Table 7 and the sample data is scored as negative or positive for resistance using the VLA standard criteria for assessing resistance using this test method. This states that sample results are to be reported as BZ resistant if the numbers of larvae counted in the 0.1mg/l TBZ are equivalent or more than 10% of that species found in the control mean count and are to be reported as 'inconclusive – possible resistance' if third stage larvae are present in very low numbers, lower than the equivalent of 10% of that species found in the control. A blank result indicates that no test was carried out and this was generally due to a low faecal egg count for that sample, resulting in insufficient egg numbers for the test protocol. One farm had low egg counts at all the visits for the 2-year period and so no LDT tests were carried out on that farm during the study. Determination of resistance using this method and scoring criteria gave inconsistent results for most farms over time. In general, resistance in the *Teladorsagia* populations on the farms was detected at more time points then in the other genera. However only 4 farms that scored positive for *Teladorsagia* resistant worms at some time during the study did so consistently across all time points. The summary results for presence of resistant individuals on each of the farms are also shown in Table 7, and a positive result was assigned if positive in any test across the study period and negative if resistant individuals were never detected. These results suggest that *Teladorsagia* resistant populations were present on all but one of the farms. Prevalence of resistance in the *Trichostrongylus* populations was lower, with 38% of the farms having resistant populations and test results on 31% of the farms suggesting the possibility of resistance, although the results were inconclusive due to low numbers. Although *Haemonchus* were present on 57% of the farms, infection levels were generally low or very low compared to other genera present and presence, as indicated by larval differentiation data, was sporadic. Few LDT test results are, therefore available for *Haemonchus*. Resistant populations were, however, detected on 5 of the study farms and one farm had sample results that indicated the possibility of a BZ-resistant population.

Comment [jl1]: Check and other species

Resistance to LEV, detected in this way, suggests that 17% of the farms had resistant *Teladorsagia* populations while 24% may have had LEV resistant *Teladorsagia* worms, although these results were inconclusive due to low test numbers. Interestingly, more farms had LEV resistant *Trichostrongylus* populations (66% positive and 7% possible) than *Teladorsagia* populations. There were no LEV resistant *Haemonchus* populations detected on any of the farms.

Results for the BZ LDT test carried out at the start of 2009, using the modified protocol are presented in Table 6 as treatment survivors as a percent of control survivors at the discriminating dose. *Teladorsagia* was the predominant surviving genus at the MIC with this compound on farms and for 86% of the farms the survival was >10%, suggesting that generally, the frequency of resistant alleles in these populations was high. *Trichostrongylus* prevalence was lower on all the farms at this time point and as a result, fewer LDT

assessments were made. The results do, however, suggest a lower frequency of resistant alleles, with 100% mortality recorded at the MIC for 71% of farms populations. Where individuals survived at the MIC, the numbers were generally lower than for *Teladorsagia* (6-33%).

Results are also shown for *Teladorsagia*, *Trichostrongylus* and *Haemonchus* survivors at the discriminating dose for LEV in LDT's in Table 6. Results suggest a much lower frequency of resistance alleles on farms generally for all genera, compared with the BZ results. Only 32% of the farms had *Teladorsagia* survivors in the tests with this compound and only one farm had *Trichostrongylus* survivors. The highest proportion surviving at the MIC was 29% and the majority of samples with survivors were <10%. Haemonchus was present in only 4 of the tests and no survivors were recorded at the dd.

Farmer's perception of the novel strategy

Results of SCOPS farmer interviews for evaluation of the novel strategy on worm control, production and costs as well as ease of use of the strategies are shown in Table 8. Nine of the 10 SCOPS farmers responded. All of the farmers described their worm control as good prior to the trial and it was as good during the trial for all but one farmer, who judged that his worm control had improved. Eight farmers said that worm control was as good during the trial as before, while 1 said it was better. Five of the farmers said that animal performance was better during the trial, while 4 said that there was no change.

Seven of the farmers found the vet advice extremely useful and the other 3 found it useful. All of the farmers that used the full SCOPS quarantine found it easy to do. Six of the farmers found it very easy to use the FEC results to target treatments and the other 3 said it was easy. Five of the farmer found the AR testing very easy or easy while 4 weren't sure. Five of the farmers weren't sure how to rate grazing management strategies, while 3 found them easy. All farmers found effective drug administration easy or very easy.

Objective 2. Validation of computer model.

Model sensitivity analysis

The total mean and variance for scenario runs are shown in Table 12 and these describe the overall uncertainty of the model outputs. For most model outputs, the mean was clearly larger than the variance but the ratio of variance to mean increased with time. For *Teladorsagia* the analysis determined the same parameter values to be of importance for all scenarios and at all time points studied. The greatest contribution to the overall variance was due to worm mortality in the host (μL_4/adults) with a range of 62.25 -71.8% for all scenarios and time points analysed. The results suggest that the next most influential lifecycle parameter value is establishment of the free-living infective stages with contributions ranging between 19.97 & 25.67% for all scenarios and time points. Some contribution to the variance was given by the parameter values used for fecundity and pre-patent period but these were relatively small (mean values of 5.14 and 1.79% respectively) compared to the other two parameters.
For *Trichostrongylus* spp. the lifecycle parameter for mortality of worms in the host also made the strongest contribution to the overall variance in the majority of cases (58.05-70.44%). For the model runs that assumed a low stocking rate and early lambing, however, there was a strong contribution by the minimum development temperature for free living larval development at the first time point (39.64%), reducing the contribution from adult worm mortality to 38.32%. As with *Teladorsagia*, the second most influential parameter was establishment of infective larvae (12.46-26%) with a relatively small effect shown with fecundity and pre-patent period (means of 4.8 and 1.52% respectively).

Although mortality of the host dependent worm stages were generally the most influential factor in the analysis for *Haemonchus*, this was not always so, with values ranging between 9.46 and 70.07%. The order of importance of the other lifecycle parameters was different from the other 2 species. Generally, the second largest contribution was from egg-second larval stage winter mortality while the majority of the remaining contribution derived from the summer mortality for this life stage and establishment of the infective third stage larvae (Figures 4 & 5), although results were generally less consistent across scenarios and time points than with the other two species. A strong contribution was seen for minimum development temperature (d) at the first time point for runs that assumed a high stocking density and early lambing.
More than 85% of variation could be explained from the main effects of parameters and so the contribution of interactions to output variance was insignificant.

Regression analysis for observed and model simulated data
Graphs showing the observed FEC data plotted against simulated model outputs for all the farms and pooled for ewes and then lambs are shown in Figures 3 and 4. Regression analysis suggests a good fit for both the ewe and lamb data with the model accounting for 64 and 63% of the variation when all data was pooled for ewes and lambs respectively. This was in spite of the fact that there was no resistance data for the ML class of drugs and so this could not be accounted for in the model.

