

# **How to pass statistics review in Acta Orthopaedica**

**Jonas Ranstam PhD**

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**Statistics** is about rational interpretation  
of incomplete and imperfect data

# **The responsibilities of a statistical reviewer**

“To make sure that the authors spell out for the reader the limitations imposed upon the conclusions by the design of the study, the collection of data, and the analyses performed.”

Shor S. The responsibilities of a statistical reviewer. *Chest* 1972;61:486-487.

# **The responsibilities of a statistical reviewer**

“To make sure that the authors spell out for the reader the limitations imposed upon the conclusions by the design of the study, the collection of data, and the analyses performed.”

And to help authors improve their manuscripts by suggesting possible solutions to their problems.

**Hint for a successful review**

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Comply with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals



http://www.icmje.org/

**ICMJE**

International Committee of Medical Journal Editors

**Uniform Requirements for Manuscripts**

Statement of Purpose  
Ethical Considerations  
Publishing and Editorial Issues  
Manuscript Preparation  
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**ICMJE Editorials**

June 2007 Update on Trials  
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May 2005 Update on Trials  
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2004 Update on Trials Registration  
Clinical Trial Registration  
Sponsorship, Authorship, and  
Accountability

# Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication

*Updated October 2007*

Publication Ethics: [Sponsorship, Authorship, and Accountability](#)

The following information is available to be viewed/printed in [Adobe Acrobat pdf format](#).

## International Committee of Medical Journal Editors

### I. Statement of Purpose

# Statistical Methods

“Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results.”

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Required for analytical methods (hypothesis tests and confidence intervals), do not describe how data are presented when this is self-evident.

## **Results**

“When possible, quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals).”

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Uncertainty indicators (p-values and confidence intervals) are necessary for generalization of results beyond examined patients, not for case reports or “qualitative” studies.

## Results

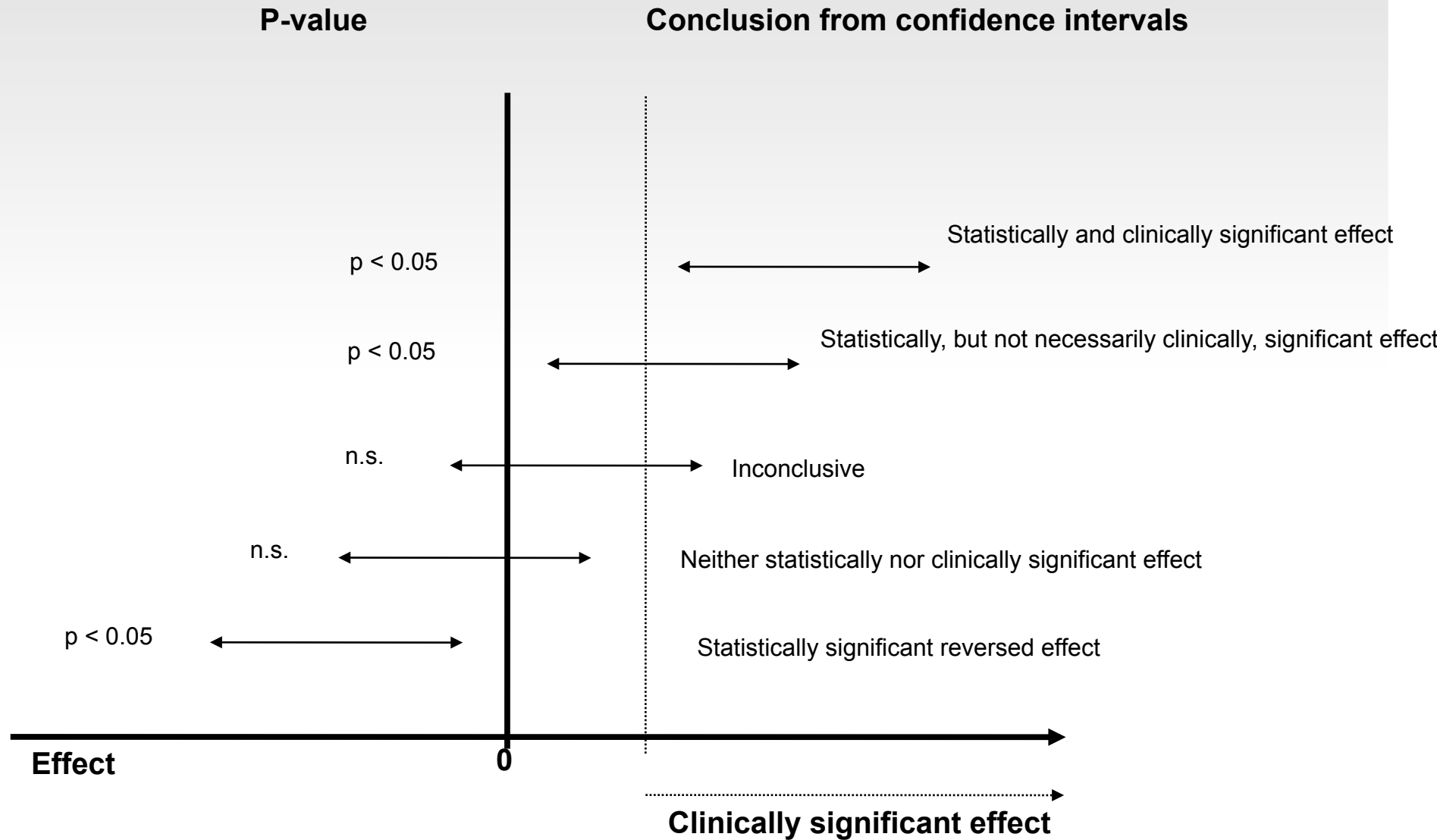
“Avoid relying solely on statistical hypothesis testing, such as the use of P values, which fails to convey important information about effect size.”

