Veterinary Parasitology 177 (2011) 231–241

Contents lists available at ScienceDirect

Veterinary Parasitology

journal homepage: www.elsevier.com/locate/vetpar

A stochastic model accommodating the FAMACHA© system for estimating worm burdens and associated risk factors in sheep naturally infected with *Haemonchus contortus*

D.P. Reynecke[a,b,c], J.A. Van Wyk[a,*], B. Gummow[b,d], P. Dorny[e], J. Boomker[a]

[a] Department of Veterinary Tropical Diseases, Faculty of Veterinary Science, University of Pretoria, Private Bag X04, 0110 Onderstepoort, South Africa
[b] Department of Production Animal Studies, Faculty of Veterinary Science, University of Pretoria, Private Bag X04, 0110 Onderstepoort, South Africa
[c] AgResearch Ltd, Hopkirk Research Institute, AgResearch Grasslands, Tennent Drive, Private Bag 11008, Palmerston North, New Zealand
[d] School of Veterinary and Biomedical Sciences, James Cook University, Townsville 4811, Queensland, Australia
[e] Institute of Tropical Medicine, Nationalestraat 155, B-2000 Antwerpen, Belgium

ARTICLE INFO

Article history:
Received 3 November 2009
Received in revised form 14 January 2011
Accepted 18 January 2011

Keywords:
Haemonchus
Sheep
Targeted Selective Treatment
Integrated Parasite Management
FAMACHA©
Mathematical model
Automated decision support

ABSTRACT

A previously developed multiple regression algorithm was used as the basis of a stochastic model to simulate worm burdens in sheep naturally infected with *Haemonchus contortus* over five consecutive *Haemonchus* seasons (November to January/February) on a farm in the summer rainfall region in South Africa, although only one season is discussed. The algorithm associates haemoglobin levels with worm counts in individual animals. Variables were represented by distributions based on FAMACHA© scores and body weights of sheep, and Monte Carlo sampling was used to simulate worm burdens. Under conditions of high disease risk, defined as the sampling event during the worm season with the lowest relative mean haemoglobin level for a class of sheep, the model provided a distribution function for mean class *H. contortus* burdens and the probability of these occurring.

A mean *H. contortus* burden for ewes ($n = 130$ per sample) of approximately 1000 (range 51–28,768) and 2933 (range 78–44,175) for rams ($n = 120$ per sample) was predicted under these conditions. At the beginning of the worm season when the risk of disease was lowest (i.e. when both classes had their highest estimated mean haemoglobin levels), a mean worm burden of 525 (range 39–4910) for ewes and 651 (range 37–17,260) for rams was predicted. Model indications were that despite being selectively drenched according to FAMACHA© evaluation, 72% of the ewes would maintain their mean worm burden below an arbitrarily selected threshold of 1000 even when risk of disease was at its highest. In contrast, far fewer rams (27%) remained below this threshold, especially towards the end of the worm season.

The model was most sensitive to changes in haemoglobin value, and thus by extrapolation, the haematocrit, which is used as the gold standard for validating the FAMACHA© system. The mean class haemoglobin level at which there was a 50% probability of worm burdens being ≤1000 worms was 7.05 g/dl in ewes and 7.92 g/dl in rams.

1. Introduction

Severe anthelmintic resistance in South Africa and elsewhere led a team of South African scientists to lay the basis for application of the principle of Targeted Selective Treatment (TST) (Malan and Van Wyk, 1992), from which

* Corresponding author at: Department of Veterinary Tropical Diseases, Faculty of Veterinary Science, University of Pretoria, Private Bag X04, 0110 Onderstepoort, South Africa. Tel.: +27 12 529 8380; fax: +27 12 529 8312.
E-mail address: jan.vanwyk@up.ac.za (J.A. Van Wyk).

0304-4017/$ – see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.vetpar.2011.01.042

the FAMACHA© system of clinical evaluation of haemonchosis was developed. The system is based on classification of the colour of the conjunctival mucous membranes of sheep and goats against a dedicated colour chart in order to identify and treat only those animals which are unable to manage unaided (i.e., without anthelmintic treatment) under severe *Haemonchus* challenge (Bath et al., 1996). While this system has potential for application under field conditions (Van Wyk and Bath, 2002), at present, labour input requirements and complexity in the face of dwindling numbers of knowledgeable advisors are serious limitating factors. This paper is part of a multi-faceted approach aimed eventually at addressing these limitations through an automated, computerised decision support system (Van Wyk and Reynecke, 2011). Risk analysis is a crucial component of this initiative, with the emphasis on, but not restricted to, stepwise retrospective analysis of clinical data collected through various methods of applying TST, for instance the FAMACHA© clinical test for anaemia.

Because most predictive models are at best representative of only a part of the whole system (Dobson, 1999), it is important that they should have as few assumptions about the system as possible. On the other hand, it is well accepted that it is not necessary to have complete knowledge of a system in order to develop a model that can be used to answer worthwhile questions about the system (Smith, 1994), and computer models relating parasite populations to anthelmintic resistance have effectively contradicted many of the recommendations of most conventional worm control programmes, such as routinely to drench all animals, and periodically to rotate anthelmintic classes. For example, a model by Barnes et al. (1995) indicated that irrespective of the drug rotation strategy, the endpoint, i.e. intractable resistance to each drug, would be reached more or less simultaneously whether two drugs are rotated or used in series. Their model also indicated that non-treatment of a few animals in order to preserve susceptible worms would delay selection for resistance, as has subsequently been supported by various field studies (Kenyon et al., 2009; Leathwick et al., 2006; Greer et al., 2009; Waghorn et al., 2008, 2009).

Learmount et al. (2006) developed a computer model for the United Kingdom to simulate expected egg counts (and therefore predict the timing of expected peaks in faecal egg counts) for a variety of inputs including regional weather data, stocking density, initial pasture contamination levels, parasite species proportions, as well as lambing dates, the timing of flock movements and removal of lambs. However, because the FAMACHA© system is effectively a test of the anaemia status of animals, and requires furthermore that the animals be evaluated often during the peak worm season (Van Wyk and Bath, 2002), data such as anaemia status and associated environmental risk factors such as rainfall and temperature are readily and frequently available directly from the point of exposure. Furthermore, the approach taken by Learmount et al. (2006) would be difficult to implement under climatic conditions in most of South Africa, where rainfall is much more limiting to this species than temperature.

With stochastic risk assessment models such as the one described in this work, inputs are in the form of mathematical distribution functions representing a pre-determined range of values, rather than a single value such as is commonly found in deterministic models (Vose, 1998, 2000), and as such they describe a continuous range of potential values that could occur according to the information known about the input parameter. Monte Carlo simulation allows the random sampling of values from within the defined input distribution functions and this occurs each time the model is run (i.e. for each iteration). The output of the model is thus also a distribution function representing the possible results that could occur and the probability of a given value occurring (Vose, 2000).

