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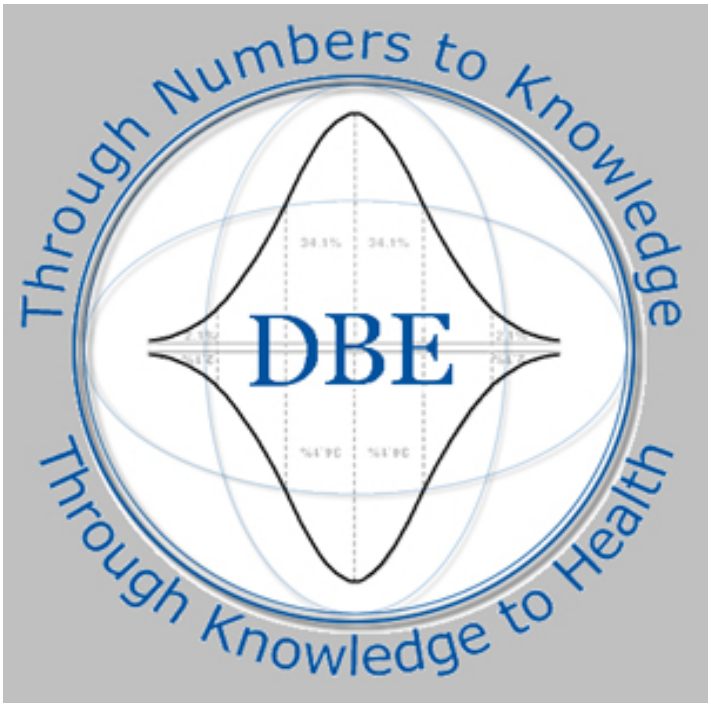

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Measuring the Impact of Biostatistical Methods on General Medical Research

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Abstract

Background: Novel statistical methods are constantly being developed within the context of biomedical research; however, the rate of diffusion of this knowledge into the field of general / internal medicine is unclear. This study highlights the statistical journal articles, the statistical journals, and the statistical methods that appear to be having the most direct impact on research in the field of general / internal medicine.

Methods: Descriptive techniques, including analyses of articles' keywords and controlled vocabulary terms, were used to characterize the articles published in statistics and probability journals that were subsequently referenced within general / internal medicine journal articles during a recent 10-year period (2000-2009).

Results: From the 45 statistics and probability journals of interest, a total of 597 unique articles were identified as being cited by 900 (out of a total of about 10,501) unique general / internal medicine journal articles. The most frequently cited statistical topics included general/other statistical methods, followed by epidemiologic methods, randomized trials, generalized linear models, meta-analysis, and missing data.

Conclusion: As statisticians continue to develop and refine techniques, the promotion and adoption of these methods should also be addressed so that their efforts spent in developing the methods are not done in vain.

Keywords: bibliometrics; biostatistical methods; general/internal medicine; journal impact factor

Introduction

Novel statistical methods are constantly being developed. The traditional routes of disseminating the new techniques typically involve presentations at local, regional, or national research meetings and publication in peer-reviewed statistical journals. However, it is unclear how effective these communication strategies are at having measureable impact on real-world problems, such as in the field of general/internal medicine research.

One way of measuring a journal article's influence is by counting how often it is cited in other publications. Although sometimes criticized for doing so [1-4], journals themselves use varieties of impact factors to measure their influence and to attract article submissions. These impact factors are based, in part, on citation frequency counts. Even though the journal impact factor is recognized as an imperfect measure, it is nonetheless considered one of the "best" ways to evaluate the "quality" or influence of a journal. For a number of reasons, prior research suggests that articles in statistical journals have slower rates of citation diffusion than are typically seen in other disciplines [5].

In this study, we were interested in determining which statistical articles, statistical journals, and statistical methods have the most direct impact on research in the field of general / internal medicine. This was accomplished using descriptive techniques involving statistical journal articles and general / internal medicine articles published during a recent 10-year period (2000-2009).

Methods

The first step was to identify the journals in the "Statistics and Probability" category so defined in the Journal Citation Reports Science Edition from Thomson Reuters, Philadelphia, PA. Sorted according to

their 2009 calculated Impact Factor, the top 40 journals (whose impact factor ranged from 1.13 to 4.00) were then selected for this study. In addition, we augmented this list with 5 other journals (*Canadian Journal of Statistics*, *Journal of Multivariate Analysis*, *Journal of Statistical Planning and Inference*, *Scandinavian Journal of Statistics*, and *Statistica Sinica*) that are focused in the area of biostatistical methodology that were believed (*a priori*) to contain methods possibly cited frequently in the general / internal medicine literature. For each of the 45 individual journals (Table 1), we searched the ISI Web of Science (ISIWoS) Science Citation Index Expanded Database to identify published articles in the ISIWoS category labeled "Medicine, General and Internal" that cited one or more articles in the statistics/probability journal of interest. For the purposes of this study, both the *citing* article and the *cited* article must have been English language manuscripts published during the years 2000 through 2009. We also counted the total number of journal articles (including original and review articles and any published corrections) categorized as "Medicine, General and Internal" during the study time period.

