

Getting Published in High-Profile Journals

Edward H. Livingston, MD, FACS, AGAF

Deputy Editor, JAMA

Professor of Surgery and Biomedical Engineering
University of Texas Southwestern School of Medicine

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 lifestyle treatment for type 2 diabetes. JAMA. 2012 Sep 12;308(10):981-2.

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

JAMA

EDITORIAL STAFF

EDITOR IN CHIEF

Howard Bauchner, MD

Executive Editor

Phil B. Fontanarosa, MD, MBA

Deputy Editors: Drummond Rennie, MD, Ronna Henry, MD, Robert M. Golub, MD, Edward H. Livingston, MD

Managing Deputy Editor: Annette Flanagan

Senior Editor: Jody W. Zyke, MD

Associate Senior Editor: Roxanne K. Young

Contributing Editors: Derek C. Angus, MD, MPH, Robert G. Badgett, MD, Anne Rentoumis Cappola, MD, ScM, Huan J. Chang, MD, MPH, Helene M. Cole, MD, Thomas B. Cole, MD, MPH, J. Michael Gaziano, MD, MPH, Richard M. Glass, MD, David H. Mark, MD, MPH, Mary McGrae McDermott, MD, Robert A. McNutt, MD, George T. O'Connor, MD, Boris Pasche, MD, PhD, Eric D. Peterson, MD, MPH, Jeanette M. Smith, MD, Janet M. Torpy, MD, Wolfgang C. Winkelmayr, MD, MPH, ScD, John L. Zeller, MD, PhD

Statistical Editor: Naomi Vaisrub, PhD

Associate Editor: Charlene Breedlove

Fishbein Fellow: Denise M. Goodman, MD, MS

Contributing Writers: Robert H. Brook, MD, ScD, Christine K. Cassel, MD, Nicholas A. Christakis, MD, PhD, MPH, Allan S. Detsky, MD, PhD, Mark Duggan, PhD, Ezekiel J. Emanuel, MD, PhD, Elliott S. Fisher, MD, MPH, Lawrence O. Gostin, JD, Kathy Hudson, PhD, John P. A. Ioannidis, MD, DSc, Ashish K. Jha, MD, MPH, David S. Ludwig, MD, PhD, Howard Markel, MD, PhD, Steven E. Nissen, MD, Bruce M. Psaty, MD, PhD, Joshua M. Sharfstein, MD, Stephen M. Shortell, PhD, MPH, MBA, Harold C. Sox, MD, Robert Steinbrook, MD, Mary E. Tinetti, MD, Abraham Verghese, MD, Jason Wang, MD, PhD, Steven H. Woolf, MD, MPH

Medical News & Perspectives: Joan Stephenson, PhD (editor); Bridget M. Kuehn, Mike Mitka (senior staff writers); Rebecca Voelker (associate managing editor)

Assistant Editors: Carrie Butt, Angela Grayson, Jennifer Reiling

Manuscript Editing: Stacy L. Christiansen (director); Emily A. Greenhow, Joy K. Jaeger, Phil Sefton, Heather A. Shebel, Kristine B. Simmons, Beverly Stewart (senior manuscript editors); Kim S. P. Campbell; Cara Wallace (freelance manuscript editor)

Editorial Graphics: Cassio Lynn, Alison E. Burke (senior medical illustrators); David Song (editorial assistant)

Electronic Media: Michelle Kurzynski (director, development and design); Christopher Hastings, Peter Kim, Craig McCaffrey (developers/designers); Reuben Rios (Web administrative assistant)

Administration: Marla A. Hall (director); Gloria Tate (supervisor); Deanna M. Willis (staff assistant)

Editorial Assistants: Mary Cannon, Susan Collister, Carmina Conley, Dawn Cortez, Cheryl Dixon, Georgia Eaton, Audrey Forman, Gwenn Gregg, Lisa Hardin, Rachell M. Lozano, Rosa E. Miranda, Lupe Morales

Workflow and Content Management Systems: Larry Bryant (director); Paul Frank (systems administrator); Monica Mungle (editorial systems manager); J.D. Neff (associate developer)