In the present work, a previously published deterministic linear regression algorithm (Roberts and Swan, 1982) was used as the basis of a stochastic simulation model, since it is based on the use of red cell parameters and body weight to estimate worm burdens in sheep. The aims of the present study were (1) to determine if the model output (i.e. the distribution for worm count in a given class of sheep) could be validated against the observed trend in FAMACHA© proportions and the attendant variability in body weight of sheep through a given worm season; (2) to estimate flock haemoglobin values which would have to be maintained by selective drenching in order to maintain the flock worm burden below a selected pathogenic worm threshold; and (3) to determine if the model would predict differential susceptibility to worm infection between the two classes of hoggets (namely young replacement ewes and rams) in the study.

2. Materials and methods

2.1. Origin of data

The series of trials, as well as the data used to develop the model, and the FAMACHA© testing procedures have been described more fully in Reynecke et al. (2011a) and Riley and Van Wyk (2009). The trials formed part of a series of trials on what was designated Farm 1 by Van Wyk (2008) and Reynecke et al. (2011a,b) to validate the FAMACHA© system, and to estimate heritability (Bisset et al., 2001; Riley and Van Wyk, 2009). Sampling occurred over five successive *Haemonchus* seasons and involved different groups of two classes of sheep, namely approximately 130 and 200 per season respectively of young replacement ewes (EWEREP), which annually replaced aging ewes in the flock, and rams of similar age (RAMREP). Although ten data sets comprising five each for the EWEREP and RAMREP classes of sheep over five consecutive *Haemonchus* seasons were analysed, the similarity of the results between years led to the analyses for only one of the sets being discussed in detail in this study.

2.2. Model system

A multiple regression equation (Roberts and Swan, 1982) was used to estimate the risk of haemonchosis. It allows the estimation of the worm burden of an animal by taking its haemoglobin level and body weight into account

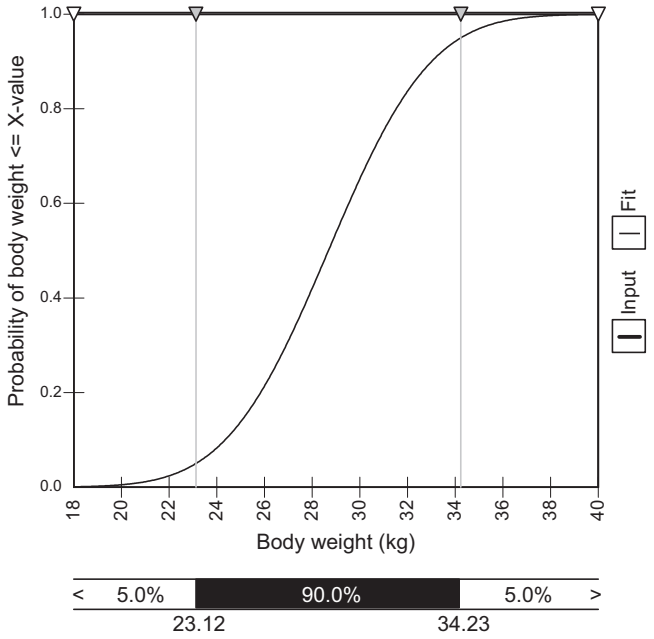

Fig. 1. Typical cumulative distribution function for the body weight of a sample of EWEREP sheep ($n = 130$). The stepped line represents the observed body weight values in the sample and the dotted line represents the @Risk-fitted Normal (28.67,3.37) distribution.

according to Eq. (1):

$$\text{Log Worm Count} = (\text{Body weight} \times 0.0168) + (\text{Haemoglobin} \times -0.20774) + 3.8936 \quad (1)$$

A typographical error in the original published model caused the constant term for body weight to be reported incorrectly as 0.0.68. Thus, back substitution of data supplied in the article was used to re-calculate the value for the body weight constant, which was thereafter validated with data included in the publication of Roberts and Swan (1982) (D. Berkvens, personal communication 2006). The correct value was calculated to be 0.0168, and when this value was substituted into Eq. (1) for a sheep weighing 20 kg and a having a haemoglobin level of 10.5 g/dl, a worm count of 111.77 was obtained, compared to an almost identical value of 112 reported by Roberts and Swan (1982). This corrected weight constant was used in all subsequent analyses.

The variables in the model were entered as distribution functions generated by "Bestfit" in the @Risk version 4.5 software. Body weight was modelled using a Normal distribution function, entered into the model with its arguments, i.e. the mean and the standard deviation of the sampled body weight data. The resulting distribution for body weight is given in Fig. 1, which predicted that 90% of the animals weighed between 23.12 kg and 34.23 kg.

Eq. (1) required that the red blood cell input parameter for anaemia, i.e. the FAMACHA© score, be in the form of blood haemoglobin level expressed in g/dl (Roberts and Swan, 1982). In the light of the well known highly significant correlation between haematocrit and haemoglobin on the one hand (Stockham and Scott, 2002), and the FAMACHA© value with haematocrit on the other (Bisset et al., 2001; Riley and Van Wyk, 2009), haemoglobin values were calculated from the haematocrit values, and a distribution function describing the haematocrit values for each FAMACHA© category was generated using @Risk. Haematocrit values for FAMACHA© categories 1–4 were found to be normally distributed within each category, while FAMACHA© category 5 ($n = 3$) had too few data values to define a distribution. Hence, in the latter case, the mean and standard deviation for this category was used to generate an assumed Normal distribution function.

The ordinated FAMACHA© scores were initially converted to haematocrit values by allowing each of the intermediate FAMACHA© categories 2, 3 and 4 to represent their most likely corresponding haematocrit values, defined as the median of the five haematocrit percentage points per category. Although this approach would be appropriate for FAMACHA© classification where the accuracy of anaemia estimation was high, the data used in the model emanated from a farm where misclassification of sheep into FAMACHA© categories occurred (Reynecke et al., 2011a,b). Therefore, for the purposes of the present analyses the mean haematocrit value for FAMACHA© category 2, with an assigned haematocrit range of 23–27%, was set to the fitted mean of its observed range at 19.5%; category 3 (18–22% assigned haematocrit range) was set to 15%, and category 4 (13–17%) was set to 11%. Category 1, with a haematocrit range of >27%, and category 5, with a range of <13%, were set at their observed mean values of 25% and 10%, respectively (Table 1).