Objective 3. To use the cohort of commercial farms and data collected for widespread knowledge transfer
The cohort of commercial farms with all data collected has been used for widespread knowledge transfer to farmers and vets to demonstrate the SCOPS recommendations and their application.
In 2007, this process began with four meetings in association with EBLEX on the project's SCOPS farms as part of a wider extension programme for the SCOPS principles. The project team demonstrated techniques, SCOPS principles and the computer model at Sheep 2008 held in Malvern in July 2008, and in September 2007 ran a CPD course for Vets and the Sheep Veterinary Society Meeting.
In 2008, a further seven meetings were carried out in conjunction with EBLEX and HCC, based on a farm walk concept on some of the SCOPS project farms and had very good attendance levels at them all. Engagement of experts active in the field industry via the SCOPS committee and promotion of this project has had an extremely positive effect and all feed back suggests that the SCOPS message is reaching an ever increasing audience in the sheep industry.

Farm case studies were used to provide publications for both the scientific and farming press. The results are to be presented at future conferences in Norway and Canada, and at further farmer meetings etc. Headline messages have already been taken to the farming press. Feedback will also be used to help the SCOPS steering group decide on priorities for the future. The presentation given in Norway has been published in a special volume of Small Ruminant Research; and at least two further papers are being drafted for submission to peer review journals.
SCOPS have also been commissioned to provide CPD training for SQPs and the project data is being used to underpin these courses. The SCOPS steering group is also looking to provide Vet CPD.

Objective 4. To update the SCOPS recommendations firstly on the basis of knowledge gained since 2003 and secondly to incorporate the findings of this project

An updated technical manual was produced in December 2007 (Abbott, Taylor and Stubbings 2007). A workshop was held in January 2009 involving the project team and participating vets, parasitologists, other interested parties and the SCOPS Steering Group. This discussed the ODO550 project results, the required updates to the technical manual together with other data published since the last workshop in 2003, and how this would affect the recommendations. The final revised manual (3rd edition) was completed at the end of March 2009 and was made available on line at the NSA website in April 2009.

Conclusions and Recommendations for Future Work

Parasitic gastroenteritis is a complex multi species disease, with the causative nematodes having both free living as well as host dependant life stages (Coop and Jackson, 2000). Life-cycle parameters differ between genera and, there may, therefore be differences in seasonality. Suppressive treatment is carried out only on the host dependant stages and free-living stages are said to be in-refugia (Gaba *et al*., 2006). This, coupled with the fact that animals are frequently moved between pastures and that ewes and lambs are often treated differently due to differences in immune states (Stear *et al*., 2000), means that resistance alleles in the worm population will often be in a state of flux. Evaluation of resistance in farm populations is not, therefore, straightforward. This observation is supported by LDT results from this study and the data suggests that extreme care must be taken when interpreting results from samples at single time points on farms as on occasion, resistant populations may be missed. The study data suggests that a robust assessment of the resistance status of the farm worm population requires monitoring over time. Our study does, however, clearly demonstrate that BZ resistant worm populations are probably well established on a large number of UK farms at least in the *Teladorsagia* worm populations and that resistant allele frequencies may be relatively high. Although LEV resistance was detected in *Teladorsagia* populations on a quarter of the study farm and *Trichostrongylus* populations on two thirds of the farms, results from the discriminating dose LDT's carried out in 2009 suggest that resistant gene frequencies may be lower. This result was supported by the data for drug class use, with LEV class of drugs being the least used across the trial period. It may, therefore, be appropriate to promote the use of LEV on farm as an alternative to the more widely used BZ drugs, as BZ resistance alleles appeared to be more frequent on the farms tested. However, it must be noted that published research suggests that resistance genes for both BZ and LEV are recessive and for this reason it is likely that survivors in a discriminating dose test are likely to be predominantly resistant homozygotes. Consequently, although the number of resistant homozygotes may be low, gene frequencies in the population may still be relatively high as a relatively large proportion of individuals may be resistant heterozygotes. For this reason, field selection with LEV drug classes may be relatively quick for those populations with low-level survival in the LDT LEV tests if their use was increased on some farms. FECRT's involving the ML class of drugs, carried out with additional support funding from EBLEX, also confirms increasing reports of possible resistance to this class in *Teladorsagia* worms (Taylor *et al.*, 2009). **Further development of a robust and reliable *in vitro* method for the ML's should be given a priority, in order that resistance to these drugs can be confirmed, general levels on farms can be evaluated and shifts in gene frequencies can be measured**. Furthermore, this study also clearly demonstrates that whilst existing *in vitro* LDT tests for the BZ and LEV compounds may be adequate for resistance detection, **increased sensitivity is required to measure temporal changes in resistance levels and this is essential in order**

that any robust evaluation of resistance delaying strategies be undertaken in the field. A comparison of LDT, drench and FECRT results, carried out with additional funding from EBLEX and reported elsewhere (Taylor *et al.*, 2009) suggest that *in vivo* tests are less sensitive than the LDT method for detecting resistance, and thus are not good methods for monitoring changes in resistance levels, and this result is intuitive. Testing the effect of drugs *in vivo* introduces significantly more variability compared to a laboratory test, so that the amount of drug actually contacting the target worm cannot be reliably measured. **Improved *in vitro* tests and further development of novel molecular tools for measuring resistance are essential to inform research into resistance delaying strategies**.

Differences in lifecycle parameters (O'Connor *et al*., 2006) may result in differences in prevalence for the different genera across the lambing season and so it is possible that resistance levels in different genera may vary on the same farm and this could allow further opportunity for selective drug use. Results from this study did support this view and suggest that selection for resistance to the BZ drugs has been less rapid for *Trichostrongylus* compared to *Teladorsagia*. This is supported by the FEC larval differentiation data that suggests a low level of infection with *Trichostrongylus* year round, and sporadic and low level infection with *Haemonchus*. **However, it is interesting to note that resistance to LEV class of drugs was more prevalent in *Trichostrongylus* populations than *Teladorsagia* populations and this may warrant further investigation**. Again, however, it must be noted that even a low level of survivors in LDT test may be indicative of a relatively high resistant gene frequency and so further selection even with the most appropriate drug classes must be promoted with caution.

Mean egg count data comparisons for the two comparative experimental groups showed that implementation of SCOPS principles on farms did not negatively affect worm control, a concern with any strategy aimed at reducing anthelmintic usage. This data is supported by the qualitative assessment at the end of the study, which showed that all farmers had as good or better worm control during as before the trial. Furthermore, of the 10 SCOPS farms, 4 found no difference in animal performance while 5 found animal performance to be improved during the trial. These results together suggest no negative effects due to implementation of SCOPS worm control guidelines on the study farms. Coupled with this, the lower drug use on the SCOPS compared to the Control-1 group suggests that a reduction in selection pressure for drug resistance is possible without negative effects on productivity. These results will be used to support further promotion of SCOPS principles across the UK sheep industry.