Editorial Systems and Administration: Elaine Williams (director); Gale Saulsberry (database specialist); Lenette Gardner-Gullens (electronic input supervisor); Delayna Brown, Fanny L. Brown (electronic input assistants)

Editorial Counsel: Joseph P. Thornton, JD

Survey Research Specialist: Joseph S. Wislar

JAMA/Archives Media Relations: Jann Ingmire (director); Jim Michalski, Deanna Bellandi, Cassie Brasseur

EDITORIAL BOARD

Daniel M. Albert, MD, MS
University of Wisconsin Hospital
and Clinics, Madison, Wisconsin
Editor, *Archives of Ophthalmology*

Donald M. Berwick, MD, MPP
Newton, Massachusetts

Philip I. Lurie, MD
The Methodist Hospital
Houston, Texas

Jordan J. Cohen, MD
The George Washington University
Washington, DC

Joseph T. Coyle, MD
Harvard Medical School
Boston, Massachusetts
Editor, *Archives of General Psychiatry*

Ezekiel J. Emanuel, MD, PhD
University of Pennsylvania
Philadelphia, Pennsylvania

Julie Freischlag, MD
Johns Hopkins University
School of Medicine
Baltimore, Maryland
Editor, *Archives of Surgery*

Thomas R. Frieden, MD, MPH
Centers for Disease Control
and Prevention
Atlanta, Georgia

Michael M. E. Johns, MD
Robert W. Woodruff Health Sciences
Center of Emory University
Atlanta, Georgia

Wayne F. Larrabee Jr, MD
University of Washington
Seattle, Washington
Editor, *Archives of Facial
Plastic Surgery*

Paul A. Levine, MD
University of Virginia
Charlottesville, Virginia
Editor, *Archives of Otolaryngology-
Head & Neck Surgery*

Donald A. B. Lindberg, MD
National Library of Medicine
Bethesda, Maryland

C. David Naylor, MD, DPhil
University of Toronto
Toronto, Ontario, Canada

Rita F. Redberg, MD, MSc
University of California, San Francisco
School of Medicine
San Francisco, California
Editor, *Archives of Internal Medicine*

Uwe E. Reinhardt, PhD
Princeton University
Princeton, New Jersey

Frederick P. Rivara, MD, MPH
University of Washington
Seattle, Washington
Editor, *Archives of Pediatrics
& Adolescent Medicine*

June K. Robinson, MD
The Feinberg School of Medicine,
Northwestern University
Chicago, Illinois
Editor, *Archives of Dermatology*

Griffin Rodgers, MD
National Institute of Diabetes and
Digestive and Kidney Diseases
Bethesda, Maryland

Roger N. Rosenberg, MD
University of Texas Southwestern
Medical Center, Dallas, Texas
Editor, *Archives of Neurology*

Joshua M. Sharfstein, MD
Maryland Department of Health
and Hygiene
Baltimore, Maryland

Harold C. Sox, MD
Dartmouth Medical School
Hanover, New Hampshire

JOURNAL OVERSIGHT COMMITTEE

Edward H. Shortliffe, MD, PhD (chair)
Columbia University
New York, New York
Arizona State University
Scottsdale, Arizona

Kent R. Anderson
Journal of Bone and Joint Surgery
Needham, Massachusetts

Karen Antman, MD
Boston University
School of Medicine
Boston, Massachusetts

Steven L. Kanter, MD
University of Pittsburgh
School of Medicine
Pittsburgh, Pennsylvania

Raynard S. Kington, MD, PhD
Grinnell College
Grinnell, Iowa

James L. Madara, MD
American Medical Association
Chicago, Illinois

Claire Pomeroy, MD, MBA
UC Davis Health System
University of California, Davis
School of Medicine
Sacramento, California

FORMER EDITORS

Nathan S. Davis, MD (1883-1888)

John B. Hamilton, MD
(1889, 1893-1898)

John H. Hollister, MD (1889-1891)

James C. Culbertson, MD (1891-1893)