The conversion to mean haemoglobin level per FAMACHA© category was initially effected by dividing the mean haematocrit percentage by 3, since the haemoglobin level is typically one-third of the haematocrit value (Hall

Table 1
Farm 1. FAMACHA© score vs. haematocrit: assigned mean haematocrit values, fitted mean values, and percentiles and standard deviations of the fitted Normal distribution for haematocrits of 675 sheep of both sexes from 2000 to 2005.

FAMACHA© score	*n*	Assigned mean value of haematocrit range	Fitted mean, @Risk Normal distribution (trial data)	Fifth percentile of haematocrit	Ninety-fifth percentile of haematocrit	Standard deviation
1	272	30	25.1	19.7	30.5	3.27
2	258	25	19.5	15.9	27.2	3.45
3	126	20	15	10.6	23.9	4.02
4	16	15	11	6.5	18.7	3.71
5	3	10	10	8.6	11.5	1.03

and Malia, 1984; Jain, 1993; Stockham and Scott, 2002) in the case of normocytic anaemia due to haemorrhagic blood loss, which is characteristic of *H. contortus* infections (Owen, 1968). However, the mean corpuscular haemoglobin concentration (MCHC) in most blood samples is in the range of 32–36 g/dl (Stockham and Scott, 2002). Therefore, the assumption made above that the MCHC is relatively constant at 33.3 g/dl, and that the conversion to haemoglobin content follows a simple linear trend according to the equation

$$\text{Haemoglobin (g/dl)} = 33.3 \times \text{haematocrit \%} \quad (2)$$

was modified, to include variability in both the MCHC and the observed haematocrit values. The FAMACHA© categories were truncated with respect to haemoglobin range per category, with similar upper but differing lower MCHC boundaries for each group. The "non-anaemic" FAMACHA© categories of 1 and 2 were assigned a lower and upper MCHC value of 32 and 36 g/dl, respectively, within the defined normal range, and the more anaemic FAMACHA© categories 3–5 a more depressed lower and normal upper limit of 26 and 36 g/dl respectively, since severely anaemic sheep could be expected to develop an iron, cobalt and/or copper deficiency that would depress the MCHC to a lower level than the normal range (F. Reyers, personal communication, 2006). The range of probable MCHC values was entered into a Uniform (32,36) distribution function for FAMACHA© categories 1 and 2, and a Uniform (26,36) distribution function for FAMACHA© categories 3, 4, and 5. The Uniform distribution was then multiplied by a Normal distribution function based on the fitted mean and standard deviation of the haematocrit data for each FAMACHA© category, to simulate the mean haemoglobin value for the FAMACHA© category. This process is illustrated at the top of Fig. 2, where it can be seen that for all animals in FAMACHA© category 1, the MCHC was modelled as Uniform (32,36) and the haematocrit as Normal (25.1,3.27), to give a distribution for the haemoglobin value in the relevant FAMACHA© category.

The final distribution for the FAMACHA© variable in each sample was obtained by incorporating the distribution for haemoglobin values for each FAMACHA© category obtained by simulation as described above, into a Discrete distribution function, with the format:

$$\text{Discrete}(\{xi\}, \{pi\}), \quad i = 1 \text{ to } n \quad (3)$$

where x represents the simulated output distribution for haemoglobin value in each FAMACHA© category present in the sample, and p represents the probability of occurrence of the particular category. The Discrete distribution in this instance represents a composite probability distribution of the occurrence of FAMACHA© categories in groups of sampled sheep, incorporating the proportional occurrence of FAMACHA© categories, by probabilistic branching (Vose, 2000). Thus, if in a particular sample only two categories of animal were present, the parameters for the distribution could be set for the proportional occurrence of those two categories; if there were three categories, the third category could be proportionally incorporated, etc. The output of the Discrete distribution function for the haemoglobin value of a sample is given in the histogram in Fig. 3, which is produced in @Risk by grouping data into several bars or classes and the number of values in any class is the frequency of the class. The probability that the output variable lies within the range of the class is determined by the frequency divided by the total number of values.

The output of the simulation model described in Fig. 2 was obtained by selecting the appropriate Excel worksheet cell as a simulation output for a given sample date, and a distribution of possible outcomes was generated for every selected output cell according to variability in the input cells. Each simulation run consisted of 10,000 iterations, which is the equivalent of 10,000 random trials being carried out. The number of iterations is an arbitrarily chosen value, selected to give a smooth distribution curve and to exceed the minimum number required for stability and convergence.

3. Results

3.1. EWEREP class

The model output for the EWEREP class is illustrated in Fig. 4a, and the corresponding percentages of sheep in the different FAMACHA© categories in Fig. 4b. The summary graph (Fig. 4a) represents the seasonal trend in the predicted variability of worm burdens, with a predicted major peak of infection in January, followed by a slight increase in worm burden towards the end of the season (April).

When the second blanket anthelmintic treatment was administered on 7 January, the proportion of animals in FAMACHA© category 1 was still higher than that in category 2, but there were also some sheep in FAMACHA© categories 3 and 4. The model reflected the above blanket treatment at the sampling of both 17 January (Fig. 4a), when the simulated worm burden decreased sharply, and 7 February, when it again closely approximated the value seen at the first sample date (Fig. 4a). Thereafter, simulated

