META-ANALYSIS OF MULTIPLE TREATMENTS EXPERIMENTS

Samuel D. Zapata
Assistant Professor and Extension Economist, Department of Agricultural Economics, Texas A&M AgriLife Extension Service, Texas A&M University, Weslaco, TX.
samuel.zapata@ag.tamu.edu

Terry W. Griffin
Assistant Professor and Cropping Systems Economist, Department of Agricutlural Econmics, Kansas State Research and Extension, Kansas State Univeristy, Manhatta, KS.
twgriffin@ksu.edu

Selected Paper prepared for presentation at the MAER-Net 2016 Colloquium, Hendrix College, Conway, AR, September, 15-17 2016

Meta-Analysis of Multiple Treatments Experiments

Many scientific experiments involve the evaluation of m treatments (i.e., $m > 2$). For example, consider a group of independent agricultural field researchers mutually interested in finding the optimal rate of nitrogen to apply to corn. To this aim, these scientists might conduct a series of asynchronous experiments to test the effect of a discrete set of different nitrogen levels on corn yield. Without loss of generality, a group of comparable independent studies can be represented by:

$$Y_{ijk} = f(X_{ij}|\boldsymbol{Z}_j) + \varepsilon_{ijk}, \quad (1)$$

where Y_{ijk} is the kth observed response associated to the ith treatment level of the jth experiment, $f(\cdot)$ is a function that represents the conditional mean function of Y_{ij} given X_{ij} and $\boldsymbol{Z}_j$, X_{ij} is the finite value of the ith treatment level in the jth experiment, $\boldsymbol{Z}_j$ is a vector of intrinsic characteristic of the jth experiment, and ε_{ijk} is an random experiment error term assumed to be indepent with mean zero and variance σ_j^2. Note that under this setting $f(X_{ij}|\boldsymbol{Z}_j) = \bar{Y}_{ij}$ represents the ith treatment effect under jth experiment conditions.

The effect size of interest (X^*) of each considered study is the optimum level of X. Namely, the level of the treatment factor X that maximizes or minimizes Y. The standard statistical technique for multiple treatment level experiments is the analysis of variance (ANOVA) utilizing a means separation test such as Fisher's Least Significance Difference (LSD) to identify the "best" treatment. However, the true X^* is commonly not observed because only a discrete set on potential values of X is evaluated on each experiment. Furthermore, given the limited number of observations considered on each experiment it might not be possible to reliably infer the value of the true effect size using individual experiment results alone, especially when those results are reported as discrete categorical rather than continuous data.

There is a need for a reliable and valid method to combine and synthetize this type of research results from existing literature. However, the analysis of multiple treatment studies is an emergent subject of research in the meta-analysis literature, and little conceptual and empirical work has been conducted to evaluate multiple treatment experiments in a meta-analysis framework. The objective of this study is to develop a flexible meta- regression analysis (MRA) method to jointly evaluate multiple treatment experiment results from different available studies.

Meta-Analysis Model

Meta-analysis methods have been used to synthesize research output in areas such as medicine [4], psychology [1], and agriculture [3]. It is common to encounter that only one effect size is reported by each individual study considered in the meta-analysis literature. However, this is not the case for multiple treatment studies, where a mean estimate is reported for each treatment level and the true size effect (X^*) is usually not observed.

When dealing with multiple outcome studies, the traditional approach is to combine the different treatment effects into an unique estimate, and then use standard meta-analysis techniques (e.g., [7,2]). There might be several disadvantages with this 'shrinking' approach. Namely, a reduced number of observations and potential explanatory variables are used on the final meta-analysis, which may result in less precise estimates. Also, in some cases the reported within-study variability cannot be incorporated in the analysis because this metric is only related to the response variable (Y), and not to the treatment factor (X) or size effect (X^*). To overcome these limitations, we proposed a novel MRA model capable to estimate the overall true effect size X^* by only using the typical information reported on each experiment: estimated mean treatment effects and a measure of variability.

Given a collection of M independent and comparable experiments with a finite number of treatment levels, a multiple treatment random effect model is defined as[1]:

$$\bar{Y}_{ij} = g\left(X_{ij}\middle|\boldsymbol{Z}_j\right) + \epsilon_{ij} + e_{ij} \qquad j = 1,2,\dots M \tag{2}$$

where $\bar{Y}_{ij}$ is the observed ith treatment effect of the jth experiment, $g(\cdot)$ is the conditional overall treatment mean, $\epsilon_{ij} \sim N(0, \sigma_\epsilon^2)$ is the between-experiment error, and $e_{ij} \sim N(0, \sigma_{e_{ij}}^2)$ is the within-experiment error. A common correlation is specified to account for the expected dependence among observations from the same experiment. In the absence of the specific variability of each treatment effect, the within-experiment error ($\sigma_{e_{ij}}^2$) could be approximated by $\hat{\sigma}_j^2 / n_{ij}$, where $\hat{\sigma}_j^2$ is replaced by the mean squared error (MSE) obtained from the LSD metric and n_{ij} represents the total number of observations under the ith treatment of the jth experiment. The overall effect size (X^*) is estimated by further defining $g(\cdot)$ as a non-monotonic function of X reaching a global extrema value at X^*. For instance, $g(\cdot)$ might be expressed as a quadratic or plateau function. Moreover, the model in (2) can be used to conduct additional analyses beyond

[1] The MRA model in (2) is a generalization of authors' previous model developed in [5].

the estimation of the true effect size. For example, it can be used to estimate the effect of the treatment factor X on $\bar{Y}$ (i.e., $\partial\bar{Y}/\partial X$), or as a functional form of $\bar{Y}$ in subsequent analyses (e.g., to estimate the economic optimal level of X).