Results from the qualitative assessment for ease of use of SCOPS methods allow us to make a subjective evaluation of their practicality on UK farms. Most found the vet advice extremely useful and the Quarantine, FEC and drug administration procedures easy or very easy. There was less confidence expressed for the use of grazing management and this may reflect the fact that this type of strategy requires more planning and has more dependant co-variants to assess compared to some of the other more straightforward strategies. Also, forty four percent of farmers were unsure about the use of AR test results and this may be as a result of the generally high prevalence of resistant populations and the lack of alternative drug classes to allow appropriate choices.

Results for the sensitivity analysis (SA) for the computer suggest that host dependant lifecycle parameters are the most sensitive in determining model outputs for both *Teladorsagia* and *Trichostrongylus*. These are, however, the most difficult parameters to measure experimentally as an effective experiment may necessitate animal slaughter. The model is

therefore a useful tool to measure the effect of variation of these parameter values on, for example, the development of resistance. For example, stochastic model simulations could be run using normally distributed data around the calculated means, to generate a range of potential outcomes. Theses scenarios will be examined in the future using the generated experimental data. The *Trichostrongylus* results also showed some sensitivity around the minimum development temperature and this data is critical when considering modelling infection under different climate scenarios. Interestingly the *Haemonchus* model showed a greater level of sensitivity around free-living life cycle parameters and this varied under alternative husbandry scenarios. This result is supported by the epidemiological data collected, with a very varied temporal pattern of infection on the farms where *Haemonchus* was present. As a consequence, the generic model inputs for the computer model were not adequate for simulation of the *Haemonchus* infections; often the species was absent at the start of the year and so there was no data to initiate the model with, although infection was detected in samples collected at later time points. **These issues will need to be addressed if further model developments are undertaken, particularly in light of incidental reports suggesting an increase in prevalence of *Haemonchus* in the UK**. Haemonchosis, although historically, relatively uncommon in the UK is an acute and therefore, extremely significant disease in sheep (Taylor *et al*., 2007).

Results from this study of the *in vivo* tests with the ML class of drugs suggest that these methods may not be sensitive enough to give an indication of levels of resistance on a farm. It was impossible, therefore, to seed model runs with this data and, indeed, the majority of the farms did not test for ML resistance even using the *in vivo* methods. **For these reasons further calibration of the model would is unrealistic at the present time and these data gaps would need to be addressed and further model development necessary before the model could be used as a predictive tool for infection levels, where ML's are used**.

Despite the limitations posed by ML resistance and *Haemonchus* results, the regression analysis for observed and predicted infection suggests model fit for both the lamb and the ewe data. This data is supported by additional work carried during the project in collaboration with the research team at the University of Geulph, to evaluate the potential of the model to simulate infection in Canadian sheep flocks and this work was presented at the WAAVP meeting (2009) in Calgary, Canada giving additional value to the commissioned research. The model shows great potential as a research tool to allow the evaluation of resistance development under proposed farm management strategies and to focus future Defra research that might require costly long-term field studies. **Further development of the model would enable, for example, assessment of the value of vaccines and approaches have been made by industry to use the model to evaluate the use of novel anthelmintic drugs and subsequent development of resistance**. The use of targeted selective treatments (TST's) has been researched in recent years but there is little scientific evidence of best practice for field application to ensure maximum benefit. For example, **evaluation of optimal time of application and selectivity of treatment for TST's for maximum effect on resistance delay would be critical to determine best practice.** Computer modelling is the most effective tool for focussing research to answer such questions, as the type and range of UK sheep farms, and therefore husbandry, is broad. The model is climate driven and could easily be used to evaluate possible effects of climate change on infection and drug resistance on UK farms. Alongside this project, the model has been used as part of an international collaborative project with the university of Geulph to evaluate its use in predicting infection in Canadian sheep flocks (Gutherie *et al*., 2009).

The inclusion of Objectives 3 and 4 into this study have meant that a very positive effort has been made to promote and advise farmers of SCOPS methods and the continuous update of the technical manual ensures that a comprehensive and current guide is widely available to the veterinary and farming communities. The study results ensure that the knowledge base remains applicable and appropriate and allows end users to build confidence in this novel approach. This type of extension work underpinned by focused science provides an extremely effective resource for policy makers and all involved in the livestock community and is essential to ensure effective and sustainable farming in the UK.

Table 1. Farm profiles based on criteria used to pair SCOPS and Control-1 farms.

Farm No	Test group	Farm Type	Met Region	Mean No ewes	% permanent grass	Peak Lambing	Cattle ?
17	C1	Lowland	8	224	60-90%	18 March	Yes
16	SCOPS	Lowland	8	112	60-90%	09 March	Yes
51	C1	Lowland	2	407	30-60%	10 April	No
63	SCOPS	Lowland	2	373	60-90%	28 March	No
28	C1	Hill	2	359	90-100%	22 April	Yes
26	SCOPS	Upland	2	367	90-100%	28 March	Yes
58	C1	**Upland**	2	350	90-100%	14 March	Yes
27	SCOPS	Upland	2	810	90-100%	20 April	No
37	C1	Hill	8	496	90-100%	19 March	No
33	SCOPS	Upland	8	325	90-100%	22 March	No
42	C1	Upland	8	508	90-100%	20 March	Yes
35	SCOPS	Upland	8	890	60-90%	30 March	Yes
41	C1	Upland	8	726	90-100%	01 April	Yes
36	SCOPS	Upland	8	303	90-100%	10 March	No
43	C1	Upland	7	750	90-100%	15 March	Yes
40	SCOPS	Upland	7	592	60-90%	10 March	Yes
72	C1	Lowland	8	627	60-90%	27 Feb	Yes
49	SCOPS	Lowland	8	244	90-100%	25 March	No
69	C1	Lowland	5	670	90-100%	19 Feb	No
54	SCOPS	Lowland	5	1883	60-90%	10 April	No
48	C2	Lowland	4	707	60-90%	20 Feb	Yes
12	C2	Upland	8	461	90-100%	15 April	Yes
15	C2	Lowland	8	413		18 March	No
45	C2	Upland	7	484	90-100%	12 March	Yes
62	C2	Upland	2	546	90-100%	28 March	Yes
68	C2	Lowland	5	872	60-90%	05 March	Yes
31	C2	Lowland	2	1014	60-90%	28 March	No
46	C2	Upland	7	890	90-100%	15 March	Yes
44	C2	Upland	7	1368	90-100%	10 April	Yes
59	C2	Upland	2	995	60-90%	02 April	Yes

Table 2. Model input data for UK sheep farms (data sets = 47).