## Results

“Avoid relying solely on statistical hypothesis testing, such as the use of P values, which fails to convey important information about effect size.”

Clinical and statistical significance are two completely different things. Present clinically interpretable effect estimates and their precision (confidence intervals or p-values).

# P-values vs. confidence intervals



## Results

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Observational studies usually require adjustment for known and suspected confounding factors.

Automatic stepwise regression is not an adequate method for selecting adjustment factors.

## **Clinical trials**

“The ICMJE member journals will require, as a condition of consideration for publication in their journals, registration in a public trials registry.”

“The ICMJE recommends that journals publish the trial registration number at the end of the Abstract.”

**Uniform Requirements for Manuscripts**

Redundant Publication  
Secondary Publication  
Privacy

Reporting Guidelines  
Manuscripts  
Authorship  
Reference Styles

**Separate Statements**

Peer Review

Editorial Freedom  
Conflict of Interest  
Industry Support  
Corrections, Retractions  
Confidentiality  
Journals and Media  
Internet  
Advertising  
Supplements  
Correspondence Columns  
Competing Manuscripts

**About the ICMJE****Frequently Asked Questions****Journals that Follow URM**

## Is This Clinical Trial Fully Registered?: A Statement from the International Committee of Medical Journal Editors

Catherine De Angelis, MD, MPH; Jeffrey M. Drazen, MD; Frank A. Frizelle, MBChB, MMedSc, FRACS; Charlotte Haug, MD, PhD, MSc; John Hoey, MD; Richard Horton, FRCP; Sheldon Kotzin, MLS; Christine Laine, MD, MPH; Ana Marusic, MD, PhD; A. John P.M. Overbeke, MD, PhD; Torben V. Schroeder, MD, DMSc; Harold C. Sox, MD; and Martin B. Van Der Weyden, MD

In September 2004, the members of the International Committee of Medical Journal Editors (ICMJE) published a joint editorial aimed at promoting registration of all clinical trials ([1](#)). We stated that we will consider a trial for publication only if it has been registered before the enrollment of the first patient. This policy applies to trials that start recruiting on or after July 1, 2005. Because many ongoing trials were not registered at inception, we will consider for publication ongoing trials that are registered before September 13, 2005. Our goal then and now is to foster a comprehensive,

## Clinical trials

“The ICMJE member journals will require, as a condition of consideration for publication in their journals, registration in a public trials registry.”

“The ICMJE recommends that journals publish the trial registration number at the end of the Abstract.”

Many trials are registered with [Clinicaltrials.gov](http://Clinicaltrials.gov), see [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

Note: the registers of national medical products agencies and the Eudract are not public.

## **Clinical trials**

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Example: The trial was approved by the ethics committee of ... and performed in compliance with the Helsinki Declaration of 1975, as revised in 2000.