Empirical Application

As proof of concept, an existing series of nitrogen field experiments on corn production were collected from [6]. Fourteen small-plot studies were conducted between 1989 and 1999 in nine counties across southwestern Minnesota. [6] tested a series of nitrogen rates ranging from 0 to 180 pounds per acre in approximately 30 pound increments; with the number of treatment levels differing among experiments. MSE and total number of replications by treatment were calculated from the reported information relative to LSD for each study[2], and used as a proxy for the within-experiment error ($\sigma^2_{e_j}$). The meta-database consists of 86 useful observations.

For illustration purposes, the conditional overall treatment mean $g(\cdot)$ was defined as a linear plateau function. Namely, the model in (2) was specified in terms of the nitrogen rate (N) and a time trend (T):

$$\bar{Y}_{ij} = \beta_0 + \beta_1 N_{ij} + \beta_2 T_j + \epsilon_{ij} + e_{ij} \quad \text{if } N_{ij} < N^* \tag{3}$$

$$\bar{Y}_{ij} = Y^* + \epsilon_{ij} + e_{ij} \quad \text{if } N_{ij} \geq N^*,$$

where the β's are yield response parameters, N_{ij} is the treatment level associated with $\bar{Y}_{ij}$, $N^*$is the nitrogen level required to reach the plateau (i.e. where additional nitrogen has no effect on yield), Y^* is the expected yield plateau, and independence is assumed across the two random components. Furthermore, the variance-covariance matrix is specified as a block diagonal matrix with block corresponding to the experiments and with each block having a compound-symmetry structure (i.e., diagonal elements equal to $\sigma^2_\epsilon + \sigma^2_{e_{ij}}$ and off-diagonal elements equal to σ^2_ϵ).

Estimation results are presented in Table 1. Empirical results suggest that before corn yield reaches a plateau, yield increases at a rate of 0.40 bu/acre with each additional pound of nitrogen applied. Also, corn yield has been increasing by 3.73 bu/acre every year. Lastly, corn yield is expected to reach a plateau at a nitrogen rate of 82.75 lb/acre such that increased yield was not expected beyond this level of nutrient application.

[2] Two experiments reported no numerical LSD, in those cases the LSD was replaced by the yield range as a conservative proxy. The number of replications were stated to be between four to six although no information were given specifically to each field study; therefore it was assumed that each field study had four replications.

Table 1. Model Parameter Estimates

Parameter	Estimate	Standard Error	*t*-value	*p*-value
β_0	116.95	11.03	10.60	<0.001
β_1	0.40	0.04	11.30	<0.001
β_2	3.73	1.67	2.24	0.028
N^*	82.75	10.12	8.18	<0.001
σ_ϵ^2	504.06	213.95	2.36	0.020

Summary and Conclusions

Despite the growing interest of meta-analysis, limited attention has been given to analyze and combine research output from multiple treatment studies. The main objective of this study was to extend the current meta-analysis literature by developing a flexible econometric model to evaluate multiple treatment data. The proposed method is based on random effects meta-regression and mixed effects models. Estimation approach was illustrated on an agricultural application.

References

[1] Barrick, M.R. and M.K. Mount. 1991. The Big Five Personality Dimensions and Job Performance: A Meta-Analysis. Pers Psychol 44(1): 1-26.

[2] Borenstein, M., L.V. Hedges, J.P.T. Higgins, and H.R. Rothstein eds. 2009. Introduction to meta-analysis. John Wiley & Sons, Ltd., New York, New York, USA 450 pp.

[3] Burzaco, J.P., I.A. Ciampitti, and T.J. Vyn. 2014. Nitrapyrin impacts on maize yield and nitrogen use efficiency with spring-applied nitrogen: Field studies vs. meta-analysis comparison. Agron J 106(2): 753-760.

[4] Caldwell, B., S. Aldington, M. Weatherall, P. Shirtcliffe, and R. Beasley. 2006. Risk of cardiovascular events and celecoxib: a systematic review and meta-analysis. J Roy Soc Med 99(3): 132-140.

[5] Griffin, TW. and S.D. Zapata. 2016. Optimal Cotton Insecticide Application Termination Timing: a Meta-Analysis. *Journal of Economic Entomology*. 109 (4): 1698-1705.

[6] Randall, G., M. Schmitt, J. Strock and J. Lamb. 2013. Validating N rates for corn on farm fields in southern Minnesota. University of Minnesota Extension. Available at: http://ow.ly/km1z300fQGJ [April, 2016].

[7] Rosenberg, M.S., K.A. Garrett, Z. Su, and R.L. Bowden. 2004. Meta-analysis in plant pathology: Synthesizing research results. Phytopathology 94(9): 1013-1017.