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Geometric means provide a biased efficacy result when conducting a faecal egg count reduction test (FECRT)

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ABSTRACT

The process of conducting a faecal egg count reduction test was simulated to examine whether arithmetic or geometric means offer the best estimate of efficacy in a situation where the true efficacy is known. Two components of sample variation were simulated: selecting hosts from the general population which was modelled by the negative binomial distribution (NBD), and taking an aliquot of faeces from the selected host to estimate the worm egg count by assuming a Poisson distribution of sample counts. Geometric mean counts were determined by adding a constant (C) to each count prior to log transformation, C was set at 25, 12 or 1. Ten thousand Monte Carlo simulations were run to estimate mean efficacy, the 2.5% (lower) and the 97.5% (upper) percentile based on arithmetic or geometric means. Arithmetic means best estimated efficacy for all different levels of worm aggregation. For moderate levels of aggregation and with $C = 1$ the geometric mean substantially overestimated efficacy. The bias was reduced if C was increased to 25 but the results were no better than those based on arithmetic means. For very high levels of aggregation (over-dispersed populations) the geometric mean underestimated efficacy regardless of the size of C. It is recommended that the guidelines on anthelmintic resistance be revised to advocate the use of arithmetic means to estimate efficacy.

1. Introduction

As anthelmintic resistance emerges in a parasite population it has been recommended that resistance be declared when a faecal egg count reduction test (FECRT) result is less than 95% efficacy or if the lower confidence limit is below 90% (Anon, 1989; Coles et al., 1992). Both these publications advocate the use of arithmetic means in preference to geometric means to estimate efficacy and provide methodology for determining the 95% confidence interval for the estimate of efficacy. However, more recent publications have advocated the use of geometric means (Wood et al., 1995; Smothers et al., 1999; Vercruysse et al., 2001) for determining efficacy in controlled slaughter test and FECRT.

There is little disagreement that when conducting an ANOVA or testing the differences between two means of a parasite population the data should be transformed (e.g. using logs or roots) so that variances between groups are more homogenous. However it cannot be assumed that the best transformation to stabilise variances is also the best to determine efficacy (Dash et al., 1988). We set out to explore this question using Monte Carlo simulation where the true efficacy was set at the "critical" point of 95% (Miller et al., 2006). If efficacy is 100%, or so low that all treated animals exhibit positive counts, then the choice of either geometric or arithmetic mean is of little consequence. However, when a proportion of the pre- or post-treatment counts are zero the choice of mean can make a substantial difference to the resulting efficacy. To

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estimate the geometric mean where some zero counts are present in a data set, a constant (C) must be added prior to a log transformation as otherwise the geometric mean becomes zero. Donald et al. (1978) found that log (count+25) was most effective for stabilizing variances when analysing tracer sheep worm counts. Dash et al. (1988) suggested that the value added to each count should be half the minimum detection level. We therefore explored different values for C for estimating the geometric mean for comparison with the arithmetic mean and assumed a detection level of 25. Vidyashankar et al. (2007) present methods for determining efficacy, particularly for relatively small samples, that do not require transformation of the data. They achieve this by developing a statistical model for the change in pre- to post-treatment counts which is independent of distributional assumption for the raw data.

The negative binomial distribution (NBD) is considered to adequately model egg and worm count data (Morgan et al., 2005; Barger, 1985), and the aggregation parameter k for the NBD typically varies from 0.2 to 2.3 for commercial flocks. If k is large (say greater than 10) the NBD of parasite counts within a flock begins to approach the normal distribution where the mean is a good measure of central tendency. When k is small then the NBD is skewed towards the vertical (left) axis with many animals having a relatively low count and a few animals having very high counts (i.e. highly aggregated or "over-dispersed" populations). Separate Monte Carlo simulations were run to explore the impact of a range of k values on the appropriate mean to use in a FECRT. The Poisson distribution is used to describe counts that arise as a result of a random process or if objects are randomly distributed, such as worm eggs in a sample volume of liquid drawn from a larger agitated volume. When the expected number of counts is low the Poisson is skewed to the left (like the NBD) but as the expected number of counts increases (say greater than 15) the Poisson distribution tends to become symmetric about the mean.

Table 1
Sample data from one Monte Carlo iteration for NBD with mean 300 and $k = 2$.

Pre-treatment count		Post-treatment count	
True count	Observed count	True count	Observed count
146	100	7	50
354	225	18	25
420	325	21	50
188	175	9	0
250	300	13	0
255	300	13	0
125	100	6	0
313	350	16	0
422	450	21	0
496	325	25	0
292	275	15	25
220	175	11	50
156	100	8	0
367	275	18	0
185	125	9	0
219	150	11	0
178	250	9	0
428	675	21	0
336	300	17	0
41	50	2	0
AM			
270	251	13	10
GM $C = 1$			
238	213	12	1
Efficacy from arithmetic mean			96.0%
Efficacy from geometric mean $C = 1$			99.3%
Efficacy from geometric mean $C = 12$			97.6%
Efficacy from geometric mean $C = 25$			96.9%

Efficacy was determined for observed counts from arithmetic (AM) and geometric means (GM). For the latter the constant (C) of 1, 12 or 25 was added to each count prior to log transformation.

2. Materials and methods

2.1. Data Generation

In Table 1 the 20 "true" counts were a random sample drawn from a negative binomial distribution (NBD) with a mean of 300 and a dispersion parameter k of 2. The "observed" count was obtained from the true count by taking a random Poisson sample (Morgan et al., 2005) for each true value as follows. Each true count was divided by the detection or multiplication factor (set here to 25); this result was set as the expected number of eggs to be found in the Poisson distribution from which the observed sample count was drawn (total eggs counted); the randomly sampled eggs counted were then multiplied by the detection factor to give the observed count. To obtain a 95% reduction in an FECRT the true post-treatment count was set to 5% of the true pre-treatment count, the observed post-treatment count was obtained by taking a Poisson sample as described above. For example, in line 1 of Table 1: 146/25 = 5.84 expected eggs; however only 4 eggs were drawn for this particular random sample (assuming a Poisson distribution with mean 5.84) to yield an observed count of 100. Random variables (NBD and Poisson) and Monte Carlo simulations were generated using PopTools (CSIRO, Australia) within Excel (Microsoft, Inc., USA).

2.2. Efficacy Estimates

For n animals with count X_i for the i-th animal, efficacy was determined by:

Arithmetic mean count $\mu = \frac{\sum X_i}{n}$ for $i = 1, \ldots, n$

Geometric mean count $\mu = \left\{10^{\left(\left[\sum \log(X_i + C)\right]/n\right)}\right\} - C$ for $i = 1, \ldots, n$ and $C \geq 1$

Percent efficacy $E = 100\left(1 - \frac{\mu_t}{\mu_u}\right)$ where μ_t and μ_u are the mean for