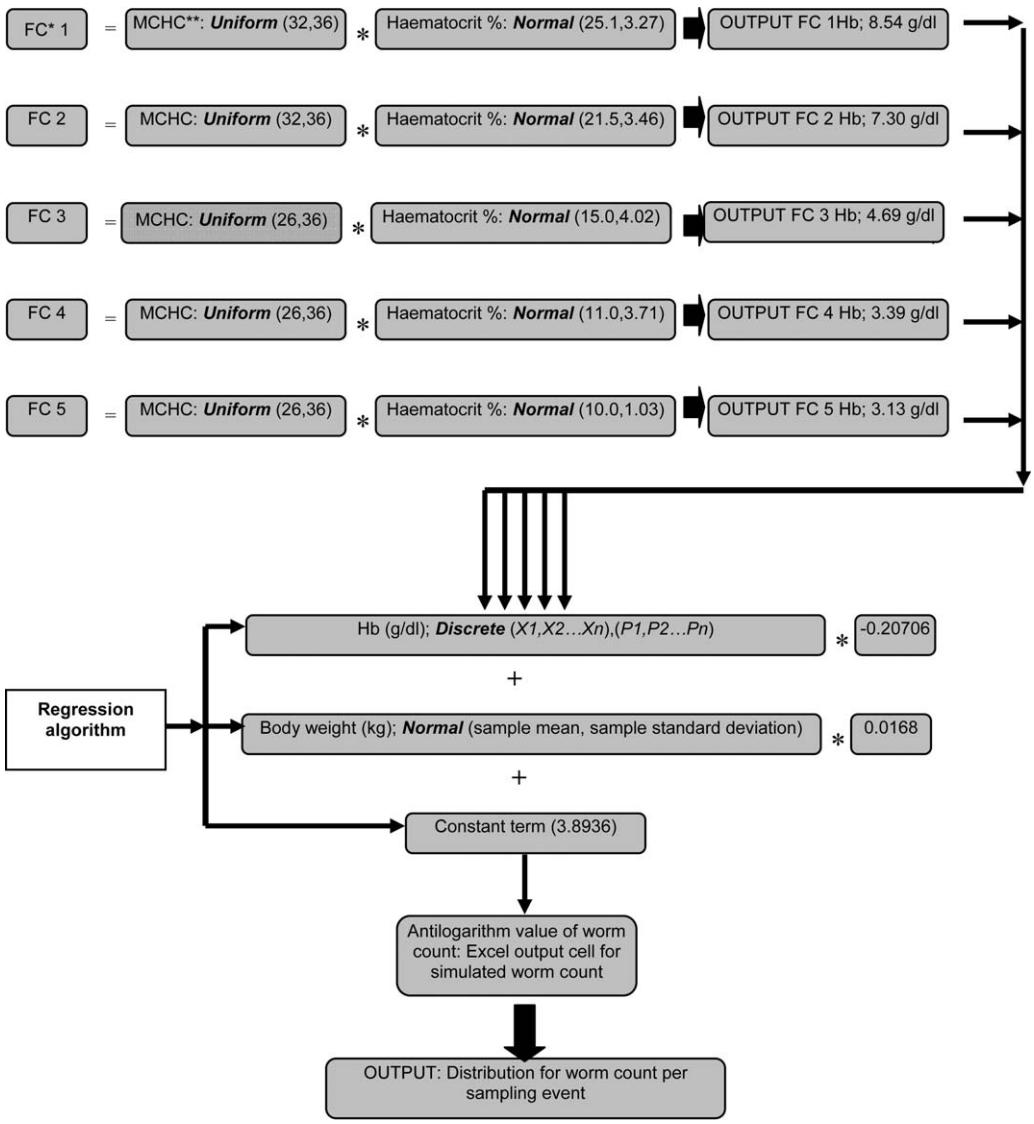

Fig. 2. Schematic diagram of the model used to simulate mean worm count of sampled sheep. Fitted statistical distributions are given in bold italicised letters. Bold black arrows indicate Monte Carlo simulated outputs of the model (*FC represents FAMACHA©, **MCHC represents mean corpuscular haemoglobin concentration).

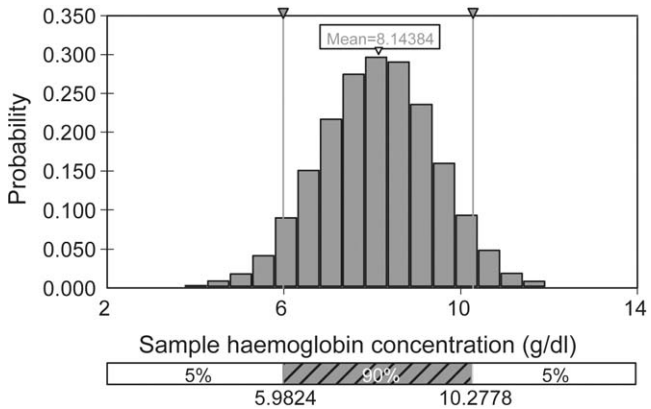

Fig. 3. Discrete haemoglobin distribution for the FAMACHA© variable for a EWEREP sample ($n = 133$). The mean haemoglobin value was 8.14 g/dl, and 90% of the simulated haemoglobin values were between 5.98 and 10.27 g/dl.

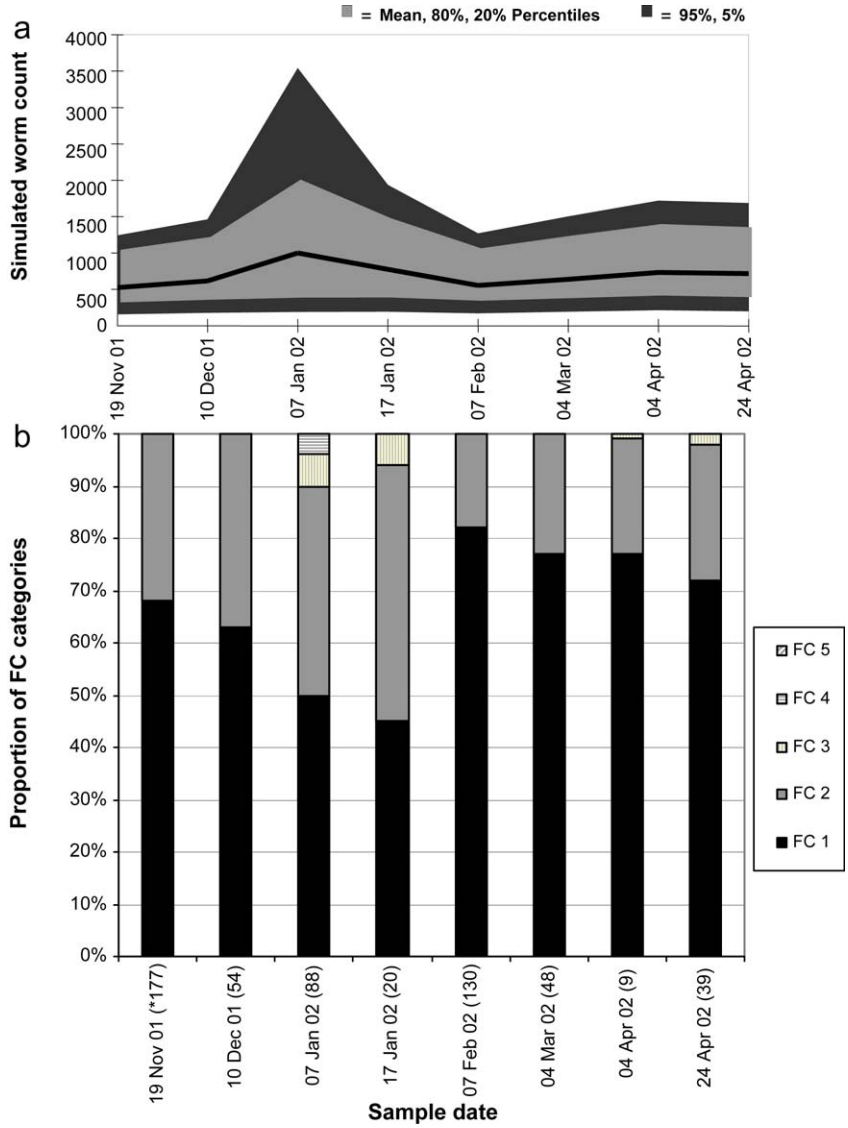

Fig. 4. (a) EWEREP (n = 130). Model output for simulated worm count. The black line represents the simulated mean worm count. (b) EWEREP: Proportional representation of the FAMACHA© categories per sample. Rainfall between sampling events is given in parentheses, in mm (*rainfall for preceding 4 weeks). FC represents FAMACHA©.