Farm	Year	Reg	Pasture L3KG	Ewe epg	MF n	lamb %	Field size	First lamb date	lamb wk	Wean Date
17	2007	8	107 (100:0:0)	188 (60:40:0)	30	167	6	20-Feb-07	11	15-Jul-07
	2008		24 (100:0:0)	105 (53:47:0)	36	100	6	25-Feb-08	9	15-Jul-08
16	2007	8	0	146 (38:62:0)	32	181	3	26-Feb-07	9	25-Jul-07
	2008		26 (50:50:0)	693 (84:16:0)	71	161	3	01-Jan-08	2	14-Jul-08
51	2007	2	42 (50:50:0)	174 (78:22:0)	90	0	14	01-Apr-07	14	02-Oct-07
	2008		30 (100:0:0)	276 (0:100:0)	100	15	8	23-Jan-08	13	28-Nov-08
28	2007	2	0	361 (56:44:0)	58	200	13	13-Apr-07	16	07-Sep-07
	2008		48 (100:0:0)	165 (78:22:0)	40	63	7	15-Apr-08	16	13-Sep-08
26	2007	2	17 (100:0:0)	96 (16:84:0)	230	200	17	16-Mar-07	12	25-Jul-07
	2008		63 (100:0:0)	218 (92:8:0)	375	195	58	10-Mar-08	11	23-Jul-08
58	2007	2	41 (67:33:0)	13 (100:0:0)	200	200	5	11-Mar-08	10	01-Aug-07
	2008		11 (100:0:0)	338 (100:0:0)	40	200	5	25-Mar-08	12	18-Aug-08
27	2007	2	42 (67:33:0)	0	250	200	40	15-Apr-07	15	21-Aug-08
	2008		93 (100:0:0)	50	280	171	33	15-Apr-08	15	21-Aug-08
37	2007	8	46 (67:0:33)	263 (83:17:0)	300	100	4	28-Feb-07	11	12-Aug-07
	2008		79 (78:22:0)	376 (78:22:0)	175	143	14	27-Feb-08	11	12-Aug-08
33	2007	8	0	249 (85:15:0)	120	100	2	08-Mar-07	11	30-Jul-07
	2008		176 (65:35:0)	75 (90:10:0)	58	112	2	10-Mar-08	11	30-Jul-08
42	2007	8	0	38 (48:52:0)	200	165	8	10-Mar-07	11	03-Aug-07
	2008		348 (61:39:0)	250 (84:16:0)	75	200	11	10-Mar-08	11	30-Jul-08
35	2007	8	12 (100:0:0)	70 (84:16:0)	125	120	7	28-Feb-07	12	17-Aug-07
	2008		111 (100:0:0)	584 (95:5:0)	73	185	8	27-Feb-08	10	30-Jul-08
41	2007	8	93 (61:39:0)	102 (7:93:0)	130	154	6	16-Mar-07	13	15-Jul-07
	2008			169 (42:58:0)	100	160	15	20-Mar-08	12	
36	2007	8	19 (100:0:0)	270 (83:17:0)	80	200	4	13-Feb-07	9	13-Aug-07
	2008		318 (70:30:0)	770 (45:55:0)	35	189	4	22-Feb-08	10	11-Aug-08
43	2007	7	33 (0:100:0)	140 (65:23:13)	80	200	8	15-Feb-07	10	04-Sep-07
	2008		0	289 (87:13:0)	80	163	13	10-Mar-08	10	04-Sep-08
40	2007	7/8	0	157 (81:19:0)	180	133	15	18-Feb-07	9	14-Jul-07
	2008		221 (67:33:0)	374 (74:26:0)	200	150	10	29-Feb-08	8	20-Jun-08
72	2007	8	34 (100:0:0)	691 (75:19:6)	105	200	19	24-Feb-07	8	01-Jul-07
			9 (0:100:0)	268 (97:3:0)	90	222	7	03-Mar-08	10	15-Jul-08
49	2007	8	0	149 (94:5:1)	260	177	4	11-Mar-07	12	22-Jul-07
	2008		427 (87:13:0)	200 (100:0:0)	223	170	3	19-Mar-08	13	07-Aug-08
69	2007	5	177 (100:0:0)	351 (44:36:20)	150	160	10	5-Feb-07	7	26-Jun-07
	2008		292 (75:25:0)	250 (99:1:0)	60	167	10	5-Feb-08	7	26-Jun-08
54	2007	5	0	618 (58:42:0)	220	150	17	25-Mar-07	14	20-Jul-07
	2008		280 (59:41:0)	594 (100:0:0)	150	150	17	20-Mar-08	13	15-Jul-08
48	2007	4	836 (23, 77, 0)	94 (22,64,14)	120	167	8	02-Feb-07	7	01-Jul-07
	2008		50 (0, 100, 0)	198 (79, 17, 4)	180	133	8	14-Jan-08	5	20-Jun-08
15	2007	8	29 (100, 0, 0)	567 (88, 13, 0)	120	183	4	20-Feb-07	11	20-Jul-07
	2008		18 (0, 100, 0)	375 (98, 2, 0)	400	0	3	09-Mar-08	11	20-Jul-08
45	2007	7	71 (76, 24, 0)	413 (69, 31, 0)	465	140	7	07-Mar-07	10	01-Jul-07
	2008		542 (78, 22, 0)	521 (92, 8, 0)	430	140	17	01-Mar-08	9	14-Jul-08
62	2007	2	13 (100, 0, 0)	311 (97, 3, 0)	100	200	9	24-Mar-07	12	31-Jul-08
68	2007	5	25 (100, 0, 0)	250 (64, 16, 20)	124	167	11	18-Feb-07	9	17-Jul-07
	2008		326 (72, 28, 0)	169 (60, 37, 4)	90	167	6	22-Feb-08	9	28-Jul-09
44	2007	7	80 (63, 0, 38)	95 (75, 25, 0)	234	100	10	01-Apr-07	14	01-Aug-07

Table 3. Model parameters investigated for model sensitivity analysis for *Teladorsagia, Trichostrongylus* and *Haemonchus*.

Species specific parameters

	***Teladorsagia* spp.**			***Trichostrongylus* spp.**			***Haemonchus* spp.**		
Parameter	**Mean**	**Max**	**Min**	**Mean**	**Max**	**Min**	**Mean**	**Max**	**Min**
λ	202	265	131	202	265	131	3436	3752	3038
μEgg-L_2	0.23	ND	ND	0.13	0.18	0.1	0.9	ND	ND
μEgg-L_2	0.002	ND	ND	0.008	ND	ND	0.014	ND	ND
μL_3 (summer)	0.0085	0.009	0.008	0.043	ND	ND	0.12	0.35	0.01
μL_3 (winter)	0.00094	ND	ND	0.023	ND	ND	0.027	ND	ND
d	4	ND	ND	10	11	9	10	11	9
d_i	42	79	25	42	79	25	42	79	25
t_i	33	42	21	113	210	56	113	210	56
Generic parameters									
h	1797	2027	1412						
c_{ewes}	2.3	2.3	2.2						
e	0.39	0.655	0.138						
s_{ewes}	2300	ND	ND						
s_{lambs}	2000	ND	ND						
m	20	21	18						
μL_4/adults	0.07	0.12	0.03						

Table 4. Mean faecal egg counts for study farms over a 2-year period (n=8)

Farm pair		Mean epg Control 1		Mean epg SCOPS		Mean epg Control 2
17/16		844		300		1033
51/63		425		531		106
28/26		194		208		369
58/27		266		190		304
37/33		440		829		177
42/35		190		423		2369
41/36		278		898		739
43/40		844		310		233
72/49		544		292		704
69/54		1202		843		178
Mean		**523**		**482**		**621**

Table 5. Treatments for thirty UK farms during 2007 and 2008.

