

USING SAS® FOR A BOOTSTRAP ANALYSIS OF REPEATED MEASURES ECTOPARASITICIDE DATA

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Introduction

A basic experiment to test the effects of several ectoparasiticide formulations consists of several treatments applied once plus a negative control where the effect of the parasiticides are observed at several time points. At each time point all animals in the experiment have a fixed number of parasites (e.g. fleas or ticks) applied to them, and after a set time such as a day or so, each animal is inspected and the number of remaining parasites are counted. The usual counting technique is to thoroughly comb the animal in the case of companion animals such as dogs or cats. The efficacy of a formulation is estimated by Abbott's formula:

$$\% \text{ Efficacy} = [(C - T) / C] * 100$$

where C is the mean count of the control animals and T is the mean count of the formulation treatment. In practice, either arithmetic or modified geometric means may be used. The efficacy estimate is computed at each time point for each formulation and tabulated. The time points do not need to be uniformly spaced but are spaced to observe the profile of efficacy over time.

The usual question for this type of experiment is whether a formulation shows adequate efficacy at a given time where "adequate" is defined by the regulatory authorities to be 90% or better. In practice, this level is applied to experiments where each treatment and the control all have the same number of animals tested, usually 3 to 6 animals per treatment. While various formulations may be compared to each other at a fixed time, the first point of the experiment is to estimate an effect, and there is no real reason to test a treatment against the control for significance. The time in the experiment where there is no significant difference between the control and the treatment is long past the time the formulation would be useful. So, following the orientation of my parasitologist colleagues, the focus will be on the primary measurement of efficacy and not on the means themselves.

The reason a bootstrap analysis is used as opposed to more common analyses is that a non-parametric method is needed. Particularly for earlier times, the count for a treatment may be zero on all animals tested. However, the count on each control animal might be 50 to 100, and for the last couple of time points the count for a treatment will tend to rise. Hence, the means may have very different variances both within and between treatments. Neither the assumption of a normal nor a Poisson distribution can be justified for these data. Also, the efficacy statistic is a ratio so that the distribution would have an extra level of complexity.

While the techniques in this paper allow for comparisons of treatments, the emphasis will be first on estimation and the establishment of standard errors of estimates. Comparisons between treatments at a fixed time and comparisons within a treatment between times will be made using confidence intervals instead of hypothesis tests. By taking the differences between these estimates, an analog to treatment by time interaction can be estimated and differences in efficacy over time compared.

Standard Errors

In order to establish an estimated standard error of efficacy a bootstrap computation may be carried out (Efron and Tibshirani, 1993). Table 1 gives an example set of ectoparasiticide data showing ectoparasite counts at five time points. At each time 100 ectoparasites were applied to each animal and after a fixed period the remaining parasites were counted.

Table 1. A Repeated Measures Ectoparasiticide Efficacy Study

Dog	Trt*	Count Time 1	Count Time 2	Count Time 3	Count Time 4	Count Time 5
A11	1	6	0	0	1	1
A12	1	8	0	0	0	3
A13	1	11	0	0	0	1
A14	1	5	0	0	2	5
A15	1	19	1	0	4	8
A16	1	7	0	7	3	36
A21	2	9	0	0	0	1
A22	2	3	0	0	0	1
A23	2	14	0	1	1	0
A24	2	2	0	0	3	2
A25	2	3	3	2	0	25
A26	2	6	0	0	0	1
A31	3	0	0	0	4	83
A32	3	10	0	0	2	15
A33	3	8	0	0	1	27
A34	3	13	0	0	41	92
A35	3	21	1	5	3	51
A36	3	14	0	11	0	36
AC1	C	71	83	89	87	77
AC2	C	77	72	76	82	84
AC3	C	81	91	90	93	91
AC4	C	79	96	83	88	80
AC5	C	86	76	72	59	73
AC6	C	94	79	80	78	88

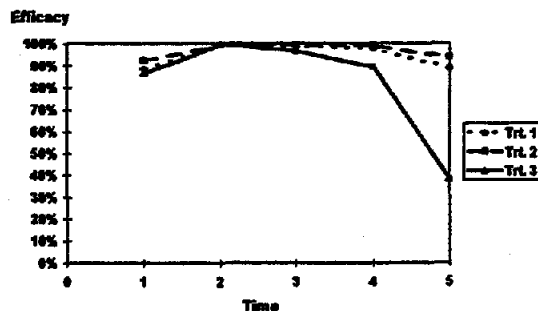
* Note: "C" is the control; 3 is a standard formulation; 1 & 2 are new formulations.