worm burdens rose continually from the fifth to the seventh samples on 7 February, 4 March, and 4 April, when a second, lesser peak in infection was indicated, concomitant with an increase in the number of FAMACHA© categories per sampling event. This trend can partly be explained by relatively high and well-distributed rainfall that fell up to the sixth sample on 4 March, after which a downward trend in simulated mean worm burden was seen from 4 April, probably occasioned by a combination of lower rainfall and increased host immunity.

3.2. RAMREP class

The model output for the RAMREP class is illustrated in Fig. 5a, and the percentages of sheep in the different FAMACHA© categories in Fig. 5b. The sheep in the RAMREP trial were blanket drenched on 10 November and again on 7 January. The seasonal trend in predicted worm counts was similar in both classes of sheep, but the RAMREP class was clinically more apparent as suffering from worm infection as can be seen from the sample on 7 January, where only FAMACHA© categories 1, 2, 3 and 4 were present in the EWEREP class, whereas FAMACHA© categories 1–5 were present in the RAMREP class. Additionally, on 7 January, approximately 50% of the sheep in the EWEREP class were in FAMACHA© category 1, compared to only 5% of the sheep in the RAMREP class (Figs. 4b and 5b).

4. Discussion

As was to be expected, in each trial the risk of haemonchosis indicated by the Roberts and Swan (1982) model

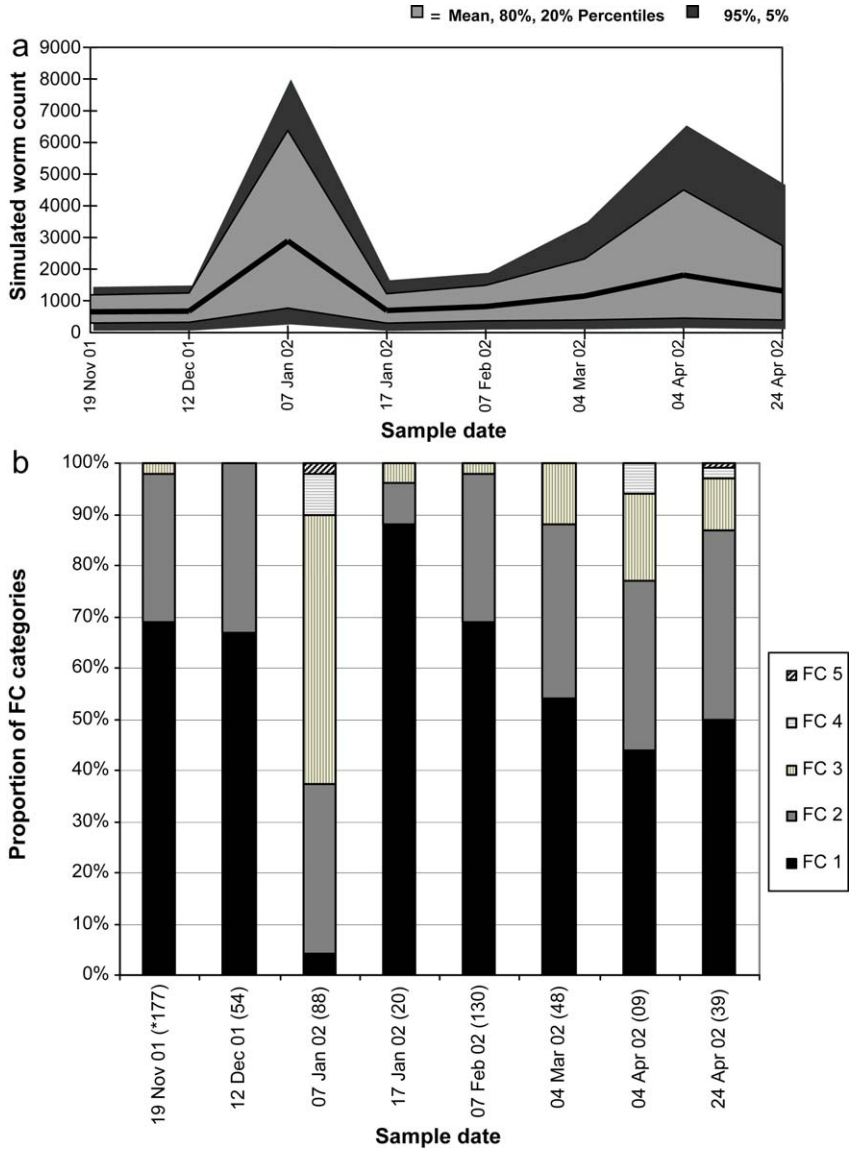

Fig. 5. (a) RAMREP (n = 120). Model output for simulated worm count. The black line represents the simulated mean worm count. (b) RAMREP: Proportional representation of the FAMACHA© categories per sample. Rainfall between sampling events is given in parentheses, in mm (*rainfall for preceding 4 weeks). FC represents FAMACHA©.

was lowest at the start of the worm season. For instance, all of the trial sheep were initially dewormed on 19 November, when only FAMACHA© categories 1 and 2 were present in the sample. Worm burdens then increased slowly until the second sampling event on 10 December, and then sharply to the third event on 7 January, at which time there was a peak in infection and FAMACHA© categories 1–4 were present. This sharp increase in simulated worm burden, accompanied by a downward shift in the mean haemoglobin level in the flock, can largely be related to 177 mm of rain recorded on the farm over a period of 12 days during the four-week period immediately preceding the time of the first sampling event on 19 November. Between this date and the third event on 7 January a further 142 mm of rain was recorded. However, from the example of the work of McCulloch et al. (1984), it is clear that the initial 177 mm of rainfall and its spread over 12 days had probably laid the foundation for much of the increased risk of disease that was apparent at the time of the third sampling.