The processes described above resulted in two lists, one of articles in the general/internal medicine category that cited one or more articles in the statistics/probability category, and the other a list of articles in the statistics/probability category cited by one or more articles in the general/internal medicine category. The lists were managed in MS Excel 2007 (Redmond, WA) and Thomson Reuters EndNote X3 (Philadelphia, PA). For each of the statistics/probability articles, we counted the number of times each was cited by articles in the general/internal medicine listing.

For each of the cited articles, we also retrieved the National Library of Medicine's controlled vocabulary Medical Subject Headings (MeSH) and/or author-assigned keywords, when available. In order to obtain some type of understanding of the nature of the articles being cited, these MeSH and author-assigned keywords were mapped to one or more of the following broader methodological categories: analysis of

correlated data, Bayesian methods, bias, bioinformatics methods, computer simulation, diagnostic testing, econometrics, epidemiology, general/other statistical terms, generalized linear models, meta-analysis, missing data, multiple comparisons, non/semi-parametrics, psychometrics, randomized trials, reproducibility of results, sample size / power estimation, statistical software, study design, survival analysis, and non-statistical terms (including demographics, medical terms, etc.). The mapping was independently reviewed by two biostatisticians (PJN and AEW), and a consensus was reached on each term's / keyword's category mapping for any discrepancies.

Using the techniques described, several characteristics of the cited articles were examined, including the most frequently cited journal articles and journals. In addition, we were able to characterize the most frequently cited biostatistics methods using a simple descriptive analysis of the MeSH / keyword mappings.

Results

From 2000 through 2009, the ISIWoS search resulted in the identification of a total of 10,501 unique English language journal articles published in the field of general / internal medicine. Of these 10,501 articles, 900 (8.6%) included a citation of at least one of the 45 statistics and probability journals of interest published during the assigned time frame. Some of the general medical articles cited more than one statistics and probability article, for a total of 1,636 citations of 597 unique statistics and probability articles. Among individual cited articles, the median number of citations was four, with 19.7% of the articles being cited only once. Table 2 lists the top 10 most frequently cited statistics and probability journal articles, which together accounted for 18.5% of all the citations. Of these 10 articles, the focal topics that emerged included meta-analysis, publication bias, missing data, econometrics, and prognostic models.

Table 3 lists the top 10 most frequently cited statistics and probability journals from the general / internal medicine journal articles. Of the 1,636 citations, *Statistics in Medicine* accounted for n=744, or 45.0%, of the total, followed by *Statistical Methods in Medical Research* (n=157, 9.6%) and *Biometrics* (n=136, 8.3%). Some of the 45 journals were never cited in the general medical literature during this study time frame.

In Table 4, each of the keyword mapping categories is displayed, along with the most frequently occurring individual keyword terms included in the categories and the citation frequencies associated with the categories. Aside from non-statistical terms, general/other statistical keywords were cited most often (n=2,959 citations), followed by terms classified under the headings of epidemiology (n=1,023), randomized trials (n=998), generalized linear models (n=656), meta-analysis (n=547), and missing data (n=482). There are more citations than articles simply due to the fact that each citing article may cite multiple statistics and probability articles, which, in turn, often include multiple keywords.

Discussion

This study highlights relative trends from 2000-2009 in the applications of statistics and probability within the general and internal medicine research literature. Less than 9% of the medical journal articles cited an article published in any statistics and probability journal during this time period. Among 597 cited statistics and probability articles, the 10 most frequently cited articles address topics including meta-analysis, publication bias, methods for handling missing data, econometrics, and prognostic models. Three journals (*Statistics in Medicine*, *Statistical Methods in Medical Research,* and *Biometrics*) accounted for 62.9% of all the citations within 900 unique general / internal medicine journal articles. Overall, the most frequently cited statistical keywords were classified as general/other statistical terms,

followed by epidemiology, randomized trials, generalized linear models, meta-analysis, and missing data.