		Ewes			Lambs			Totals	
Farm pair		Control-1	SCOPS		Control-1	SCOPS		Control-1	SCOPS
17/16		7	2		8	0.72		15	2.72
51/63		2	0		5	1		7	1
28/26		2	0		3	8		5	8
58/27		3	1		3	6		6	7
37/33		5	2		4	6		9	8
42/35		5	3		9	5		14	8
41/36		3	1.6		6	3		9	4.6
43/40		3	3		6	6		9	9
72/49		3	2		3	1.75		6	3.75
69/54		1	2		6	3		7	5
Mean		**3.4**	**1.7**		**5.3**	**4.0**		**8.7**	**5.7**

Table 6. Indication of BZ resistance over time using LDT tests and standard assessment criteria for resistance.

Farm	*Genus*	Visit 1 Spring /07 (ewe)	Visit 2 Autumn 07 (lamb)	Visit 3 Spring 08 (ewe)	Visit 4 Autumn 08 (lamb)	Positive Any visit
17	*Haemonchus*	No	No	No	Inconclusive	**No**
	Teladorsagia	Yes	Yes	No	Yes	**Yes**
	Trichostrongylus	No	Yes	No	No	**Yes**
16	*Haemonchus*	No	No	No	-	**No**
	Teladorsagia	Inconclusive	Yes	Yes	-	**Yes**
	Trichostrongylus	No	Yes	Inconclusive	-	**Yes**
51	*Haemonchus*	No	No	No	-	**No**
	Teladorsagia	Yes	No	Yes	Yes	**Yes**
	Trichostrongylus	Yes	Yes	Yes	No	**Yes**
63	*Haemonchus*	-	No	-	No	**No**
	Teladorsagia	-	Yes	-	Yes	**Yes**
	Trichostrongylus	-	No	-	Yes	**Yes**
28	*Haemonchus*	No	No	-	No	**No**
	Teladorsagia	Inconclusive	Yes	-	Inconclusive	**Yes**
	Trichostrongylus	No	No	-	No	**No**
26	*Haemonchus*	No	-	No	No	**No**
	Teladorsagia	Inconclusive	-	Yes	No	**Yes**
	Trichostrongylus	No	-	Inconclusive	No	**Poss**
58	*Haemonchus*	-	-	No	No	**No**
	Teladorsagia	-	-	Inconclusive	Yes	**Yes**
	Trichostrongylus	-	-	No	No	**No**
27	*Haemonchus*	-	No	No	-	**No**
	Teladorsagia	-	Yes	Inconclusive	-	**Yes**
	Trichostrongylus	-	No	No	-	**No**
37	*Haemonchus*	No	-	No	-	**No**
	Teladorsagia	Yes	-	No	-	**Yes**
	Trichostrongylus	No	-	No	-	**No**
33	*Haemonchus*	No	Yes	No	No	**Yes**
	Teladorsagia	Yes	Yes	Yes	Yes	**Yes**
	Trichostrongylus	No	No	No	No	**No**
42	*Haemonchus*	No	No	No	-	**No**
	Teladorsagia	Yes	Yes	Inconclusive	-	**Yes**
	Trichostrongylus	No	No	Yes	-	**Yes**
35	*Haemonchus*	No	No	No	-	**No**
	Teladorsagia	Yes	Yes	Yes	-	**Yes**
	Trichostrongylus	No	Inconclusive	Inconclusive	-	**Poss**
41	*Haemonchus*	No	No	No	-	**No**
	Teladorsagia	Yes	Yes	No	-	**Yes**
	Trichostrongylus	No	No	No	-	**No**
36	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	Inconclusive	Inconclusive	Inconclusive	Yes	**Yes**
	Trichostrongylus	No	Yes	No	No	**Yes**
43	*Haemonchus*	No	Yes	No	No	**Yes**
	Teladorsagia	Yes	Yes	Yes	No	**Yes**
	Trichostrongylus	Yes	Inconclusive	No	Inconclusive	**Yes**
40	*Haemonchus*	No	No	No	-	**No**
	Teladorsagia	Yes	Yes	Yes	-	**Yes**
	Trichostrongylus	Yes	No	No	-	**Yes**
72	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	Yes	Inconclusive	Yes	Yes	**Yes**
	Trichostrongylus	No	No	No	Inconclusive	**Poss**
49	*Haemonchus*	No	No	No	Yes	**Yes**
	Teladorsagia	Yes	Yes	Yes	Yes	**Yes**
	Trichostrongylus	No	No	Yes	Yes	**Yes**
69	*Haemonchus*	Yes	No	No	No	**Yes**
	Teladorsagia	Yes	Yes	No	Yes	**Yes**

	Trichostrongylus	No	Inconclusive	No	No	**Poss**
54	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	Yes	Yes	Yes	No	**Yes**
	Trichostrongylus	No	Inconclusive	No	Inconclusive	**Poss**
44	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	Yes	Yes	Yes	Yes	**Yes**
	Trichostrongylus	No	Inconclusive	Yes	Inconclusive	**Yes**
31	*Haemonchus*	No	No	-	-	**No**
	Teladorsagia	Yes	Yes	-	-	**Yes**
	Trichostrongylus	No	Inconclusive	-	-	**Poss**
68	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	Yes	Inconclusive	Yes	Yes	**Yes**
	Trichostrongylus	No	No	No	Inconclusive	**Poss**
62	*Haemonchus*	No	-	No	-	**No**
	Teladorsagia	No	-	No	-	**No**
	Trichostrongylus	No	-	No	-	**No**
46	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	Inconclusive	Yes	Inconclusive	Inconclusive	**Yes**
	Trichostrongylus	No	No	No	No	**No**
45	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	Yes	Yes	Yes	Yes	**Yes**
	Trichostrongylus	No	Yes	No	No	**Yes**
13	*Haemonchus*	Inconclusive	-	No	-	**Poss**
	Teladorsagia	Inconclusive	-	Yes	-	**Yes**
	Trichostrongylus	No	-	Inconclusive	-	**Poss**
15	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	Inconclusive	Yes	Yes	Yes	**Yes**
	Trichostrongylus	No	No	No	No	**No**
48	*Haemonchus*	No	No	No	Yes	**Yes**
	Teladorsagia	Yes	No	Inconclusive	Yes	**Yes**
	Trichostrongylus	Inconclusive	No	No	Inconclusive	**Poss**

Table 7. Indication of LEV resistance over time using LDT tests and standard assessment criteria for resistance.