Truman W. Miller, MD (1899)

George H. Simmons, MD (1899-1924)

Morris Fishbein, MD (1924-1949)

Austin Smith, MD (1949-1958)

Johnson F. Hammond, MD
(1958-1959)

John H. Talbot, MD (1959-1969)

Hugh H. Hussey, MD (1970-1973)

Robert H. Moser, MD (1973-1975)

William R. Barclay, MD (1975-1982)

George D. Lundberg, MD
(1982-1999)

Catherine D. DeAngelis, MD, MPH
(2000-2011), Editor in Chief Emerita

JAMA

The Journal of the American Medical Association

August 22/29, 2012

CLINICIAN'S CORNER

CLINICAL REVIEW

Lipid-Modifying Therapies and Risk of Pancreatitis: A Meta-analysis

804

D. PREISS, M. J. TIKKANEN, P. WELSH, I. FORD, L. C. LOVATO, M. B. ELAM, J. C. LAROSA, D. A. DEMIGGIO, H. M. COLHOUN, E. GOLDENBERG, M. J. MURPHY, T. M. MACDONALD, T. R. PEDERSEN, A. C. KEECH, P. M. RIDKER, J. KIEKSHUS, N. SATTAR, J. J. V. MCMURRAY

JAMA CLINICAL CHALLENGE

Cutaneous Nodule in a Young Man

812

J. QIAO, H. FANG

Letters

Cardiac Device Infective Endocarditis and Patient Survival

761
X. WU, D. YANG, A. SHARMA, A. VALLAKATI, E. ATHAN, A. WANG

Neonatal Abstinence Syndrome

H. E. JONES, K. KALTENBACH, S. W. PATRICK, R. E. SCHUMACHER, M. M. DAVIS

Research Letter

Competitive Sports Participation in Athletes With Congenital Long QT Syndrome

764
J. N. JOHNSON, M. J. ACKERMAN

VIEWPOINTS

Ending the Tobacco Epidemic

767
H. K. KOH, K. SEBELIUS

Preventing Patient Harms Through Systems of Care

769
P. J. PRONOVOST, G. W. BO-LINN

Transforming Quality of Care and Improving Outcomes After Acute MI: Lessons From the National Registry of Myocardial Infarction

771
W. J. FRENCH, V. S. REDDY, H. V. BARRON

The Value of Statistical Analysis Plans in Observational Research: Defining High-Quality Research From the Start

773
L. THOMAS, E. D. PETERSON

A PIECE OF MY MIND

Poolside

775
D. SHAPIRO

ORIGINAL CONTRIBUTIONS

Effect of Biolimus-Eluting Stents With Biodegradable Polymer vs Bare-Metal Stents on Cardiovascular Events Among Patients With Acute Myocardial Infarction: The COMFORTABLE AMI Randomized Trial

777

L. RÄBER, H. KELBÆK, M. OSTOJIC, A. BAUMBACH, D. HEG, D. TÜLLER, C. VON BIRGELEN, M. ROFFI, A. MOSCHOVITIS, A. A. KHATTAB, P. WENAWESER, R. BONVINI, G. PEDRAZZINI, R. KORNOWSKI, K. WEBER, S. TRELLE, T. F. LÜSCHER, M. TANIWAKI, C. M. MATTER, B. MEIER, P. JUNI, S. WINDECKER; FOR THE COMFORTABLE AMI TRIAL INVESTIGATORS

Comparison of Novel Risk Markers for Improvement in Cardiovascular Risk Assessment in Intermediate-Risk Individuals

788

J. YEBOAH, R. L. MCCLELLAND, T. S. POLONSKY, G. L. BURKE, C. T. SIBLEY, D. O'LEARY, J. J. CARR, D. C. GOFF JR, P. GREENLAND, D. M. HERRINGTON

Common Carotid Intima-Media Thickness Measurements in Cardiovascular Risk Prediction: A Meta-analysis

