Getting Published in High-Profile Journals

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Where Do You Want to Publish?

- NEJM
- JAMA
- Lancet
Issues

• Very few surgeons routinely publish in the very high impact literature

• Why?
  – Types of research done by surgeons
  – Surgeons are not well funded
  – Surgeons have little presence at the major journals
  – Credibility
  – Quality of Science
What Do the Big Journals Want?

• RCTs
• Meta-analyses (rigorous)
• Practice Changing Findings
• Important Discoveries

• Citations/Impact Factor
Types of research done by surgeons

- Observational
- Case Series
- Quality/Outcomes
RCTs

• Routinely done in Medical Subspecialties (Cardiology, Oncology, GI)
• Need more in Surgery
• More difficult to design than drug trials but not impossible

• JAMA Evidence: Users Guide to the Medical Literature. Guyatt et al.
• Ludwig DS, Ebbeling CB, Livingston EH. Surgical vs
Meta analyses

• Must use rigorous methods
• Follow Guidelines (PISMA, MOOSE etc)
What Does Not Work

- Logistic Regression of Administrative Data
- Volume Outcome
- Single Center Studies
- Case Series
- Retrospective Analyses
- Obvious COI
Business is About Relationships

• So is Publishing
• Get to know editors
• Review papers (in depth)
• Write editorials, reviews
• The big journals are always looking for reviewers and authors
• We tend to publish who we know
Stability

• Editors and staff-15 years with JAMA
• Purposeful-prospective authors should learn who their contacts are
• Work with societies to publish presented papers
• It may not seem like it-but we are in the business of publishing your papers!
How Do Papers Move Through JAMA?

- 6,000 MS’s received each year
- Approximately 4 major papers/week
- Assigned to a specialty contributing editor
- Editor decides to reject/send for peer review
- 2 Content/1 Statistical Reviewer
Editorial Process

- Discuss reviewed papers at bi-weekly editors meeting
- ERBR (editorial review before revision)/Reject/Refer
- ERBR-Repeat re-present at editors meeting
- Accept-Contributing editor edits paper for publication along with copy editors
Paper Structure

• Brevity and Clear Writing
• Abstract-
  – Context: What is the clinical question?
  – Conclusion: Ensure it follows the data
• Introduction
  – 3 Paragraphs
    • Introduction to topic-avoid a summary of what everyone already knows
    • What specific aspect of the clinical problem you will address
    • Explicit statement of a study hypothesis
Paper Structure

• Methods
  – Sufficient detail so others can duplicate study

• Results
  – Include confidence intervals or IQRs for data-never only show point estimates

• Discussion
  – Focused
  – How your findings change clinical thought

• Figure/Tables
  – Visually appealing and simple

• References
  – Complete-make sure you find all pertinent papers-the one you miss is always written by (a now pissed off) reviewer
Common Pitfalls

• Trial registration
  – Intervention trials must be registered BEFORE patients are enrolled

• Study Power
  – Reference prior studies providing assumptions about expected mean, SD etc.
  Rationale for expected differences between groups (MCID)
Common Pitfalls

- Study Design
  - Equivalence
  - Superiority
  - Noninferior
Reporting of Noninferiority and Equivalence Randomized Trials
An Extension of the CONSORT Statement

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The CONSORT (Consolidated Standards of Reporting Trials) Statement, including a checklist and a flow diagram, was developed to help authors improve their reporting of randomized controlled trials. Its primary focus was on individually randomized trials with 2 parallel groups that assess the possible superiority of one treatment compared with another but is now being extended to other trial designs. Noninferiority and equivalence trials have methodological features that differ from superiority trials and present particular difficulties in design, conduct, analysis, and interpretation. Although the rationale for such trials occurs frequently, those designed and described specifically as noninferiority or equivalence trials appear less commonly in the medical literature. The quality of reporting of those that are published is often inadequate. In this article, we present an adapted CONSORT checklist for reporting noninferiority and equivalence trials and provide illustrative examples and explanations for those items amended from the original CONSORT checklist. The intent is to improve reporting of noninferiority and equivalence trials, enabling readers to assess the validity of their results and conclusions.

JAMA, 2006;295:1152-1160
Trial Design

• Superiority
  – Minimal Detectable Difference
  – Minimal Clinically Important Difference

• Equivalence/Noninferiority
  – Equivalence Margin
Figure 3. Hazard Ratios Comparing Overall Survival Between the ALND and SLND-Alone Groups.
Common Pitfalls

• Clear definition of Primary Outcome Variable

• Secondary Outcomes
  – Rarely adequately powered
  – Best if secondary analysis is included in study protocol as an a priori analysis
Study Protocol

• We will ask for original study protocol and IRB documents

• These must be consistent with the paper (bad news if it is not—and that has happened—see “ethical problems”)

Statistics

• Differences between groups should be clinically significant and important.

