Editorial

Conducting Clinical Research and Getting the Report Published

Providing satisfactory care and making a living are probably the two most common goals of the everyday practicing surgeon, whereas the goal implied by "publish or perish" is probably not very important to anyone who is not employed at an academic institution. Nonetheless, publication of the results of clinical research is a crucial part of the transfer of knowledge, and remains a worthwhile endeavor for foot and ankle surgeons everywhere. For this reason, clinicians should understand the way in which clinical questions become publishable research projects. For surgeons who want to publish their work, attention to a few important concepts will increase the likelihood that their work will get accepted for publication in a peer-reviewed biomedical journal. These key elements include reliable results, protocol development, prospective versus retrospective approaches, and attention to the particular journal's guide for authors.

The basis of a publishable paper is reliable results, the kind that can be used to formulate valid conclusions. Reliable results, and conclusions that are likely to be valid, are procured with the use of a study design (Table 1) that employs the building blocks of good clinical evidence (Table 2). Without results, there really is nothing to publish. To obtain useful results, surgeons need to plan their investigation so that their methodology reduces bias and answers the research question. To this end, perhaps the most fundamental consideration is whether or not the investigation proceeds in a prospective or retrospective fashion.

A prospective investigation is one that entails designing the study, including the specific data to be collected and the statistical plan, prior to collecting any of the data. A prospective investigation conveys a number of advantages, not the least of which is that the investigators can decide from the start whether they want to conduct an experiment to compare treatments (a randomized controlled trial), or if they want to observe a cohort of patients over time to see what outcomes develop. All of the important variables can also be identified prior to data collection. Prospective investigations provide the highest level of clinical evidence (Table 3). Drawbacks to the prospective design are the time and money necessary to conduct the investigation, difficulty studying a rare disease or treatment, the need to monitor safety and outcomes prior to the planned conclusion of the study, and the statistical quandary brought on by the influence that multiple looks at the data (over time) have on the assumption of data independence, since many of the most commonly used statistical analyses are based on the probability that the measured variables are unrelated and normally distributed. Thus, prospective investigations yield the highest level of clinical evidence even though they are not easy to do in a clinical setting unless a research-oriented infrastructure is already in place. And this is the difficulty faced by most busy surgeons trying to conduct a quality clinical investigation, and the reason why most authors write about cases that they have already treated in the past.

A retrospective investigation entails collecting and analyzing data that already exist. The primary advantage of a retrospective investigation is the availability of data, whether the topic of interest is a rare case or a treatment that has already been undertaken. Beyond this, however, the retrospective design imparts a number of obstacles that confer bias and threaten the validity of any claim to a causal relationship. The most common problems include missing variables and changes to the relationship between patients and their environment over time. To overcome the problem of unmeasured variables, say, for instance, the number of cigarette smokers in a study that focuses on bone healing, a sensitivity analysis can be useful (1). A sensitivity analysis is an analytical tool that is used to determine the resistance of one's results, and the conclusions based on those results, to the presence of a hypothetical variable that has an association with the outcome of interest as well as the independent variables that were actually measured. Without knowing the results of a sensitivity analysis, readers will question the authors' conclusions since variables that any reasonable surgeon would consider important were not taken into account.

Other fundamental elements of the investigative protocol (Table 4) include clearly stated primary and secondary aims. By convention, published reports typically specify the hypothesis, as well as the study design (Table 1), at the end of the introduction, immediately preceding the detailed description of the patients (materials) and methods used to conduct the investigation. It is also necessary to define the patient population, or sample, that was studied; in particular, recruitment and selection methods, as well as specific inclusion and exclusion criteria, need to be clearly

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Table 1
Clinical study designs

Study design	Description
Analytical (hypothesis testing)	
Randomized controlled trial	Experimental (intervention), prospective
Prospective cohort study	Observational, N ≥ 30
Retrospective cohort study	Observational, N ≥ 30
Case-control study	Observational, retrospective
Descriptive (hypothesis forming)	
Analysis of secular trends	Cohort, change over a long period, ecologic
Cross-sectional study	Events at a point in time, prevalence
Case series	Group, retrospective or prospective
Case report	Rare disease or treatment, retrospective

understood. For interventional experiments, the method of random treatment allocation (sealed envelopes, random number generator, coin flip, or some other method) needs to be described, as it does not suffice to simply say that participants were randomized to different treatments. For prospective investigations, the sample size and statistical power (the ability to detect a significant difference at the desired level of certainty), as well as the level of statistical significance (usually 5%, or $P \leq 0.05$; consistent with a willingness to be incorrect just once out of 20 times), also need to be stated. For retrospective studies, a post hoc power analysis should be undertaken in order to tell the reader just how much power the investigators had to identify a statistically significant difference, especially if such a difference was not identified. This is important because a Type 2 statistical error may have been made, where the authors claimed that a statistically significant difference was not present, however their sample may have actually been too small to allow the difference to be identified.