From the data in Table 1, the efficacy results using Abbott's formula are summarized in Table 2 and Figure 1. Arithmetic means were used, but by adding one to each value a geometric mean can be computed and one subtracted from this mean to give a modified geometric mean. The modification is needed to handle the zero values.

Table 2. Efficacy of Treatments as Measured by Abbott's Formula.

Treatment	Time 1	Time 2	Time 3	Time 4	Time 5
1	89%	100%	99%	98%	89%
2	92%	99%	99%	99%	94%
3	86%	100%	97%	90%	38%

Figure 1. Efficacy over Time as Computed by Abbott's Formula.



To compute a bootstrap estimate of efficacy and the standard error of the efficacy, a sample with replacement of size six (the number of observations in the treatment group) is selected from a treatment group and a sample with replacement of size six is selected from the control group. The efficacy is computed by Abbott's formula, and the whole process is repeated many times, say 1000. The mean and standard deviation of the 1000 efficacy values computed from the bootstrap samples provide an estimate of the efficacy and a standard error of the efficacy, respectively. A simple confidence interval can be constructed using percentiles of the 1000 efficacy values.

The actual computations to establish the bootstrap samples and the efficacy computations for each bootstrap sample can be accomplished using the SAS® data steps within a set of macros (SAS Institute Inc., 1990a). These macros are briefly described in the Appendix. For each treatment, select a sample of animals with replacement equal in size to the number of animals observed with the treatment. Using this so called bootstrap sample, compute the mean at each time point. These means are an observation in a temporary data set established for that treatment. Each possible bootstrap sample is selected and the means computed for the sample. Hence, for the data in Table 1, there are 46,656 possible bootstrap samples for Treatment 1 and 46,656 observations in the temporary data set. These observations are essentially vectors of means with each variable representing a different time and are created by the macro SETUP described in the Appendix. Once the data sets are established, an observation is randomly selected from the Treatment 1 data set of means and an observation is randomly selected from the control treatment data set of means. This is accomplished using the SET statement with a POINT option where the pointer is a randomly selected value. The NOBS option on the SET statement informs the data step how many vectors of means there are for the treatment. Assuming the option is NOBS=numobs, the pointer is selected by the code: $i = \text{int}(\text{ranuni}(\text{seed}) * \text{numobs}) + 1$. The array statement allows the data step to store a series of means from the Treatment in temporary variables before reading the means from the control. For each time point, the efficacy is computed so that a vector of efficacies is established with the efficacy at each time in a different variable. The vector of efficacies is added to a new data set. The random selection and creation of a vector of efficacies is repeated many times, say 1000, and is a set of bootstrap samples. This set may be investigated with procedure MEANS (SAS Institute Inc., 1990b) or procedure CAPABILITY (SAS Institute Inc., 1989b) to compute point estimates (the mean of the 1000 values for each time), standard errors (the standard deviation of the 1000 values for each time), and confidence intervals (the 5th and 95th percentiles of the 1000 values for each time for 90% confidence intervals).

Efron and Tibshirani (1993) suggest that for estimating a standard error, there need be 25 to 100 repeated sets of bootstrap samples, but for computing confidence intervals 500 to 1000 repeats are needed (see Ch. 19). Since confidence intervals will be used to make comparisons and establish a range of possible efficacy, the number of bootstrap samples is taken as the larger amount.

Since the data are repeated measures on the same animal, the bootstrap samples are not taken independently at each time point. Rather, the animals are sampled and a vector of counts at the observation times is recorded. The bootstrap sample is reduced to the sufficient statistics, the means, containing all useful information from the sample. This sampling retains the relationship among the means through time. Hence, when a vector of efficacies is computed from a randomly selected vector of treatment means and a randomly selected vector of control means, the relationship of the efficacies through time is also retained. The treatment and control samples are taken separately because we are not interested in creating a permutation test of the treatment against the control. A quick inspection of the data shows the obvious difference between each treatment and control. (Formal statistical tests bare out the significance of this difference.) Once the computational price is paid to create these vectors of means, the rest of the computations in this paper are quite rapid. The results of a bootstrap computation are summarized in Table 3. Arithmetic means were used in the analysis.

Table 3. Efficacy of Treatments by Bootstrapping Abbott's Formula.