Very similar general trends in mean worm burden were indicated for RAMREP and EWEREP, although with considerably higher worm burdens for RAMREP. As happened in every one of the five *Haemonchus* seasons spanned by this study, peaks in infection occurred in mid season (on 7th January) and again late in the season, in both classes of sheep, but with the level of infection being consistently higher in the rams than in the ewes. Possibly this phenomenon can be ascribed to the immunomodulatory effect of male sex hormones, the androgens, which could cause

males to be more susceptible than females to parasitic infections (Klein, 2000; Gauly et al., 2002).

Riley and Van Wyk (2009) showed that, using BLUP (Best Linear Unbiased Prediction) analysis of the present data set, the evaluations of the farmer were so consistent that very highly significant levels of both genetic and phenotypic correlation were obtained between the FAMACHA© and haematocrit values. However, it was also shown by Reynecke et al. (2011a,b) that, despite the above misclassification in category 2–5 sheep, the farmer concerned was on average consistently one FAMACHA© category out with his classifications, i.e. FAMACHA© category 3 sheep were classified into category 2, etc.

As pointed out by Gettinby (1989), a complication of computational models is that with diseases such as haemonchosis which cycle annually, identical patterns of disease outbreaks rarely occur, even on farms that are close together, or from year-to-year on a given farm. He stated further that qualitative patterns or long-term predictions of disease were of little value at farm level, where weather and management practices can so alter the course of disease that only site specific models can be of any use to estimate the risk of disease. This was an important reason for use in the present study of a model that simulates levels of worm infection repeatedly from time to time per given site for TST and tactical anthelmintic intervention, instead of the conventional approach of attempting at the beginning of a given worm season to predict worm outbreaks with the aim of preventing them by prophylactic, strategic drenching.

For both classes of sheep, the model strikingly reflected the changing epidemiological situation as regards *H. contortus* challenge during the course of the worm season, especially in relation to FAMACHA© evaluation and the shift in FAMACHA© categories during the course of the season (Figs. 4a, b and 5a, b). Also, while the results of only one of the five years' duration of the trials are presented here, those of the other four were very similar as regards the extent to which the model reflected differences in levels of *H. contortus* challenge over each worm season. If the Roberts and Swan (1982) model were to be used deterministically by the input of single point-estimate values rather than stochastically as in this study, the variability in probable worm burdens would not be apparent due to the fact that there could be only one output – a single worm count value – for any two single input combinations of haemoglobin and body weight.

The results of model simulations indicated that if rainfall, as a major factor in the development of haemonchosis, were to be used as a risk indicator at some time between the two samples on 10 December and 7 January and if the animals had been FAMACHA©-evaluated to enable application of the risk model during this period, then the model would probably have indicated that the incidence of clinical disease was increasing rapidly. The logical step would then have been to drench somewhat more liberally, for instance to treat sheep in FAMACHA© categories 2–5, as opposed to only those in FAMACHA© categories 3–5, as recommended for general use by Van Wyk and Bath (2002).

Reynecke et al. (2011a,b) found that it would be realistic to specify a sensitivity of at least 90% at a haematocrit cut-off of not less than 19%, and a FAMACHA© cut point of 2 (i.e. to treat FAMACHA© categories 2–5 inclusive), in order to ensure that at least 90% of truly diseased individuals on this farm are detected and treated for the defined haematocrit cut-off value. Importantly, a selected cut point of 2 would also ensure that at a more conservative cut-off of ≤22%, 83% of sheep with a haematocrit of ≤22% would also be included in the treatment. Realistically, however, the classification error of the evaluator on the farm had the implication that in effect only animals in FAMACHA© categories 4 and 5 were being treated, instead of all those in categories 3–5 throughout the year, as recommended by Van Wyk and Bath (2002). Had the latter occurred, it seems likely that the levels of worm infection would not have been as high as was recorded.

The high level of infection reached on 7 January was exacerbated by an extended period of almost four weeks between sampling events, with no anthelmintic treatments, instead of the weekly evaluations recommended for the relatively short period of the peak worm season (Van Wyk and Bath, 2002). Had the recommended approach been followed, the large peak in infection on 7 January, with cases of sheep at grave risk in FAMACHA© categories 4 and 5, would probably have been considerably lower, since stragglers would have been detected and dewormed at an earlier stage while leaving sufficient sheep truly in FAMACHA© categories 1 and 2 untreated for sustainable levels of refugia (Van Wyk, 2001).

The RAMREP class was at a higher risk of disease than the EWEREP class throughout the season, even in "low-risk" samples such as on November 19 and January 17, when respectively 70% and 90% of the RAMREP sheep were evaluated to be in FAMACHA© category 1 (Fig. 5b). Also, at the last sampling event all five of the FAMACHA© categories were present for the RAMREP class, compared to only categories 1, 2, and 3 for EWEREP. It is also apparent from Fig. 6a and b that the probability that animals in the EWEREP and RAMREP classes had respectively more than 3300 and 8000 worms is small, and the probability that an animal sampled from the EWEREP class had ≤1000 worms was approximately 0.75, compared to only 0.27 for the RAMREP class. Also, at the highest risk of disease on 7th January, the minimum haemoglobin level resulting in a worm count of ≤1000 worms for the EWEREP and RAMREP classes was estimated to be 7.05 g/dl and 7.92 g/dl, respectively, representative of an acute (Reinecke, 1983) or moderate (Hansen and Perry, 1994) infection.

Rams are usually heavier than ewes of similar age, but in the present case the difference in mean body weight was only 2.3 kg on 24 April, although with a higher degree of variability of mean body weight for RAMREP than for EWEREP. While it is unlikely that the two flocks were exposed to similar worm challenge, as they had never shared a pasture but were only rotated on the same pastures with other animals not in the trials, it is noteworthy that the RAMREP had much higher simulated worm burdens than the EWEREP in every one of the five years of the study.

The mean haemoglobin values listed above for the two classes of sheep would be the minimum that would have to be maintained by selective drenching, to be able to maintain worm burdens under the selected pathogenic