In many respects, the results of the keyword analysis in this citation study are not entirely surprising. General and internal medicine research is essentially focused on identifying risk factors for disease, identifying optimal treatments, and finding ways to prevent disease, which typically rely on epidemiologic techniques and randomized clinical trials. If we had conducted a similar study from an earlier decade (e.g. 1980-1989 or 1990-1999), the topics identified may have been quite similar to the ones we highlight in this paper. In fact, a paper in 2005 featured the then top 25 most-cited statistical papers of all time[6], and the top 10 papers addressed topics including survival analysis[7-10], multiple comparisons[11], least squares estimation[12], measurement agreement[13], randomized trials[9, 14], bootstrapping[15], epidemiological methods[16].

From our study it is clear that general/internal medicine researchers definitely recognize the need for sound biostatistical methods related to meta-analysis, handling missing data within studies, using computer simulation, analysis of correlated data, and understanding the influence of various biases. In some respects however, our study may illustrate a different problem - the fact that relatively few general/internal medicine research articles are referencing novel statistical methods. Perhaps the biostatistical community needs to consider better ways of disseminating their findings. Van Nierop (2009) argues using diffusion curve analysis that it simply takes longer for articles in statistical journals to become frequently cited[5]. There is an entire branch of translational research dealing with the science of dissemination (typically of evidence-based treatments)[17], and there may be lessons learned in that arena which could help biostatisticians promote better methodological practices. Using an analogy involving drug development, if resources spent on the successful discovery of a new drug do not result in the drug being used to treat/prevent disease, then resources have been wasted. Similarly, if

resources are used to develop novel/improved statistical methods that are never utilized, then resources have again been wasted. As with a new treatment that has been developed, successful communication and dissemination of novel biostatistical methods will likely need to involve *promoting* the ideas, *adapting* them to different settings, and *revising* the methods to make them better.

Our study is limited by several factors. There are novel and improved statistical methods that are published in journals that do not focus on statistical methods (e.g. clinical journals, bioinformatics journals) and would not have met the criteria for being included in this study; however, identifying such articles would have required more resources (e.g. having to search and review perhaps tens of thousands of journal articles) than were available for this study. Also, since our time frame for the cited articles coincided with that of the citing articles, it is possible that there may already exist published novel statistical methods, not identified in this study, that may ultimately be extremely influential in future general/ internal medicine research. In other words, a highly innovative and useful statistical method published in 2009 may not start being cited frequently for a few years outside of this study's time frame.

The field of developing statistical methods has a bright future. With emerging emphases from the National Institutes of Health on topics such as translational research, comparative effectiveness research, community-based participatory research, and personalized medicine, it will be imperative that statisticians continue to develop and refine techniques to ensure accurate analyses and efficient uses of resources. However, they should also be mindful of finding optimal ways to promote and market their methods so that the effort for having developed the methods is not done in vain. Such techniques might include writing easily adapted computer programs (e.g. SAS ® macros, R packages), presenting methods within clinical scientific settings (from local journal clubs to international gatherings), or providing more user-friendly descriptions of the techniques on internet sites and/or via social media

applications.

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4. Ryan TPW, W.H. The most-cited statistical papers. *Journal of Applied Statistics.* 2005;32(5):461-474.

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10. Marquardt DW. An algorithm for least squares estimation of non-linear parameters. *Journal of the Society for Industrial and Applied Mathematics.* 1963;2:431-441.

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12. Litchfield JT, Jr., Wilcoxon F. A simplified method of evaluating dose-effect experiments. *J Pharmacol Exp Ther.* Jun 1949;96(2):99-113.

13. Felsenstein J. Confidence limits on phylogenies: an approach using the bootstrap. *Evolution.* 1985;39:783-791.

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15. Dearing JW. Evolution of diffusion and dissemination theory. *J Public Health Manag Pract.* Mar-Apr 2008;14(2):99-108.

Table 1. Journals used in the analysis (in alphabetical order).