Treatment	Time 1*	Time 2	Time 3	Time 4	Time 5
1	88% (2.4%)	100% (0.2%)	99% (1.2%)	98% (0.8%)	89% (5.9%)
2	92% (2.1%)	99% (0.6%)	99% (0.4%)	99% (0.5%)	94% (4.6%)
3	86% (3.2%)	100% (0.2%)	97% (2.1%)	90% (7.4%)	38% (14.4%)

* Bootstrap Efficacy Estimate (Standard Error of Estimate)

In comparing Tables 2 and 3, the estimated efficacies are nearly equal. The size of the standard error relative to the estimate shows that there is some skewness to the distribution of the estimate. Finally, the estimates and standard errors are sufficient to make some conclusions overall. The treatments do not differ through Time 3, and Treatments 1 and 2 do not differ and are effective through Time 5. The results in Table 3 also point to an obvious problem with the regulatory standard of declaring protection to be adequate with a point estimate of 90% efficacy. A better practice would be to make a lower limit on a lower confidence limit of a specified level of confidence. Using the percentiles of the 1000 bootstrap samples, a 90% lower confidence limit at Time 5 for Treatment 1 is 81% and for Treatment 2 is 89%. Given the current standard, insisting that a lower 90% confidence limit exceed 90% to show adequate efficacy would be a far more stringent requirement, but changing the standard to require this limit to exceed 80% or 85% might be reasonable.

Comparisons Between Treatments within a Time Point

A more thorough answer may be given to the basic question in formulation experiments of whether a formulation is improved at a particular time over another. The data of Table 1 are from an experiment where Treatment 3 is a standard treatment of known efficacy, and an improvement at Time 5 was desired. In what follows, T_{ij} = the mean of the i^{th} treatment at the j^{th} time, C_j = the mean of the control at the j^{th} time, and E_{ij} = the efficacy of the i^{th} treatment at the j^{th} time. The difference in Treatments 1 and 3 at Time j is

$$E_{1j} - E_{3j} = (C_j - T_{1j})/C_j - (C_j - T_{3j})/C_j = (T_{3j} - T_{1j})/C_j$$

which can be bootstrapped the same as the efficacy itself. In this case, three samples with replacement of size six are taken, one from each treatment and one from the control. The difference in efficacy is computed, and the process is again repeated many times.

All of this can be accomplished in a SAS® data step. Three random pointers are selected and the data sets containing the means for Treatments 1 and 3 and for the control are each read using the SET statement with a POINT option. As each data set is read, the values are stored using an array into temporary variables, and once the means are all read in, the formula can be computed for each time point and the results outputted to a new data set. This process is repeated many times to build up the bootstrap distribution. Again, procedure MEANS and other SAS summary procedures can be used to generate the basic statistics for the bootstrap distribution.

Table 4 gives the comparison results at the various times for the example data:

Table 4. Efficacy Differences at Fixed Times
Computed by the Bootstrap.

Treatment Difference	Time 1*	Time 2	Time 3	Time 4	Time 5
1-3	1.7% (3.2%)	0.0% (0.2%)	1.5% (2.0%)	7.1% (6.1%)	42% (12%)
2-3	5.1% (3.0%)	-0.3% (0.5%)	2.2% (1.7%)	8.2% (6.2%)	46% (12%)
1-2	-3.2% (2.5%)	0.3% (0.5%)	-0.6% (1.1%)	-1.0% (0.7%)	-3.8% (6.1%)

* Bootstrap Estimate of Difference in Efficacy (Standard Error of Estimate)

Many of the entries in Table 4 are smaller than a simple subtraction of entries in Table 3 suggest should be the case. While in most cases the differences are only slightly smaller than expected, and in fact are hardly bigger than rounding would account for, the differences between Treatments 1 or 2 and Treatment 3 at Time 5 are considerably less than expected and are 0.6 to 0.9 of the standard error. Hence, when the differences are large, there is a downward bias in the method, but the bias is not too serious for comparing efficacies in the 90% and higher range. While in this case there is no mistaking that Treatment 3 is considerably reduced in effectiveness at Time 5 relative to the other two treatments, if the situation were a closer call, techniques to correct for bias might be useful. Finally, a comparison of the standard errors shows the positive correlation between the two efficacy measurements in the computation. This correlation stems from the fact that although the treatment means are independent, both efficacies are shifted down or up together according to the observed control values.