796

H. M. DEN RUIJTER, S. A. E. PETERS, T. J. ANDERSON, A. R. BRITTON, J. M. DEKKER, M. J. EIJKEMANS, G. ENGSTRÖM, G. W. EVANS, J. DE GRAAF, D. E. GROBBEE, B. HEDBLAD, A. HOPMAN, S. HOLEWIJ N, A. IKEDA, M. KAVOUSI, K. KITAGAWA, A. KITAMURA, H. KOFFIJBERG, E. M. LONN, M. W. LORENZ, E. B. MATHIESEN, G. NIJPELS, S. OKAZAKI, D. H. O'LEARY, J. F. POLAK, J. F. PRICE, C. ROBERTSON, C. M. REMBOLD, M. ROSVALL, T. RUNDEK, J. T. SALONEN, M. SITZER, C. D. A. STEHOUWER, J. C. WITTEMAN, K. G. MOONS, M. L. BOTS

EDITORIALS

New-Generation Drug-Eluting Stents for Patients With Myocardial Infarction

814
S. CASSESE, A. KASTRATI

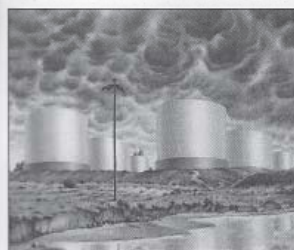
Cardiovascular Risk Assessment in the 21st Century

816
J. M. GAZIANO, P. W. F. WILSON

129 Years of CONTINUOUS PUBLICATION

EDITOR IN CHIEF
Howard Bauchner, MD

JAMA



Clarence Holbrook Carter (1904-2000), *Port Huron, 1936*, American.

Humanities

THE COVER 744

Port Huron
M. TORPY

POETRY AND MEDICINE 745

Torsades de Pointes
A. POSSNER

JAMA 100 YEARS AGO 746

The Practical Value of Direct Transfusion of Blood
The Therapeutic Use of Blood
Wholesale Geographic Surgery

Reader Service

This Week in JAMA 739

Masthead 741

Author in the Room
Teleconference 745

Archives Journals Abstracts 747

Correction 765

Online CME Article 804

CME Information 821

Classified Advertising 822

Journal Advertiser Index 826

JAMA Contact Information 828

Instructions for Authors
<http://jama.com>

The Key and Critical Objectives of JAMA
January 4, 2012

All articles published, including editorials, letters, and book reviews, represent the opinions of the authors and do not reflect the official policy of the American Medical Association or the institution with which the author is affiliated, unless this is clearly specified.

www.jama.com

BOOK AND MEDIA REVIEWS 818

Made in India: A Film About Surrogacy (Haimowitz, Sinha)

REVIEWED BY S. Y. SESSIONS

International Health and Aid Policies: The Need for Alternatives (Unger et al)

REVIEWED BY D. CHINITZ

JAMA PATIENT PAGE 829

Ectopic Pregnancy

News and Analysis

MEDICAL NEWS & PERSPECTIVES 749

Methadone Overdose Deaths Rise With Increased Prescribing for Pain
Experts Question Recommendations for Universal Lipid Screenings in Children
news@JAMA: From JAMA's Daily News Site

VISUALIZING HEALTH POLICY 752

Medicaid: Its Role Today and Under the Affordable Care Act

HEALTH AGENCIES UPDATE 753

Military PTSD Care
Egg Allergy Treatment
Smoking Cessation Reminders
Fetal Alcohol Exposure

FROM THE CENTERS FOR DISEASE CONTROL AND PREVENTION 754

Unexplained Respiratory Disease Outbreak Working Group Activities—
Worldwide, March 2007–September 2011
Work-Related Asthma—38 States and District of Columbia, 2006–2009

JAMA Beyond Print at www.jama.com



Video Interview with Stephan Windecker, MD,
author of Effect of Biolimus-Eluting Stents
With Biodegradable Polymer vs Bare-Metal Stents
on Cardiovascular Events Among Patients
With Acute Myocardial Infarction