## **Clinical trials**

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“For reports of randomized controlled trials authors should refer to the CONSORT statement.”

The CONSORT Statement is an evidence-based, minimum set of recommendations for reporting RCTs.

<http://www.consort-statement.org>

Include the CONSORT checklist and flowchart when submitting a manuscript.

Include to Acta, and many other journals, also a copy of the study protocol.



# CONSORT

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## Welcome to the CONSORT Statement Website

CONSORT, which stands for Consolidated Standards of Reporting Trials, encompasses various initiatives developed by the CONSORT Group to alleviate the problems arising from inadequate reporting of randomized controlled trials (RCTs).

The main product of CONSORT is the [CONSORT Statement](#), which is an evidence-based, minimum set of recommendations for reporting RCTs. It offers a standard way for authors to prepare reports of trial findings, facilitating their complete and transparent reporting, and aiding their critical appraisal and interpretation.

The CONSORT Statement comprises a 22-item [checklist](#) and a [flow diagram](#), along with some brief descriptive text. The checklist items focus on reporting how the trial was designed, analyzed, and interpreted; the flow diagram displays the progress of all participants through the trial. The Statement has been translated into [several languages](#).

Considered an evolving document, the CONSORT Statement is subject to periodic changes as new evidence emerges.

## News

### Now published: CONSORT for Non-Pharmacologic Treatments

The CONSORT Group is pleased to announce that the CONSORT extension for reporting RCTs assessing non-pharmacologic treatments (NPT) is now published.

[Read more](#)

### Registration now open: EQUATOR Network Launch Meeting

Register now for the EQUATOR Network Launch Meeting "Achieving Transparency in Reporting Health Research" including the 1st EQUATOR Annual