Comparisons Across Time

In order to determine how long a treatment needs to establish initial effectiveness and to determine if a treatment is maintaining effectiveness at later times, the efficacy can be compared across time. The improvement in efficacy for treatment i from Time 1 to Time 2 is

$$E_2 - E_1 = (C_2 - T_{2i})/C_2 - (C_1 - T_{1i})/C_1$$

and similar formulas can be written down for each pair of times. These differences can be bootstrapped to get estimates of differences, but care must be taken that the same animals are used for both times within the same bootstrap sample as described earlier. The SAS® code in a data step implementing the estimation of the comparisons is similar to the code used to compute the vector of efficacies when building the bootstrap data set of efficacies. An observation of means from the treatment is randomly selected, an observation of means from the control is randomly selected, and the computation is completed and stored in a new data set. For convenience, several comparisons can be made using a single pair of randomly selected observations of means. The resulting new data set of bootstrap values can be investigated using summary procedures. Example results are presented in Table 5.

Table 5. Bootstrapped Efficacy Differences Between Times for Each Treatment.

Treatment	Time 1 - Time 2*	Time 2 - Time 3	Time 3 - Time 4	Time 4 - Time 5
1	-11.1% (2.3%)	1.2% (1.3%)	0.7% (1.2%)	9.0% (5.8%)
2	-6.9% (2.3%)	-0.0% (0.3%)	0.3% (0.7%)	5.1% (4.7%)
3	-13.3% (3.2%)	3.1% (2.0%)	7.2% (8.2%)	51.1% (10%)

* Bootstrap Estimate of Difference in Efficacy (Standard Error of Estimate)

Interpreting Table 5, for all three treatments there is a significant improvement in efficacy for each treatment from Time 1 to Time 2. Also, there is a significant drop in efficacy from Time 4 to Time 5 for Treatment 3 and there is evidence that Treatment 1 is coming to the end of its usefulness by Time 5. A 98% confidence interval for the difference for Treatment 1 between Times 4 and 5 is [1.2%, 25%], so the drop in efficacy in the last period is significant.

Comparing Tables 2 or 3 with Table 5, there is little bias in the estimated differences. The standard error for the comparison of Times 4 and 5 for Treatment 3 (10%) is much smaller than might be expected from Table 3 if the efficacy measurements were independent [$15.8\% = \sqrt{(7.4\% \cdot 7.4\% + 14\% \cdot 14\%)}$]. The correlation through time due to repeated measurement of the same animal has been captured by the sampling of vectors of counts through time.

In addition to pairwise comparisons of efficacies, more complicated combinations are useful for determining the length of effectiveness. Often the length of time between observations in the design of the experiment reflects an assumption that within one time interval, if the treatment is near the end of its useful protection, the change will be obvious in the efficacy measurement. In the current data, once the startup of efficacy is completed by Time 2, there is a period of extremely high efficacy followed by a slight decline and ultimately total failure of the treatment to continue protection. To observe these changes, a series of contrasts can be set up comparing each efficacy with the mean of the prior efficacies observed at earlier times. In the repeated measures analysis of variance (ANOVA) setting, these contrasts would be orthogonal and can be implemented with procedure GLM (SAS Institute Inc., 1989a). The time variables must be entered in reverse order in the model statement, and the Helmert option would be used in the repeated statement. For the current data set, since the full efficacy is reached only by Time 2, the Time 1 efficacy results are omitted from these contrasts. (This is common and expected in certain cases of these experiments.) The SAS® data step code would be modified only in the formula for the efficacy comparison. The random selection of two vectors (observations) of means would be the same. Table 6 shows the outcome of these contrasts for each treatment.

Table 6. Bootstrapped Efficacy Contrasts Among Times for Each Treatment.

Treatment	[Times 2 + 3 + 4]/3 - Time 5*	[Times 2 + 3]/2 - Time 4	Time 2 - Time 3
1	9.7% (5.5%)	1.2% (0.7%)	1.2% (1.3%)
2	5.4% (4.3%)	0.2% (0.8%)	0.0% (0.3%)
3	58.1% (13%)	8.8% (7.7%)	3.0% (2.1%)

* Bootstrap Estimate of Contrast in Efficacy (Standard Error of Estimate)

Although perhaps not apparent from Table 6, all the drops in efficacy at Time 5 from the mean of the other times are significant. The lower 1% confidence limit is greater than zero in all cases. For Treatment 1, the drop at Time 4 has a lower 5% confidence limit of 0.2%, and so the small drop in efficacy is significant. No other contrasts in the table are significant. While the drop in Treatment 3 at Time 5 has already been noted, the other treatments are not quite as effective at Time 5, and had the experiment continued, efficacy may have dropped well below the 90% cutoff.