Journal Title
American Statistician
Annals of Applied Probability
Annals of Applied Statistics
Annals of Probability
Annals of Statistics
Biometrical Journal
Biometrics
Biometrika
Biostatistics
Canadian Journal of Statistics*
Chemometrics and Intelligent Laboratory Systems
Computational Statistics and Data Analysis
Econometric Reviews
Econometrica
Environmental and Ecological Statistics
Finance and Stochastics
Fuzzy Sets and Systems
IEEE/ACM Transactions on Computational Biology and Bioinformatics
Journal of Business and Economic Statistics
Journal of Chemometrics
Journal of Computational and Graphical Statistics
Journal of Computational Biology
Journal of Multivariate Analysis*
Journal of Quality Technology
Journal of Statistical Planning and Inference*
Journal of Statistical Software
Journal of the American Statistical Association
Journal of the Royal Statistical Society (A: Statistics in Society)
Journal of the Royal Statistical Society (B: Statistical Methodology)
Multivariate Behavioral Research
Pharmaceutical Statistics
Probabilistic Engineering Mechanics
Probability Theory and Related Fields
Scandinavian Journal of Statistics*
Stata Journal
Statistica Sinica*
Statistical Applications in Genetics and Molecular Biology
Statistics and Computing
Statistical Methods in Medical Research
Statistical Science
Statistics in Medicine
Stochastic Environmental and Research Risk Assessment
Stochastic Processes and their Applications
Technometrics
TEST

* Not one of the top 40 journals as ranked by the 2009 Science Citation Index impact factor

Table 2. Top 10 statistical journal articles most frequently cited within general / internal medicine research articles, 2000-2009.

Full Citation	Citation Count
Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics*, 2000, 56(2): 455-463.	66
Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine*, 2002, 21(11): 1539-1558.	44
Duval S, Tweedie R. A nonparametric "trim and fill" method of accounting for publication bias in meta-analysis. *Journal of the American Statistical Association*, 2000, 95(449): 89-98.	36
Altman DG, Royston P. What do we mean by validating a prognostic model? *Statistics in Medicine*, 2000, 19(4): 453-473.	31
Royston P. Multiple imputation of missing values. *Stata Journal*, 2004, 4(3): 227-241.	29
Thompson SG, Higgins JP. How should meta-regression analyses be undertaken and interpreted? *Statistics in Medicine*, 2002, 21(11): 1559-1573.	24
Bradburn MJ, Deeks JJ, Berlin JA, Russell Localio A. Much ado about nothing: a comparison of the performance of meta-analytical methods with rare events. *Statistics in Medicine*, 2007, 26(1):53-77.	23
Royston P. Multiple imputation of missing values: Update of ICE. *Stata Journal*, 2005, 5(4): 527-536.	18
Bang H, Tsiatis AA. Estimating medical costs with censored data. Biometrika, 2000, 87(2): 329-343.	16
Barber JA, Thompson SG. Analysis of cost data in randomized trials: an application of the non-parametric bootstrap, *Statistics in Medicine*, 2000, 19(23): 3219-3236.	16

Table 3. Top 10 most frequently cited statistics and probability journals

Journal Title	Citation Frequency
Statistics in Medicine	744
Statistical Methods in Medical Research	157
Biometrics	136
Stata Journal	122
Biostatistics	104
Journal of the American Statistical Association	74
American Statistician	51
Pharmaceutical Statistics	37
Statistical Science	36
Biometrika	32

Table 4. Keyword mappings categories and citation frequencies

Keyword mapping category	Common individual keywords within mapping category	Number of times keyword mapping category was cited
General/other statistical	models, statistical; data interpretation, statistical; biometry	2,959
Epidemiology	risk factors; risk; epidemiologic methods	1,023
Randomized trials	randomized controlled trials as topic; clinical trials as topic; treatment outcome	998
Generalized linear models	analysis of variance; regression analysis; logistic models	656
Meta-analysis	meta-analysis; metaregression; inverse probability weighted estimation	547
Missing data	missing data; multiple imputation; missing at random	482
Study design	research design; design; 2-period crossover design	415
Computer simulation	computer simulation; Monte Carlo method; Markov chains; bootstrap	388
Analysis of correlated data	cluster analysis; longitudinal studies; mixed models	348
Bias	bias (epidemiology); publication bias; file drawer problem	347
Survival analysis	survival analysis; proportional hazards models; survival-time	347
Statistical software	Software; st0067 (a stata program for multiple imputation); databases, factual	307
Bioinformatics methods	models, biological; oligonucleotide array sequence analysis; gene expression profiling	241
Bayesian methods	Bayes' theorem; Winbugs; empirical Bayes	238
Sample size / power estimation	sample size; power; statistical	185

	power	
Econometrics	cost-benefit analysis; cost analysis; costs and cost analysis	175
Non/Semi-parametrics	statistics, nonparametric; semiparametrics; nonparametric estimation	161
Diagnostic testing	sensitivity and specificity; ROC curve; predictive value of tests	137
Psychometrics	psychometrics; kappa statistic	69
Reproducibility of results	reproducibility of results	68
Multiple comparisons	Bonferroni procedure; false discovery rate; multiple comparisons procedures	42
Non-statistical terminology	humans; female; male	6,830

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