• Pharma studies: we will ask for independent statistical review with publication of the independent and not industry statistical analysis.
Presentation

• Follow author instructions—we will reject on

• If sent elsewhere first:
  – Not as much of a problem as many authors think
  – Ensure that you address prior reviewers critiques. We may ask for the prior reviews
Statistical Matters

• Missing Data
  – Missing at Random?
  – Dropping observations is suboptimal
  – Random Effects Regression
  – Multiple Imputation
  – Last Observation Carried Forward (LCOF)
    • Can bias towards more favorable results if patients drop out
  – First Observation Carried Forward (FOCF)
Analysis of Observational Studies in the Presence of Treatment Selection Bias
Effects of Invasive Cardiac Management on AMI Survival Using Propensity Score and Instrumental Variable Methods

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Context Comparisons of outcomes between patients treated and untreated in observational studies may be biased due to differences in patient prognosis between groups, often because of unobserved treatment selection biases.

Objective To compare 4 analytic methods for removing the effects of selection bias in observational studies: multivariable model risk adjustment, propensity score risk adjustment, propensity-based matching, and instrumental variable analysis.

Design, Setting, and Patients A national cohort of 122,124 patients who were elderly (aged 65–84 years), receiving Medicare, and hospitalized with acute myocardial infarction (AMI) in 1994–1995, and who were eligible for cardiac catheterization. Baseline chart reviews were taken from the Cooperative Cardiovascular Project and linked to Medicare health administrative data to provide a rich set of prognostic variables. Patients were followed up for 7 years through December 31, 2001, to assess the association between long-term survival and cardiac catheterization within 30 days of hospital admission.

Main Outcome Measure Risk-adjusted relative mortality rate using each of the analytic methods.

Results Patients who received cardiac catheterization (n = 73,238) were younger and had lower AMI severity than those who did not. After adjustment for prognostic factors by using standard statistical risk-adjustment methods, cardiac catheterization was associated with a 50% relative decrease in mortality (for multivariable model risk adjustment: adjusted relative risk [RR], 0.51; 95% confidence interval [CI], 0.50–0.52; for propensity score risk adjustment: adjusted RR, 0.54; 95% CI, 0.53–0.55; and for propensity-based matching: adjusted RR, 0.54; 95% CI, 0.52–0.56). Using regional catheterization rate as an instrument, instrumental variable analysis showed a 16% relative decrease in mortality (adjusted RR, 0.84; 95% CI, 0.79–0.90). The survival benefits of routine invasive care from randomized clinical trials are between 8% and 21%.

Conclusions Estimates of the observational association of cardiac catheterization with long-term AMI mortality are highly sensitive to analytic method. All standard risk-adjustment methods have the same limitations regarding removal of unmeasured treatment selection biases. Compared with standard modeling, instrumental variable analysis may produce less biased estimates of treatment effects, but is more suited to answering policy questions than specific clinical questions.

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# Propensity Match

| Table 1. Select Baseline Characteristics According to Receipt of Cardiac Catheterization* |
|------------------------------------------|-----------|-----------|
| Overall Cohort                          | Propensity-Based Matched Cohort | Unmatched Patients Receiving Cardiac Catheterization |
| Received Cardiac Catheterization Within 30 Days | No (n = 48 836) | Yes (n = 73 236) | Standardized Difference | No (n = 31 193) | Yes (n = 31 193) | Standardized Difference | No (n = 42 045) |
| Predicted 1-year mortality (AMJ severity), mean (SD) | 32.3 (18.3) | 20.9 (13.3) | 73.7 | 25.8 (15.8) | 27.8 (12.5) | 6.5 | 15.8 (7.9) |
| **Demographics**                         |          |           |     |          |           |     |          |
| Age range, y                             |          |           |     |          |           |     |          |
| 65-74                                    | 40.2     | 64.4      | 49.9 | 45.2     | 46.5     | 0.3 | 70.6 |
| 75-84                                    | 59.8     | 35.6      | 49.9 | 54.8     | 54.7     | 0.1 | 21.4 |
| Sex                                       |          |           |     |          |           |     |          |
| Male                                     | 49.7     | 50.4      | 17.6 | 53.2     | 49.6     | 7.2 | 68.9 |
| Black                                    | 7.5      | 4.8       | 11.3 | 5.7      | 6.6      | 3.7 | 3.5 |
| Social Security income ≥$25 000          | 30.0     | 29.7      | 0.9 | 30.2     | 30.2     | 0.0 | 28.2 |
| **Comorbidities**                        |          |           |     |          |           |     |          |
| History of diabetes                      | 44.1     | 40.9      | 11.8 | 46.0     | 46.5     | 0.5 | 50.2 |
| Previous myocardial infarction           | 32.0     | 26.4      | 14.3 | 26.7     | 31.9     | 6.6 | 22.3 |
| Diabetic nephropathy                     | 17.6     | 20.0      | 7.7 | 16.6     | 20.0     | 5.7 | 94.0 |
| Congestive heart failure                 | 27.2     | 10.4      | 45.7 | 16.6     | 10.3     | 4.4 | 46.6 |
| Diastolic dysfunction                     | 36.9     | 28.6      | 17.1 | 31.1     | 24.1     | 7.0 | 24.5 |
| Peripheral vascular disease              | 12.6     | 9.1       | 12.0 | 10.6     | 11.5     | 2.8 | 7.3 |
| Chronic obstructive pulmonary disease    | 24.9     | 17.6      | 16.3 | 20.9     | 20.3     | 5.0 | 10.3 |
| Smoked                                   |          |           |     |          |           |     |          |
| AMI clinical presentation characteristics |          |           |     |          |           |     |          |
| Non-ST-segment elevation AMI             | 41.8     | 38.9      | 6.9 | 40.8     | 40.1     | 0.5 | 38.3 |
| Shock                                    | 1.9      | 1.5       | 3.0 | 1.8      | 2.3       | 1.5 | 0.1 |
| Hypertension                             | 3.5      | 2.3       | 7.4 | 3.1      | 3.6       | 2.6 | 1.2 |
| Received CPR                             | 1.8      | 1.6       | 1.6 | 2.5      | 3.5       | 7.3 | 0.2 |
| Peak creatinine kinase >10 000 U/L       | 28.1     | 32.4      | 1.2 | 31.7     | 31.6     | 0.2 | 32.9 |
| Hospital characteristics                 |          |           |     |          |           |     |          |
| Annual AMI volume ≥200 patients          | 20.1     | 30.4      | 22.6 | 22.9     | 20.5     | 5.4 | 37.8 |
| Mortality                                |          |           |     |          |           |     |          |
| Died within 1 y                          | 38.6     | 14.2      | 24.6 | 36.6     | 10.0     | 10.6 |
| Died within 4 y                          | 62.0     | 27.8      | 35.4 | 55.4     | 36.5     | 21.4 |