The fact that Treatment 2 has a significant drop at Time 5 relative to the mean of Times 2 through 4 shows that the bootstrap distribution of values can be quite skewed. Although the point estimate of the drop is 5.4% with a standard error of 4.3%, the 5th percentile is 0.5% and the lower 1st percentile is 0.2%. Because of the skewness care needs to be taken in the use and interpretation of the standard errors for any of bootstrap estimates.

Comparing the estimates in Table 6 with Tables 2 or 3, there is again little bias in the estimated contrasts. The magnitude of

the standard errors as compared to Table 3 again shows the effect of correlation between time points.

Interaction of Time and Treatment

Basic to repeated measure experiments is the comparison of the pattern of changes over time among treatments. In an ANOVA setting, this would be a test of interaction. Rather than attempt an overall test for interaction, we can more usefully make a series of orthogonal contrasts which when tested in an ANOVA setting would partition the interaction sum of squares. These contrasts have an interpretation directly related to a meaningful result concerning efficacy. As an example, while it is obvious that Treatments 1 and 2 differ in their pattern over time from Treatment 3, we can directly measure how much Treatments 1 and 2 differ from each other. For each contrast through time in either Table 5 or 6, the bootstrap technique may be applied to the difference between Treatments 1 and 2 in that contrast. As in the comparison within a single time between treatments, the bootstrap sampling must be done taking a single sample with replacement of control animals and a sample with replacement from each of the two treatments to be compared. Since all treatments and the control have six animals, all three samples are of size six. Again as in the comparisons over time, the whole vector of counts is sampled, and the treatments are not sampled separately at each time.

The SAS® data step code must select a vector (observation) of means at random from each of two treatments and a vector of means from the control. The formulas for comparing each treatment across time are computed, and the difference between these results for the two treatments is the estimate of interaction. The code is very similar to that previously discussed.

Table 7 shows the outcome of the interaction of time and treatment for the difference in the first two times and for each time contrast in Table 6 with each pair of treatments.

Table 7. Bootstrapped Efficacy Interactions of Time and Treatment.

Treatment Comparison	Time 1 - Time 2*	[Times 2 + 3 + 4]/3 - Time 5	[Times 2 + 3]/2 - Time 4	Time 2 - Time 3
1 v 2	-4.5% (3.2%)	4.4% (6.7%)	1.0% (1.0%)	1.2% (1.4%)
1 v 3	2.0% (3.7%)	-48.8% (14.4%)	-7.6% (7.7%)	-1.9% (2.5%)
2 v 3	6.2% (4.0%)	-52.2% (14.4%)	-8.5% (8.2%)	3.1% (2.0%)

* Bootstrap Estimate of Interaction Between Time Contrast in Efficacy with Treatment Pair (Standard Error of Estimate)

The first column of comparisons in Table 7 is for the initial establishment of efficacy. While Treatments 1 and 2 appear that they might have an interaction over the first two periods, a 90% confidence interval for the interaction contrast is [-9.8%, 0.6%], so that a significant interaction does not exist. (The limits are the 5th and 95th percentiles of the 1000 bootstrap samples.) An 80% confidence interval is [-8.4%, -0.2%], so at the 20% level of significance there is an interaction. Similarly for Treatments 2 and 3, a 90% confidence interval is [-0.9%, 13%], and an 80% confidence interval is [0.8%, 12%]. Again the existence of an interaction has only marginal evidence. If an interaction existed, the rate of attaining optimum efficacy would differ between treatments. The significantly large (in magnitude) interactions concern Time 5 and Treatment 3. There is no significant interaction between Treatments 1 and 2, so that their behavior over the total time period studied is the same.

By comparison of Table 7 with Table 6, there is little or no bias in the estimates.

Speed Considerations

The computations to produce the analyses in this paper were done on a Compaq Deskpro 4000 running at 166 MHz with 32 Mb of RAM using SAS Version 6.12 under Windows 3.1. They took only a couple of minutes. However, a key technique was to use half of the RAM as a ram disk and use this disk as the working directory. If a hard disk is used to house the working directory, the computations take much longer, as much as 10 to 15 times as long.

The programming was not as efficient as could be achieved in some cases by computing only, say, 1000 vectors of means chosen at random from each treatment and then using all of this same sample to compute the efficacies and their comparisons. This is in contrast to the algorithm actually used which first created all possible vectors of means for each treatment and then drew a sample from this set. For 6 animals per treatment, there are 6⁶ or 46,656 possible vectors of means, so the savings would be substantial especially if a hard disk was required for the working directory, and for more than 6 per treatment, reprogramming to sample the vector of means would be required. For 5 animals per treatment, there are 5⁵ or 3125 possible vectors, so the savings is neither much nor really necessary. For 3 or 4 animals per treatment, computing all possible vectors of means is more efficient. The method used was chosen to allow for the creation of a single set of macros that would handle all the situations normally faced at Schering-Plough.