After defining the population, the dependent (outcome) and independent (demographic exposure or risk factor) variables need to be defined, along with the methods by which these factors were measured. Preferably, health measurement instruments that have been shown to produce valid results are used for this purpose. Such measurements include the 10-cm visual analog scale (VAS) for pain assessment (2-5), the SF-12 (6,7) and SF-36 (8-12) health assessment questionnaires, the Bristol Foot Score (13), and the ACFAS (14) and AOFAS (15) clinical outcome scores, to name a few. In order to limit the influence of bias, outcomes assessors should be blinded to the intervention. Still further, the statistical methods used in the analyses need to be appropriate for the type and distribution of the data, and it is always easiest to employ the expertise of a biostatistician when a prospective investigation is being planned, or prior to collection of already measured data when a retrospective study is undertaken. To be considered publishable, most manuscripts have to include descriptive, comparative, and associative analyses. Descriptive analyses report averages and dispersions, as well as counts and proportions, for the different variables. Typically, the mean is reported with a standard deviation, and a median is reported with a range, for normally distributed continuous numeric and nonparametric categorical data, respectively. Comparative analyses report the results of null hypothesis tests, in order to determine whether or not measured differences were statistically significant, and not just as likely to have been chance observations. Associative analyses calculate odds ratios, relative risks, risk differences, and the like, in order to define the influence that independent variables had, alone and in combination, with the outcome of interest (dependent variable). And, as stated above in regard to retrospective studies, a sensitivity analysis should be reported in order to determine the potential influence that an unmeasured variable (confounder) may have had on the results of a retrospective study.

Table 2
Building blocks of good clinical evidence

1. Explicitly defined research question, population, and end points
2. Randomized treatment allocation and intention-to-treat analysis
3. Participants and outcomes assessors blind to treatment allocation
4. Use of a valid health measurement (quality of life) instrument
5. Power and sample size determined *a priori*
6. Statistical analyses compatible with type and distribution of the data
7. Point estimate and 95% confidence interval reported

Table 3
Levels of clinical evidence

Level	Study design
1	Randomized controlled trial
2	Cohort study
3	Case-control study
4	Case report or series
5	Animal, bench top, computer study

When it comes to preparing a manuscript that reports the results of an investigation, it is extremely important for authors to download, read, and implement the instructions provided in the journal's Guide for Authors, which contains important information on manuscript preparation and revision. The Guide for Authors also details the specific format and style that the particular journal requires. For instance, at *The Journal of Foot & Ankle Surgery*, this information can be downloaded from the Author Information section of the journal's webpage at http://ees.elsevier.com/jfas/default.asp. The contents of the Guide for Authors was also published, as Information for Authors, in the January-February 2009 print issue of *JFAS* (16). Review and implementation of the instructions in the Guide for Authors reduces the likelihood that authors will be required to further revise their manuscript prior to publication, assuming that the editors and peer reviewers find the article relevant and meaningful.

As a rule, authors should read and re-read their work several times before submitting it, and recruit one or two colleagues to read the paper prior to submission since many common errors, such as misspellings and ambiguous references, can be corrected prior to presenting the manuscript to the journal's editors and invited peer reviewers. Let's face it: by the time an author gets a paper to the stage where they feel it is ready for submission to a journal, they are probably so familiar with the contents that their perceived concepts and meanings may not actually match the words on the page. For this reason, asking a colleague to proofread the manuscript can be very helpful. Authors often fail to

Table 4
Elements of the clinical investigational protocol

Aims	Primary, secondary
Population	Who, source, selection; inclusion, exclusion criteria
Dependent variables	Valid health measurements
Independent variables	Risk factors, exposures, demographics
Intervention	Random allocation, consecutive
Assessors	Blinded, biased
Statistical plan	Level of significance; descriptive, comparative, associative results

see the shortcomings of their manuscript until other surgeons with similar expertise and interests have reviewed it. Another helpful tool is to have the manuscript edited by a professional author's editor prior to submission. This type of service is only available at a cost; however the benefits are usually well worth the price when one considers the improvements relative to format, style, and clarity. At *JFAS*, many authors have found the services of a professional medical editor (http://www.tomlangcommunications.com/A1) very helpful in this regard. Authors who have their work reviewed prior to submission are at an advantage in comparison to those that do not, and are more likely to get their paper published.

In conclusion, clinical investigation requires attention to a number of important factors, including the building blocks of good clinical evidence and study design, in order to obtain publishable results. Planning before collecting data is very helpful, and increases the likelihood that one's efforts will not be wasted due to bias that fatally flaws the investigation. Moreover, careful attention to the particular journal's Guide for Authors, as well as their style and formatting requirements, increases the likelihood that the report will get accepted for publication. Having a colleague review the manuscript prior to submission also pays dividends that far exceed the extra work that it takes to ask a fellow surgeon to consider the paper. This overview only scratches the surface of clinical investigation and publication, but does provide a general guide to how to approach an investigation aimed at shedding light on a clinical question.

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