Farm	*Genus*	Visit 1 (ewe)	Visit 2 (lamb)	Visit 3 (ewe)	Visit 4 (lamb)	Positive Any visit
17	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	No	No	No	No	**No**
	Trichostrongylus	No	No	No	No	**No**
16	*Haemonchus*	No	No	No	-	**No**
	Teladorsagia	Inconclusive	No	No	-	**Poss**
	Trichostrongylus	No	Inconclusive	No	-	**Poss**
51	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	Inconclusive	No	Inconclusive	Yes	**Yes**
	Trichostrongylus	Inconclusive	Yes	Yes	Yes	**Yes**
63	*Haemonchus*	-	No	-	No	**No**
	Teladorsagia	-	No	-	No	**No**
	Trichostrongylus	-	Yes	-	No	**Yes**
28	*Haemonchus*	No	No	-	No	**No**
	Teladorsagia	No	No	-	No	**No**
	Trichostrongylus	No	No	-	No	**No**
26	*Haemonchus*	No	-	No	No	**No**
	Teladorsagia	No	-	No	No	**No**
	Trichostrongylus	No	-	No	No	**No**
58	*Haemonchus*	-	-	No	No	**No**
	Teladorsagia	-	-	No	No	**No**
	Trichostrongylus	-	-	No	Yes	**Yes**
27	*Haemonchus*	-	No	No	-	**No**
	Teladorsagia	-	No	No	-	**No**
	Trichostrongylus	-	No	No	-	**No**
37	*Haemonchus*	No	-	No	-	**No**
	Teladorsagia	No	-	No	-	**No**
	Trichostrongylus	No	-	No	-	**No**
33	*Haemonchus*	No	No	-	No	**No**
	Teladorsagia	No	No	-	No	**No**
	Trichostrongylus	Inconclusive	Yes	-	No	**Yes**
42	*Haemonchus*	No	No	No	-	**No**
	Teladorsagia	Inconclusive	No	No	-	**No**
	Trichostrongylus	No	Yes	Inconclusive	-	**Yes**
35	*Haemonchus*	No	No	No	-	**No**
	Teladorsagia	No	No	No	-	**No**
	Trichostrongylus	No	Yes	Inconclusive	-	**Yes**
41	*Haemonchus*	No	No	No	-	**No**
	Teladorsagia	Inconclusive	Yes	No	-	**Yes**
	Trichostrongylus	Yes	Yes	Yes	-	**Yes**
36	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	No	No	No	No	**No**
	Trichostrongylus	No	Yes	Inconclusive	Yes	**Yes**
43	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	No	No	No	No	**No**
	Trichostrongylus	Yes	Yes	No	Yes	**Yes**
40	*Haemonchus*	No	No	No	-	**No**
	Teladorsagia	No	Yes	No	-	**No**
	Trichostrongylus	No	Yes	Inconclusive	-	**Yes**
72	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	No	No	No	Inconclusive	**Poss**
	Trichostrongylus	No	Yes	No	Yes	**Yes**
49	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	Inconclusive	No	Inconclusive	No	**Poss**
	Trichostrongylus	No	Yes	No	Inconclusive	**Yes**
69	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	No	No	No	No	**No**

	Trichostrongylus	Yes	Inconclusive	No	No	**Yes**
54	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	No	Yes	No	No	**Yes**
	Trichostrongylus	Yes	Yes	No	Inconclusive	**Yes**
44	*Haemonchus*	No	No	No	-	**No**
	Teladorsagia	No	Inconclusive	Inconclusive	-	**Poss**
	Trichostrongylus	No	Yes	Yes	-	**Yes**
31	*Haemonchus*	No	No	-	-	**No**
	Teladorsagia	Yes	Inconclusive	-	-	**Yes**
	Trichostrongylus	No	No	-	-	**No**
68	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	No	No	No	No	**No**
	Trichostrongylus	Yes	No	No	Inconclusive	**Yes**
62	*Haemonchus*	No	-	No	-	**No**
	Teladorsagia	Inconclusive	-	No	-	**Poss**
	Trichostrongylus	No	-	No	-	**No**
46	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	No	Inconclusive	No	No	**Poss**
	Trichostrongylus	No	No	No	No	**No**
45	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	No	No	No	No	**No**
	Trichostrongylus	No	No	Inconclusive	No	**Poss**
13	*Haemonchus*	No	-	No	-	**No**
	Teladorsagia	No	-	No	-	**No**
	Trichostrongylus	No	-	No	-	**No**
15	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	Inconclusive	Inconclusive	Inconclusive	Inconclusive	**Poss**
	Trichostrongylus	Yes	Yes	Yes	Yes	**Yes**
48	*Haemonchus*	No	No	No	No	**No**
	Teladorsagia	No	Yes	No	Inconclusive	**Yes**
	Trichostrongylus	No	Yes	No	Yes	**Yes**

- = Sample not tested due to low faecal egg count.

Table 8. Percent survival at discriminating dose of thiabendazole (TBZ) or levamisole (LEV) in modified laboratory larval development tests in 2009.

Farm	Test group	MIC BZ				MIC LEV		
		Tel	*Trich*	*Haem*		*Tel*	*Trich*	*Haem*
17	Control-1	68	21	0		0	0	0
16	SCOPS	63	0	-		0	0	-
51	Control-1	97	0	-		7	0	-
63	SCOPS	57	-	-		0	-	-
26	SCOPS	68	33	17		0	0	0
27	SCOPS	46	9	-		1	0	0
37	Control-1	39	0	-		0	0	-
33	SCOPS	73	6	-		4	0	-
35	SCOPS	42	0	-		0	0	-
36	SCOPS	29	0	-		0	0	-
43	Control-1	10	-	-		0	-	-
40	SCOPS	45	-	-		0	-	-
72	Control-1	85	0	-		2	3	-
49	SCOPS	42	-	-		0	-	-
54	SCOPS	51	0	-		0	0	-
48	Control-2	42	0	-		0	0	-
15	Control-2	65	-	-		1	-	-
62	Control-2	1	-	-		0	-	-
68	Control-2	11	0	0		0	0	0
31	Control-2	49	0	-		29	0	-
46	Control-2	3	-	-		0	-	-

Table 9. Farmer's assessment of effect and ease of novel SCOPS guidelines.