Conclusion

The bootstrap has been shown to be a reasonable tool in the analysis of an ectoparasiticide experiment retaining the essential repeated measures nature of the data in the analysis. The focus of the analysis can remain on the primary measure of efficacy used by parasitologists, yet a standard error can be provided with the estimate. The assumptions of an ANOVA or a generalized linear model are not needed, and no particular problem is raised by an abundance of zeros at some times. By constructing appropriate contrasts of the efficacies, meaningful estimates and tests can be formulated. The bootstrap estimates have little important bias except when comparing treatments far from the 90% level of efficacy, a situation with little practical importance.

The results presented vary slightly due to the sampling error introduced by taking only 1000 bootstrap samples. While this error can be reduced by taking more bootstrap samples, many runs of several different programs showed only the slightest variation between results, and 1000 samples seems adequate. All programming was done in SAS using the data step to take bootstrap samples and compute efficacies and their differences. The bootstrap estimates, standard errors, and confidence intervals were computed using procedures MEANS and CAPABILITY (SAS Institute Inc., 1989b).

References

- Efron, B. and R. J. Tibshirani. 1993. An Introduction to the Bootstrap. New York: Chapman & Hall.
- SAS Institute Inc. 1989a. SAS/STAT® User's Guide, Version 6, Fourth Edition, Volume 2. Cary, NC: SAS Institute Inc.
- SAS Institute Inc. 1989b. SAS/OC® Software: Reference, Version 6, First Edition. Cary, NC: SAS Institute Inc.
- SAS Institute Inc. 1990a. SAS® Language: Reference, Version 6, First Edition. Cary, NC: SAS Institute Inc.
- SAS Institute Inc. 1990b. SAS® Procedures Guide, Version 6, Third Edition. Cary, NC: SAS Institute Inc.

Appendix

For the macros used in the bootstrap analysis to work, the data are assumed to be structured in a repeated measures format. All

the observed counts through time for a particular animal must be in different SAS variables. The name given to each of these variables must have a common root followed by a number possibly indicating the day of the study on which parasites were applied. Also, there must be a variable to specify the treatment applied to the animal. Other variables are allowed, such as a variable to identify the animal, but they are not needed. For example, in Table 1, the variable names are ANIMAL, GROUP, TIME1, TIME2, TIME3, TIME4, TIME5 in the data set PARASITE. Only GROUP and TIME1 through TIME5 are required, and TIME1 through TIME5 could have been named TIME3, TIME7, TIME14, TIME21, and TIME28 reflecting the days of infestation.

The names of the macros used for the bootstrap analysis are listed with their calling parameters:

To establish the traditional Abbott's formula results use:

`%tradeff(data set name, treatment variable, control value, response variable names)`

To do a bootstrap analysis use:

`%setup(data set name, treatment variable, response variable names)`
- establish the working data sets needed by the other routines. This must be run prior to any of the following macros.

`%effic(treatment variable, control value, response variable names)`
- establish a bootstrap estimate of the distributions of the efficacy statistics using a sample of possibilities.

`%efficx(treatment variable, control value, response variable names)`
- establish a bootstrap estimate of the distributions of the efficacy statistics using all possibilities.

`%compare(control value, first treatment value, second treatment value, response variable names)`
- compare the efficacies of two treatments by timepoint.

`%day2day(control value, first treatment value, second treatment value, response variable names)`
- compare the efficacies across time within two treatments.

`%interact(control value, first treatment value, second treatment value, response variable names)`
- test for time by treatment interactions for two treatments.

The following are example calls to these macros using the PARASITE data set:

```
%tradeff(parasite,group,C,Time1 Time2 Time3 Time4 Time5);  
%setup(parasite,group,Time1 Time2 Time3 Time4 Time5);  
%effic(group,C,Time1 Time2 Time3 Time4 Time5);  
%efficx(group,C,Time1 Time2 Time3 Time4 Time5);  
%compare(C,1,2,Time1 Time2 Time3 Time4 Time5);  
%day2day(C,1,2,Time1 Time2 Time3);  
%interact(C,2,3,Time2 Time3 Time4 Time5);
```

The code for the macros may be obtained from the author via e-mail. Contact the author at DamonDisch@AOL.COM.