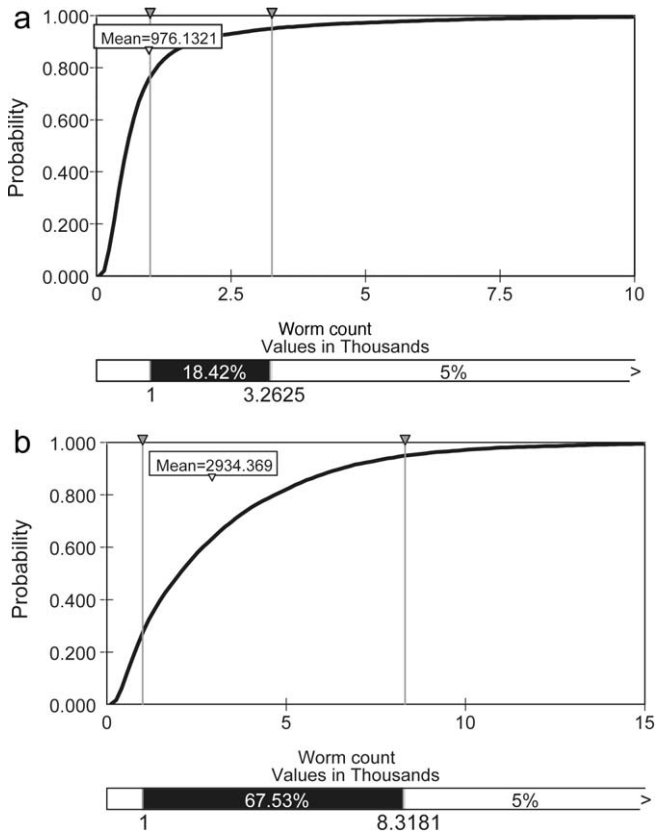

Fig. 6. (a) Ascending cumulative output distribution for worm count for the EWEREP class, 7 January. Refer to text. (b) Ascending cumulative output distribution for worm count for the RAMREP class, 7 January. Refer to text.

threshold of 1000 *H. contortus*. Rams had a three-fold higher overall probability of exceeding the threshold of 1000 worms in the sample than ewes, and the probable mean haemoglobin level for the EWEREP class on 7 January was 7.6 g/dl, compared to 5.6 g/dl for the RAMREP class (data not shown). Thus the mean EWEREP worm burden would be maintained below the threshold of 1000, while the opposite is true for the RAMREP class. Furthermore, only about 20% of the EWEREP class would have had a worm burden of between 1000 and 3262, while approximately 68% of the RAMREP class, would have had a burden of been between 1000 and 8318 (Fig. 6a and b).

In addition to other factors, such as seasonal differences in nutrition and risk of heavy worm challenge, the class of animal will play an important role in selecting a threshold for disease risk estimation. For instance, in the initial trial demonstrating the usefulness of conjunctival colour variation for evaluating the effect of *H. contortus* challenge, Malan and Van Wyk (1992) and Malan et al. (2001) reported that, compared to 83% of dry ewes and 71% of heavily pregnant ewes, only 45% of lactating ewes managed to withstand the reigning severe *Haemonchus* challenge without treatment during the five months' duration of their trial.

The relatively frequent evaluations required with the FAMACHA© system of TST, (something that is impractical for economic and logistical reasons with lab-based diagnostic tests) result in series of data sets suitable for retrogressive analysis for automated decision support modelling as in the present study. A useful spin-off is that it enables continual adjustment of the level of treatment intervention over the course of the year in relation to a variety of factors, such as reigning level for worm challenge and the susceptibility and value of the animals concerned, for instance by varying the intervals between evaluations and the proportions of animals to examine and treat per flock. While faecal worm egg counts rise to much higher levels in most TST systems than in the conventional strategic drenching approach (Van Wyk, 2008; Van Wyk et al., 2001; Van Wyk and Bath, 2002), this is offset by the relatively frequently repeated individual evaluation of the animals concerned.

The question is, however, what would alert a farmer to the possibility of malfunctioning of the FAMACHA© system, such as consistently incorrect levels of classification, which, as on the farm concerned in this paper, could endanger FAMACHA© application. While as yet there is no definite answer to this, an automated computer-assisted decision support such as envisaged by Van Wyk and Reynecke (2011), could be of benefit. For instance, Reynecke (2007) found that rainfall events, expressed as rainfall entropy, had potential as a predictor for subsequent levels of worm infection in the present data set. Thus it seems likely that a farmer could be alerted and/or the matter could be inves-

tigated on-farm if a discrepancy were to develop between FAMACHA© evaluation results and expected levels of worm infection as predicted from daily rainfall figures.

A decided disadvantage of the Roberts and Swan (1982) algorithm used in the present work is that it requires weight as an input, which is much more time-consuming than doing only clinical FAMACHA© and Body Condition Scoring evaluations. To some extent this can be overcome by weighing only a portion of each flock that is evaluated by TST systems, but even this is less than ideal since many farmers do not have scales and farmers are notoriously inaccurate at estimating live weights (Besier and Hopkins, 1988). In other words, the search should continue for a model based purely on clinical evaluation for mapping variations in the effect of rising and falling levels of worm challenge over each year.

5. Conclusion

Although further work is needed, the preliminary indications are that the model presented here should allow a rapid initial assessment of the health of a flock when used in conjunction with FAMACHA©, as the main clinical indicator of haemonchosis.

The model output was a consistently good fit to the observed trend in FAMACHA© proportions and the attendant variability in body weight of sheep through a given worm season. The model presents a unique opportunity to be able without the need for consistent laboratory intervention, for a farmer through clinical evaluation and weighing to obtain a profile for haemonchosis that is not only site-, but also flock and animal class specific.

Acknowledgments

This work was carried out within the Framework Agreement between the Directorate General for Development Cooperation, Belgium and the Institute of Tropical Medicine, Antwerpen (Belgium – Grant No AG534) with the Department of Veterinary Tropical Diseases of the University of Pretoria Faculty of Veterinary Science, and with the support of the EU "PARASOL" FOOD-CT-2005-022851 FP6 project. Without the enthusiastic disregard of Mr Johann Bührmann for the risks involved in evaluating such an unconventional new system as FAMACHA© over years under commercial farming conditions on his farm, this work could not have materialised. Mrs Rachel Coetzee was responsible for the data capture and management.

References

Barnes, E.H., Dobson, R.J., Barger, I.A., 1995. Worm control and anthelmintic resistance: adventures with a model. Parasitol. Today 11, 56–63.

Bath, G.F., Malan, F.S., Van Wyk, J.A., 1996. The FAMACHA© ovine anaemia guide to assist with the control of haemonchosis. In: Proceedings of the 7th Annual Congress of the Livestock Health and Production Group of the South African Veterinary Association , Port Elizabeth, pp. 5–7.

Besier, R.B., Hopkins, D.L., 1988. Anthelmintic dose selection by farmers. Aust. Vet. J. 65, 193–194.

Bisset, S.A., Van Wyk, J.A., Morris, C.A., Stenson, M.O., Malan, F.S., 2001. Phenotypic and genetic relationships amongst FAMACHA© score, faecal egg count and performance data in Merino sheep exposed to *Haemonchus contortus* infection in South Africa. In: Proc. 5th Internat. Sheep Vet. Congr. , Stellenbosch, S. Afr (CD).

Dobson, R.J., 1999. Modelling and forecasting. Int. J. Parasitol. 29, 93–94.