*Abbreviations: AMI, acute myocardial infarction; CPR, cardiopulmonary resuscitation.

*All data are presented as percentages. Standardized difference is the mean difference divided by the pooled SD, expressed as a percentage.

†Predicted 1-year mortality was computed using the Cox proportional hazards regression model, including all baseline patient characteristics of age, sex, race, socioeconomic status, comorbidities, and clinical presentation.

‡Defined as current smoker.

§Censored at Kaplan-Meier method.
Common Pitfalls

• Multiple comparisons
  – Alpha penalties

• Regression-Elimination Procedures
  – Order and strategy of variable entry/elimination
JELLY BEANS CAUSE ACNE!

SCIENTISTS INVESTIGATE!

WE FOUND NO LINK BETWEEN JELLY BEANS AND ACNE (P > 0.05)

THAT SETS THAT...

I HEAR IT'S ONLY A CERTAIN COLOR THAT CAUSES IT.

SCIENTISTS!

WE FOUND NO LINK BETWEEN PURPLE JELLY BEANS AND ACNE (P > 0.05)
WE FOUND NO LINK BETWEEN BROWN JELLY BEANS AND ACNE (P > 0.05)
WE FOUND NO LINK BETWEEN PINK JELLY BEANS AND ACNE (P > 0.05)
WE FOUND NO LINK BETWEEN BLUE JELLY BEANS AND ACNE (P > 0.05)
WE FOUND NO LINK BETWEEN TEAL JELLY BEANS AND ACNE (P > 0.05)

WE FOUND NO LINK BETWEEN RED JELLY BEANS AND ACNE (P > 0.05)
WE FOUND NO LINK BETWEEN TURQUOISE JELLY BEANS AND ACNE (P > 0.05)
WE FOUND NO LINK BETWEEN MAGENTA JELLY BEANS AND ACNE (P > 0.05)

WE FOUND NO LINK BETWEEN GREY JELLY BEANS AND ACNE (P > 0.05)
WE FOUND NO LINK BETWEEN CHIN JELLY BEANS AND ACNE (P > 0.05)
WE FOUND NO LINK BETWEEN GREEN JELLY BEANS AND ACNE (P > 0.05)

WE FOUND NO LINK BETWEEN YELLOW JELLY BEANS AND ACNE (P > 0.05)

NEWS

GREEN JELLY BEANS LINKED TO ACNE!
95% CONFIDENCE

ONLY 2% CHANCE OF CONFIDENCE!
Common Pitfalls

Randomized Trials Stopped Early for Benefit
A Systematic Review

• Interim

Stopping Rules

– Multiple looks and type I error

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Frequent JAMA Authors

• 10:1 Reject:Accept Ratio
• Keep Trying
  – But: Take the editors advice when rejected
  – i.e. don’t keep resubmitting the same type of paper that was rejected previously
  – “I need a JAMA publication to get promoted”
Write and Submit

• Write well—it takes practice
• 2\textsuperscript{nd} draft = 1\textsuperscript{st} draft – 10%
• Writing should be interesting to read
• Get others to review MS—especially those not intimately familiar with the topic—take their advice
• Resubmission – Address EVERY point raised by the editors and reviewers
Write and Submit

• Do not argue with peer reviewers
• You can disagree-explain why
• REALLY BAD idea to argue with the editor
• Don’t be afraid to contact editors directly
Thanks for having me!
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