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

Gilda Piaggio, PhD

Diana R. Elbourne, PhD

Douglas G. Altman, DSc

Stuart J. Pocock, PhD

Stephen J. W. Evans, MSc

for the CONSORT Group

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

www.jama.com

Trial Design

- Superiority
 - Minimal Detectable Difference
 - Minimal Clinically Important Difference
- Equivalence/Noninferiority
 - Equivalence Margin

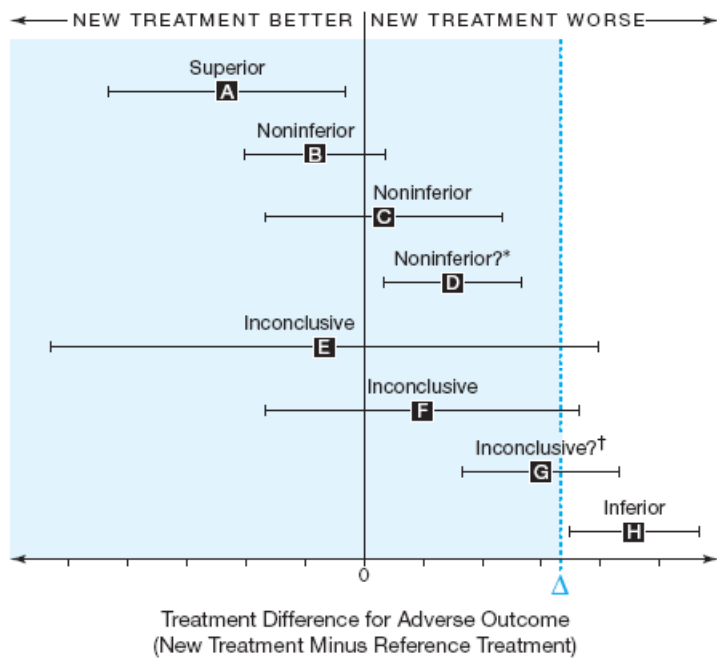
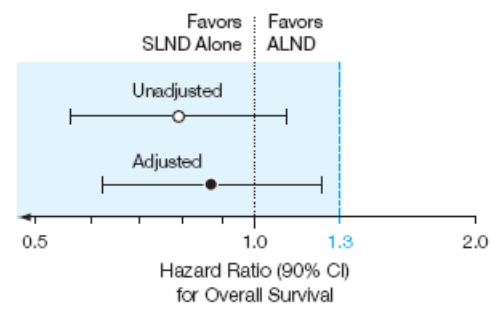


Figure 3. Hazard Ratios Comparing Overall Survival Between the ALND and SLND-Alone Groups



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 that basis alone.
- 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

Thérèse A. Stukel, PhD

Elliott S. Fisher, MD, MPH

David E. Wennberg, MD, MPH

David A. Alter, MD, PhD

Daniel J. Gottlieb, MS

Marian J. Vermeulen, MHSc

- Propensity Matching

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.

JAMA. 2007;297:278-285

www.jama.com

Propensity Match

Table 1. Select Baseline Characteristics According to Receipt of Cardiac Catheterization*