Gauly, M., Kraus, M., Vervelde, L., Van Leeuwen, M.A.W., Erhardt, G., 2002. Estimating genetic differences in natural resistance in Rhön and Merino Landsheep following experimental *Haemonchus contortus* infection. Vet. Parasitol. 106, 55–67.

Gettinby, G., 1989. Computational veterinary parasitology with an application to chemical resistance. Vet. Parasitol. 32, 57–72.

Greer, A.W., Kenyon, F., Bartley, D.J., Jackson, E.B., Gordon, Y., Donnan, A.A., McBean, D.W., Jackson, F., 2009. Development and field evaluation of a decision support model for anthelmintic treatments as part of a targeted selective treatment (TST) regime in lambs. Vet. Parasitol. 164, 12–20.

Hall, R., Malia, R.G., 1984. Medical Laboratory Haematology. Butterworth and Co, London.

Hansen, J., Perry, B., 1994. The Epidemiology, Diagnosis, and Control of Helminth Parasites of Ruminants. International Laboratory for Research on Animal Diseases, Nairobi.

Jain, N.C., 1993. Essentials of Veterinary Haematology. Lea and Febiger, New York.

Klein, S.L., 2000. The effects of hormones on sex differences in infection: from genes to behaviour. Neurosci. Biobehav. Rev. 24, 627–638.

Kenyon, F., Greer, A.W., Coles, G.C., Cringoli, G., Papadopoulos, E., Cabaret, J., Berrag, B., Varady, M., Van Wyk, J.A., Thomas, E., Vercruysse, J., Jackson, F., 2009. The role of targeted selective treatments in the development of refugia-based approaches to the control of gastrointestinal nematodes of small ruminants. Vet. Parasitol. 164, 3–11.

Learmount, J., Taylor, M.A., Smith, G., Morgan, C., 2006. A computer model to simulate control of parasitic gastroenteritis in sheep on UK farms. Vet. Parasitol. 142, 312–329.

Leathwick, D.M., Waghorn, T.S., Miller, C.M., Atkinson, D.S., Haack, N.A., Oliver, A.M., 2006. Selective and on-demand drenching of lambs: impact on parasite population and performance of lambs. New Z. Vet. J. 54, 305–312.

Malan, F.S., Van Wyk, J.A., 1992. The packed cell volume and colour of the conjunctiva as aids for monitoring *Haemonchus contortus* infestation in sheep. In: Proc. S. Afr. Vet. Ass. Biennial Nat. Vet. Congr. , Grahamstown, p. 139.

Malan, F.S., Van Wyk, J.A., Wessels, C.D., 2001. Clinical evaluation of anaemia in sheep: early trials. Onderstepoort J. Vet. Res. 68, 165–174.

McCulloch, B., Kuhn, H.G., Dalbock, R.R., 1984. The relation of climate and topography to worm egg counts of gastro-intestinal nematodes of sheep in the eastern Cape. Onderstepoort J. Vet. Res. 51, 223–238.

Owen, N.C., 1968. The pathological physiology of haemonchosis in sheep. MMedVet(Physiology) Thesis, University of Pretoria.

Reinecke, R.K., 1983. Veterinary Helminthology. Butterworth Publishers, Durban/Pretoria.

Reynecke, D.P., 2007. Software-based decision-support: a basis for the development of a predictive system for sustainable management of haemonchosis in small ruminants. PhD Thesis, University of Pretoria.

Reynecke, D.P., Van Wyk, J.A., Gummow, B., Dorny, P., Boomker, J., 2011a. Validation of the FAMACHA© eye colour chart using sensitivity/specificity analysis on two South African commercial sheep farms. Vet. Parasitol., doi:10.1016/j.vetpar.2009.08.023.

Reynecke, D.P., Van Wyk, J.A., Gummow, B., Dorny, P., Boomker, J., 2011b. Use of Receiver Operating Characteristic curves for selection of treatment thresholds using the FAMACHA© diagnostic system for anaemia in sheep. Vet. Parasitol., doi:10.1016/j.vetpar.2010.12.030.

Riley, D.G., Van Wyk, J.A., 2009. Genetic parameters for FAMACHA© score and related traits for host resistance/resilience and production at differing severities of worm challenge in a Merino flock in South Africa. Vet. Parasitol. 164, 44–52.

Roberts, J.L., Swan, R.A., 1982. Quantitative studies of ovine haemonchosis. 2. Relationship between total worm counts of *Haemonchus contortus*, haemoglobin values and body weight. Vet. Parasitol. 9, 201–209.

Smith, G.S., 1994. So you want to write a model. In: Scott, M.E., Smith, G.S. (Eds.), Parasitic and Infectious Diseases: Epidemiology and Ecology. Academic Press Limited, London (Chapter 2).

Stockham, S., Scott, M.A., 2002. Fundamentals of Veterinary Clinical Pathology. Iowa State Press, Ames.

Van Wyk, J.A., 2001. Refugia—overlooked as perhaps the most potent factor concerning the development of anthelmintic resistance. Onderstepoort J. Vet. Res. 68, 55–67.

Van Wyk, J.A., 2008. Production trials involving use of the FAMACHA© system for haemonchosis in sheep: preliminary results. Onderstepoort J. Vet. Res. 75, 331–345.

Van Wyk, J.A., Bath, G.F., 2002. The FAMACHA© system for managing haemonchosis in sheep and goats by clinically identifying individual animals for treatment. Vet. Res. 33, 509–529.

Van Wyk, J.A., Bath, G.F., Groeneveld, H.T., Stenson, M.O., Malan, F.S., 2001. Extensive testing of the FAMACHA© system for accuracy of clinical evaluation of anaemia caused by ovine haemonchosis. In: Proc. 5th Internat. Sheep Vet. Congr. , Stellenbosch, S. Afr (On CD).

Van Wyk, J.A., Reynecke, D.P., 2011. Blueprint for an automated specific decision support system for countering anthelmintic resistance at farm level. Vet. Parasitol. 177, 212–223.

Vose, D., 1998. The application of quantitative risk assessment to microbial food safety. J. Food Protect. 61, 640–648.

Vose, D., 2000. Risk Analysis: A Quantitative Guide. Wiley, Chichester.

Waghorn, T.S., Leathwick, D.M., Miller, C.M., Atkinson, D.S., 2008. Brave or gullible: testing the concept that leaving susceptible parasites in refugia will slow the development of anthelmintic resistance. N. Z. Vet. J. 56, 158–163.

Waghorn, T.S., Miller, C.M., Oliver, A.M.B., Leathwick, D.M., 2009. Drench-and-shift is a high-risk practice in the absence of refugia. N. Z. Vet. J. 57, 359–363.