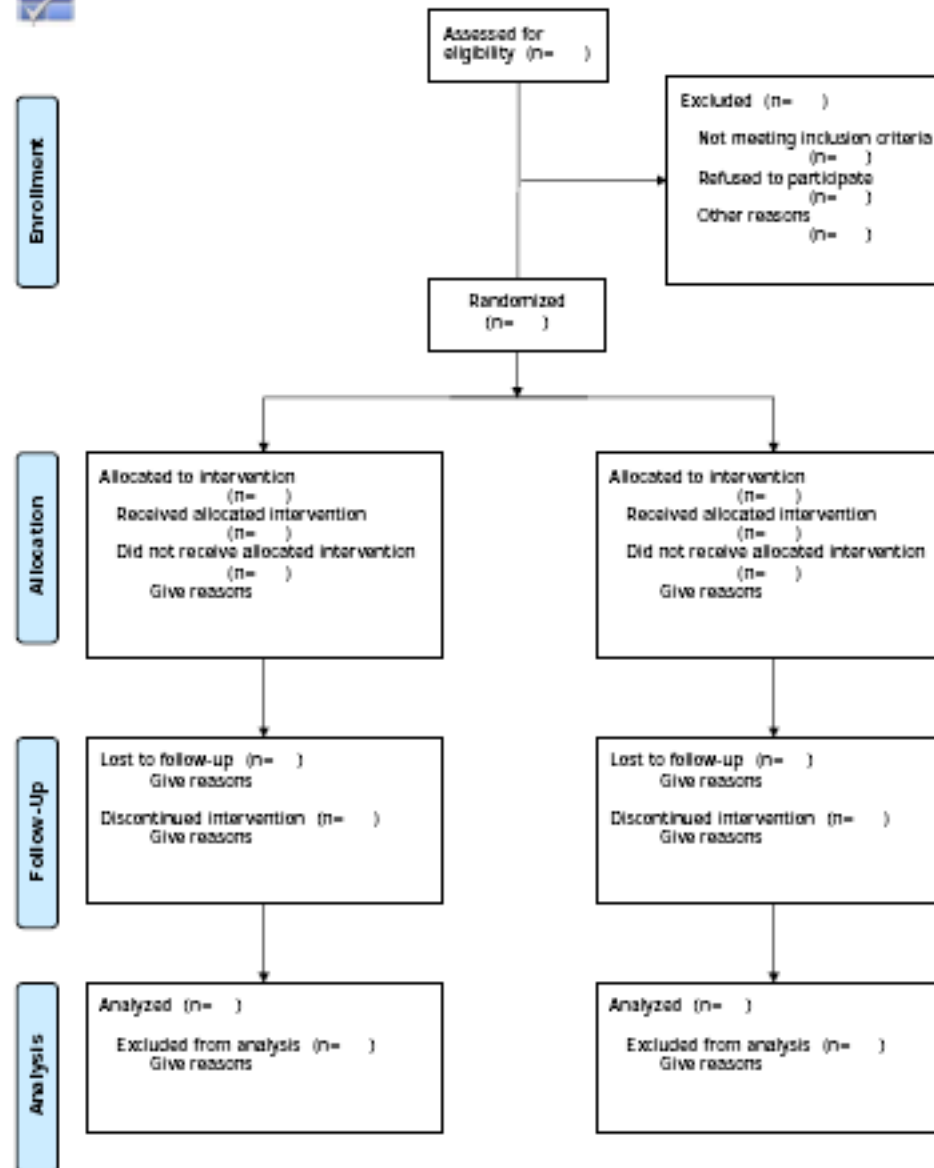
CONSORT Statement 2001 - Checklist 

Items to include when reporting a randomized trial

PAPER SECTION And topic	Item	Descriptor	Reported on Page #
TITLE & ABSTRACT	1	<u>How participants were allocated to interventions</u> (e.g., "random allocation", "randomized", or "randomly assigned").	
INTRODUCTION Background	2	<u>Scientific background and explanation of rationale.</u>	
METHODS Participants	3	<u>Eligibility criteria for participants and the settings and locations where the data were collected.</u>	
Interventions	4	<u>Precise details of the interventions intended for each group and how and when they were actually administered.</u>	
Objectives	5	<u>Specific objectives and hypotheses.</u>	
Outcomes	6	<u>Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements</u> (e.g., multiple observations, training of assessors).	
Sample size	7	<u>How sample size was determined</u> and, when applicable, <u>explanation of any interim analyses and stopping rules.</u>	
Randomization -- Sequence generation	8	<u>Method used to generate the random allocation sequence, including details of any restrictions</u> (e.g., blocking, stratification)	
Randomization -- Allocation concealment	9	<u>Method used to implement the random allocation sequence</u> (e.g., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	
Randomization -- Implementation	10	<u>Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.</u>	
Blinding (masking)	11	<u>Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment, if done, how the success of blinding was evaluated.</u>	
Statistical methods	12	<u>Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.</u>	
RESULTS Participant flow	13	<u>Flow of participants through each stage</u> (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. <u>Describe protocol deviations from study as planned, together with reasons.</u>	
Recruitment	14	<u>Dates defining the periods of recruitment and follow-up.</u>	
Baseline data	15	<u>Baseline demographic and clinical characteristics of each group.</u>	
Numbers analyzed	16	<u>Number of participants denominators in each group included in each analysis and whether the analysis was by "intention-to-treat".</u> State the results in absolute numbers when feasible (e.g., 10/20, not 50%).	
Outcomes and estimation	17	<u>For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision</u> (e.g., 95% confidence interval).	
Additional analyses	18	<u>Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.</u>	
Adverse events	19	<u>All important adverse events or side effects in each intervention group.</u>	
DISCUSSION Interpretation	20	<u>Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.</u>	
Generalizability	21	<u>Generalizability (external validity) of the trial findings.</u>	
Overall evidence	22	<u>General interpretation of the results in the context of current evidence.</u>	



## CONSORT Statement 2001 Flow Diagram



From Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. *Lancet* 2001; 357(9243):1191-1194.

For more information, visit [www.consort-statement.org](http://www.consort-statement.org).

# Clinical trials

## International regulatory guidelines

Topic E9 - Statistical Principles for Clinical Trials

EMA Points to consider

- baseline covariates
- missing data
- multiplicity issues
- etc.

These guidelines can all be found on the internet.

## **General statistical suggestions**

### **Many methods require independent observations**

A patient's multiple observations are dependent and should not be analysed using methods requiring independence, e.g. chi-squared test, Student's t-test, Mann-Whitney U-test, ANOVA.

Unless the statistical methods can deal with dependent data, analyse patients, not knees, hips, shoulders, etc.

# General statistical suggestions

## Avoid vague and ambiguous expressions

- significant                      clinically or statistically?
- no difference                      statistically insignificant?
- statistical difference              statistically significant?
- matched                              selected or just comparable?
- correlation                              relation, regression?
- etc.

**Thank you for your attention!**