	Overall Cohort			Propensity-Based Matched Cohort			Unmatched Patients Receiving Cardiac Catheterization (n = 42 045)
	Received Cardiac Catheterization Within 30 Days		Standardized Difference	Received Cardiac Catheterization Within 30 Days		Standardized Difference	
	No (n = 48 886)	Yes (n = 73 238)		No (n = 31 193)	Yes (n = 31 193)		
Predicted 1-year mortality (AMI severity), mean (SD)†	32.3 (18.3)	20.9 (13.3)	73.7	26.8 (15.5)	27.8 (12.5)	6.3	15.8 (7.5)
Demographics							
Age range, y							
65-74	40.2	64.4	49.9	45.2	45.3	0.1	78.6
75-84	59.8	35.6	49.9	54.8	54.7	0.1	21.4
Men	49.7	58.4	17.6	53.2	49.6	7.2	65.0
Black	7.5	4.8	11.3	5.7	6.6	3.7	3.5
Social Security income ≥\$2600	30.0	29.7	0.9	30.2	30.2	0.1	29.2
Comorbidities							
History of angina	44.1	49.9	11.8	46.0	45.6	0.9	53.2
Previous myocardial infarction	32.9	26.4	14.3	28.7	31.9	6.8	22.3
Previous revascularization	17.8	20.9	7.7	18.0	20.2	5.7	21.3
Congestive heart failure	27.2	10.4	45.7	16.6	18.3	4.4	4.6
Diabetes mellitus	36.6	28.6	17.1	31.8	34.1	4.9	24.5
Peripheral vascular disease	12.8	9.1	12.0	10.6	11.5	2.8	7.3
Chronic obstructive pulmonary disease	24.9	17.6	18.3	20.9	23.3	5.9	13.3
Smoker‡	16.1	18.0	5.0	16.5	17.0	1.2	18.8
AMI clinical presentation characteristics							
Non-ST-segment elevation AMI	41.8	38.9	5.9	39.8	40.1	0.8	38.0
Shock	1.9	1.5	3.0	1.8	2.3	3.4	0.9
Hypotension	3.5	2.3	7.4	3.1	3.6	2.6	1.2
Received CPR	1.8	1.6	1.6	2.3	3.5	7.3	0.2
Peak creatinine kinase >1000 U/L	29.1	32.4	7.2	31.7	31.8	0.2	32.9
Hospital characteristics							
Annual AMI volume >200 patients	20.1	30.4	23.6	22.9	20.5	5.6	37.8
Mortality§							
Died within 1 y	38.6	14.2		34.6	19.0		10.6
Died within 4 y	62.0	27.8		55.4	36.3		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.

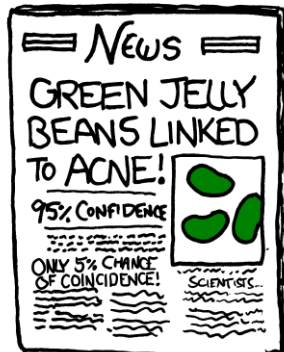
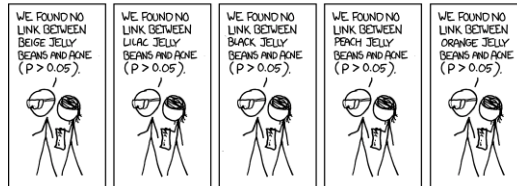
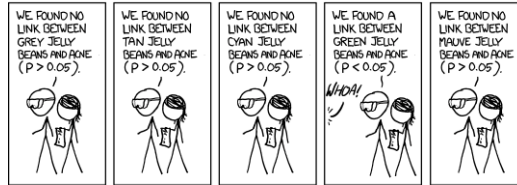
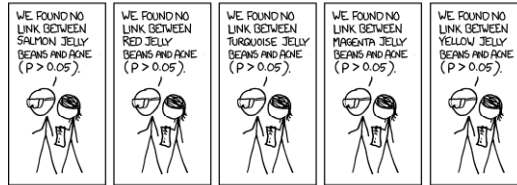
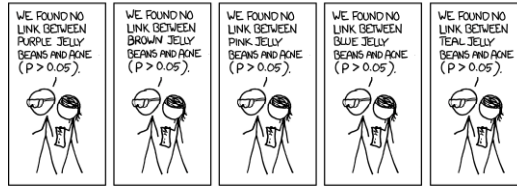
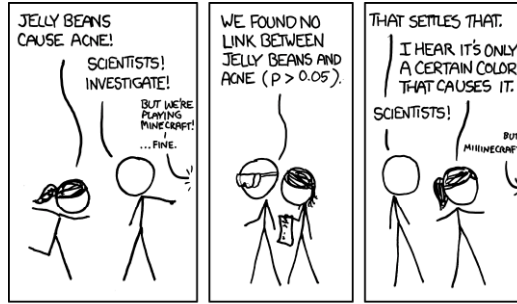
†Predicted 1-year mortality was computed using the Cox proportional hazards regression model, including all baseline patient characteristics of age, sex, race, socioeconomic status, comorbidities, and clinical presentation.