Farm	Worm control before	Worm control after	Animal performance	Rate vet advice	Rate Quarantine	Rate FEC	Rate AR	Rate Grazing	Rate effective admin
16	Good	No diff	No change	Extremely useful	Easy	Very easy	Easy	Easy	Easy
63	Good	No diff	Better	Extremely useful	NA	Very easy	Don't know	No Return	Easy
26	Good	No diff	Better	Extremely useful	NA	Very easy	Don't know	Don't know	Very easy
27	Good	No diff	No change	Extremely useful	Easy	Very easy	Easy	Easy	Easy
33	Good	No diff	No change	Useful	Easy	Very easy	Easy	Don't know	Easy
35	Good	No diff	No change	Useful	Easy	Easy	Don't know	Don't know	Easy
36	Good	Better	Better	Extremely useful	Easy	Easy	Very easy	Don't know	Easy
49	Good	No diff	Better	Extremely useful	Easy	Easy	Don't know	Don't know	Easy
54	Good	No diff	Better	Extremely useful	Easy	Very easy	Easy	Easy	Easy

Table 10. GEM-SA sensitivity and uncertainty analysis results for computer model. Each column represents a model output. The 'mean' and 'variance' rows represent the overall mean and variance of the model output taking account of all input uncertainties. The remaining entries are percent contributions of individual inputs to the overall output variance. Output codes are: H=high flock stocking rate, L=Low stock flock stocking rate, E=Early lambing, Lt=late lambing; logi indicates the natural log output for species i and _j indicates timepoint j. Grey cells are screened out as non important (sensitivity measures below an arbitrary limit of 0.1). The most important parameter is marked yellow.

a) *Teladorsagia*

		log1HE_1	log1HE_2	log1HE_3	log1HE_4	log1HE_5	log1HLt_1	log1HLt_2	log1HLt_3	log1LE_1	log1LE_2	log1LE_3	log1LLt_1	log1LLt_2	log1LLt_3
lambda	1	5.68	5.34	5.31	5.34	5.31	5.34	4.97	5.29	5.76	4.96	4.32	5.35	4.9	4.52
muEgg.L2.summer	2	0.39	0.4	0.52	0.5	0.55	0.87	0.3	0.55	0.31	0.32	0.28	0.68	0.71	0.45
muEgg.L2.winter	3	0	0	0.01	0.01	0.01	0	0.01	0.01	0	0	0	0	0	0
muL3.summer	4	0	0	0.01	0.02	0.03	0.01	0.02	0.02	0.01	0.01	0	0.03	0.03	0.03
muL3.winter	5	0	0	0	0.01	0.01	0.01	0.01	0.01	0	0	0	0	0	0
muL4.adults	6	65.02	67.59	66.51	62.25	62.28	67.36	62.92	63.12	64.55	70.48	71.8	67.43	70.54	69.33
d	7	0.03	0.01	0.01	0.03	0.04	0	0.03	0.03	0.01	0.02	0	0	0	0
m	8	2.97	2.24	1.94	1.85	1.67	2.21	2.17	1.85	2.05	1.21	1.09	1.21	1.12	1.44
di	9	0	0.01	0	0.01	0.01	0.01	0.01	0.01	0	0.01	0	0	0.01	0.01
ti	10	0	0	0.01	0.01	0.01	0	0.01	0.01	0	0	0	0	0	0
h	11	0.53	0.39	0.24	0.15	0.12	0.36	0.15	0.13	0.78	0.85	0.65	0.89	0.86	0.67
cewes	12	0	0.01	0	0.06	0.07	0	0.04	0.06	0	0.01	0	0	0	0
e	13	24.54	23	22.9	22.01	21.28	22.76	21.95	21.58	25.67	21.06	19.97	23.61	20.7	21.55
sewes	14	0.07	0.04	0.06	0.02	0.02	0.06	0.09	0.02	0.1	0.06	0.02	0.22	0.13	0.12
slambs	15	0.19	0.09	0.08	0.03	0.03	0.1	0.03	0.03	0.5	0.18	0.09	0.41	0.2	0.08
	mean	9.98942	11.6985	14.2129	19.7661	23.9615	10.921	18.1441	18.7775	6.69421	8.3885	8.90909	6.63691	7.68478	8.65882
	variance	1.89444	3.77756	9.58429	25.9852	45.294	3.56267	18.1201	21.984	0.699063	1.69836	2.72177	0.808737	1.62491	2.71275

b)

Trichostrongylus

		log2HE_1	log2HE_2	log2HE_3	log2HLt_1	log2HLt_2	log2HLt_3	log2LE_1	log2LE_2	log2LE_3	log2LLt_1	log2LLt_2	log2LLt_3
lambda	1	4.65	5.07	5.14	5.09	5.22	5.1	2.8	4.73	4.54	6.01	4.7	4.59
muEgg.L2.summer	2	1.35	2.25	2.27	2.49	2.1	1.9	0.06	0.86	1.81	4.38	2.31	2.03
muEgg.L2.winter	3	0.02	0.01	0.01	0.01	0.01	0	0.02	0.01	0.03	0	0	0
muL3.summer	4	0.02	0.07	0.12	0.05	0.05	0.08	0.05	0.01	0.06	0.19	0.13	0.14
muL3.winter	5	0.02	0	0	0	0.01	0.01	0.48	0.02	0.01	0	0.01	0.02
muL4.adults	6	61.56	65.44	65.27	66.22	65.93	66.86	38.32	69	70.44	58.05	69.62	70.31
d	7	3.94	0.79	0.5	0.02	0.02	0.02	39.64	0.92	0.02	0.61	0.03	0.02
m	8	2.59	1.68	1.76	2.04	2.19	1.84	0.27	0.79	0.73	2.45	0.99	1
di	9	0.03	0.01	0.01	0.01	0.01	0	0.02	0.01	0.01	0	0	0.01
ti	10	0	0	0.02	0	0	0	0.06	0	0.04	0	0	0.01
h	11	0.71	0.49	0.52	0.61	0.58	0.56	0.08	1.08	0.8	1.2	1.01	0.95
cewes	12	0.04	0.03	0	0.01	0.01	0	0.01	0.01	0.02	0	0.01	0.02
e	13	22.16	22.6	22.5	22.21	22.6	22.48	12.46	20.99	19.72	26	19.59	18.92
sewes	14	0.13	0.06	0.03	0.02	0.02	0.01	0.19	0.07	0.06	0.16	0.06	0.06
slambs	15	0.12	0.05	0.04	0.06	0.04	0.02	0.17	0.26	0.17	0.53	0.1	0.06
	mean	10.2892	12.4342	13.9445	13.0433	15.8328	17.4003	4.68162	7.65858	7.97262	5.7392	8.24174	9.03028
	variance	1.937	5.44934	9.57276	7.00261	12.7926	17.7041	1.42524	0.980279	2.05827	0.706004	3.13171	5.1515

c)