‡Defined as current smoker.

§Derived by Kaplan-Meier method.

Common Pitfalls

- Multiple comparisons
 - Alpha penalties
- Regression-Elimination Procedures
 - Order and strategy of variable entry/elimination



Common Pitfalls

- Interim Analysis- Stopping Rules
 - Multiple looks and type I error

Randomized Trials Stopped Early for Benefit A Systematic Review

Victor M. Montori, MD, MSc

P. J. Devereaux, MD

Neill K. J. Adhikari, MD

Karen E. A. Burns, MD

Christoph H. Eggert, MD

Matthias Briel, MD

Christina Lacchetti, MHSc

Teresa W. Leung, BHSc

Elizabeth Darling, RM, BHSc

Dianne M. Bryant, PhD

Heiner C. Bucher, MD, MPH

Holger J. Schünemann, MD, PhD

Maureen O. Meade, MD, MSc

Deborah J. Cook, MD, MSc

Patricia J. Erwin, MLS

Amit Sood, MD

Richa Sood, MD

Benjamin Lo, MD

Carly A. Thompson, BHSc

Qi Zhou, PhD

Edward Mills, PhD

Gordon H. Guyatt, MD, MSc

Context Randomized clinical trials (RCTs) that stop earlier than planned because of apparent benefit often receive great attention and affect clinical practice. Their prevalence, the magnitude and plausibility of their treatment effects, and the extent to which they report information about how investigators decided to stop early are, however, unknown.

Objective To evaluate the epidemiology and reporting quality of RCTs involving interventions stopped early for benefit.

Data Sources Systematic review up to November 2004 of MEDLINE, EMBASE, Current Contents, and full-text journal content databases to identify RCTs stopped early for benefit.

Study Selection Randomized clinical trials of any intervention reported as having stopped early because of results favoring the intervention. There were no exclusion criteria.

Data Extraction Twelve reviewers working independently and in duplicate abstracted data on content area and type of intervention tested, reporting of funding, type of end point driving study termination, treatment effect, length of follow-up, estimated sample size and total sample studied, role of a data and safety monitoring board in stopping the study, number of interim analyses planned and conducted, and existence and type of monitoring methods, statistical boundaries, and adjustment procedures for interim analyses and early stopping.

Data Synthesis Of 143 RCTs stopped early for benefit, the majority (92) were published in 5 high-impact medical journals. Typically, these were industry-funded drug trials in cardiology, cancer, and human immunodeficiency virus/AIDS. The proportion of all RCTs published in high-impact journals that were stopped early for benefit increased from 0.5% in 1990-1994 to 1.2% in 2000-2004 ($P < .001$ for trend). On average, RCTs recruited 63% (SD, 25%) of the planned sample and stopped after a median of 13 (interquartile range [IQR], 3-25) months of follow-up, 1 interim analysis, and when a median of 66 (IQR, 23-195) patients had experienced the end point driving study termination (event). The median risk ratio among truncated RCTs was 0.53 (IQR, 0.28-0.66). One hundred thirty-five (94%) of the 143 RCTs did not report at least 1 of the following: the planned sample size ($n=28$), the interim analysis after which the trial was stopped ($n=45$), whether a stopping rule informed the decision ($n=48$), or an adjusted analysis accounting for interim monitoring and truncation ($n=129$). Trials with fewer events yielded greater treatment effects (odds ratio, 28; 95% confidence interval, 11-73).

Conclusions RCTs stopped early for benefit are becoming more common, often fail to adequately report relevant information about the decision to stop early, and show implausibly large treatment effects, particularly when the number of events is small. These findings suggest clinicians should view the results of such trials with skepticism.

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
- 2nd draft = 1st 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

VA HSRD

- Thanks for having me!
- Edward H. Livingston, MD, FACS, AGAF
- Deputy Editor for Clinical Content
- Journal of the American Medical Association
- 515 N. State Street
- Chicago, Illinois, 60654
- Tel: 312-464-2459
- Fax: 312-464-5824
- edward.livingston@jamanetwork.org