Haemonchus

		log3HE_1	log3HE_2	log3HE_3	log3HLt_1	log3HLt_2	log3HLt_3	log3LE_1	log3LE_2	log3LE_3	log3LLt_1	log3LLt_2	log3LLt_3
lambda	1	0.07	0.32	0.16	0.36	0.32	0.32	0.55	0.35	0.15	0.01	0.34	0.25
muEgg.L2.summer	2	2.16	35.2	29.6	36.26	35.71	31.39	0	13.7	10.47	0.35	30.93	24.89
muEgg.L2.winter	3	0	0.02	0.01	0.03	0.03	0	0	0	0	0.01	0.03	0.02
muL3.summer	4	0.01	2.97	5.05	9.1	7.87	8.32	0	4.18	12.45	77.17	13.8	19.78
muL3.winter	5	0.27	0.01	0.02	0	0	0	1.5	0.25	0.11	0.03	0.02	0
muL4.adults	6	20.24	42.81	46.4	37.99	39.64	45.05	70.07	62.8	64.37	9.46	38.28	41.82
d	7	64.6	0.25	0.77	0	0.23	1.19	0	1.31	0.99	0.34	0	0
m	8	0.1	0.56	0.27	0.9	0.7	0.43	1.13	0.38	0.04	0.02	0.24	0.19
di	9	0.02	0.01	0.01	0	0	0	0	0	0	0.01	0.01	0
ti	10	0.02	0	0.01	0	0.01	0	0	0	0.01	0.01	0	0
h	11	0.28	0.22	0.18	0.45	0.42	0.27	0.06	0.25	0.17	0.01	0.55	0.51
cewes	12	0.01	0.01	0.02	0	0.01	0.01	0	0.01	0.01	0.01	0.01	0.01
e	13	5.36	12.58	12.11	13.14	13.02	11.42	26.08	15.36	9.41	0.6	13.33	10.58
sewes	14	0.05	0.1	0.12	0.07	0.07	0.06	0	0.02	0.02	0.06	0.13	0.06
slambs	15	0.02	0.1	0.08	0.08	0.05	0.03	0.48	0.18	0.07	0.03	0.17	0.07
	mean	5.85156	8.51167	8.44517	8.40961	10.0366	9.24275	6.63125	7.05146	5.96208	-2.97222	5.46825	5.38834
	variance	3.18314	2.07509	3.5762	3.87016	12.738	15.1292	0.681611	1.78248	3.91266	6.96543	1.77157	4.03886

Figure 1. Example of faecal egg counts with speciation across study period (Farm A)

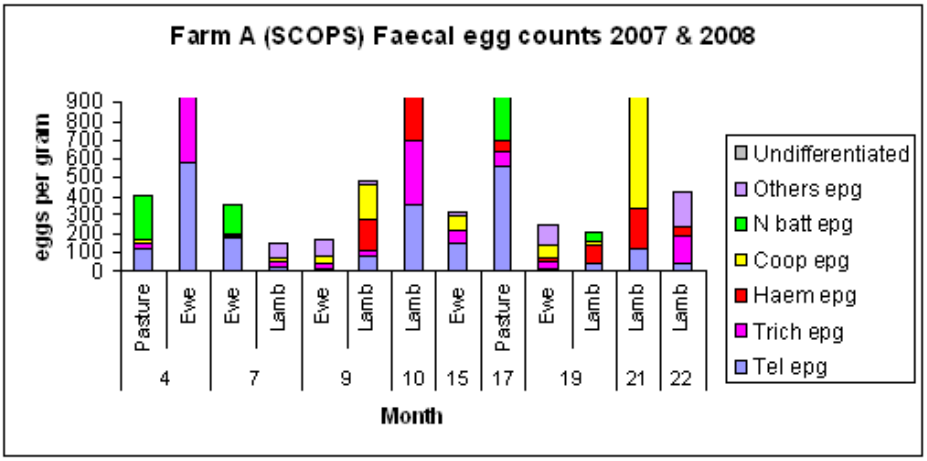


Figure 2. Example of faecal egg counts with speciation across study period (Farm B)

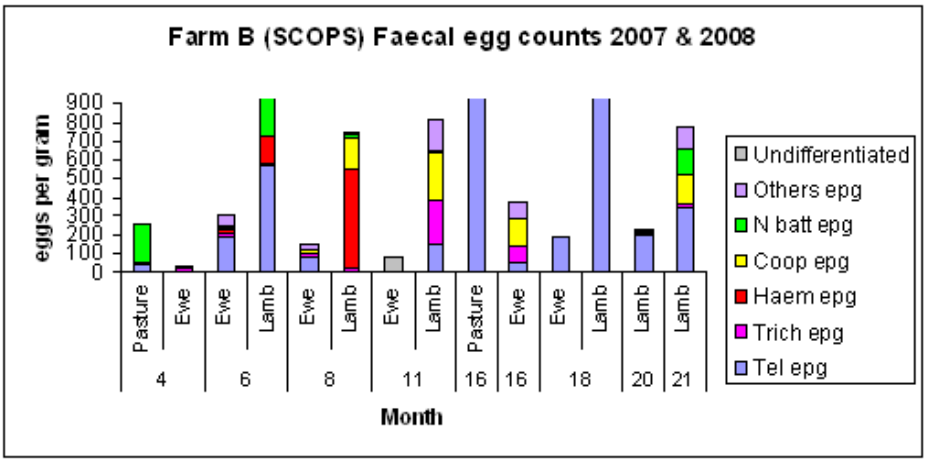


Figure 3. Ewe egg count observed results plotted against model-simulated results.

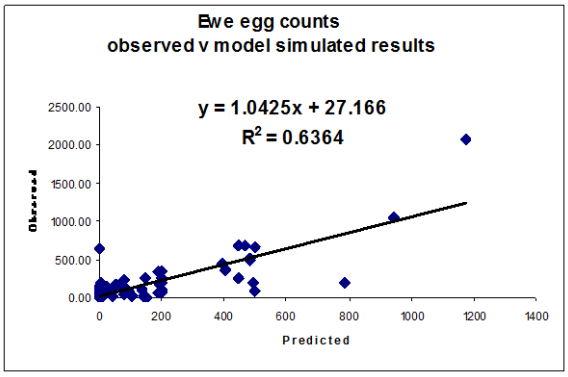
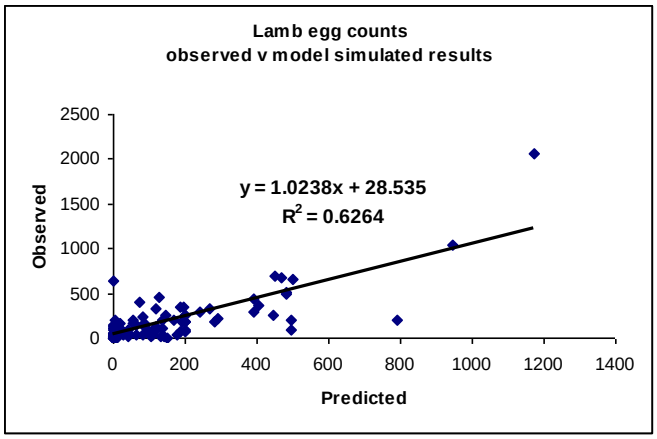


Figure 4. Lamb egg count observed results plotted against model-simulated results.



References to published material

9. This section should be used to record links (hypertext links where possible) or references to other published material generated by, or relating to this project.

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