“ESHRE Journals Course for Authors”

28 June 2009
Amsterdam
The Netherlands
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ESHRE Journals course for authors

Learning objectives: After attending this Course the Author who has completed a clinical or basic science study will be able to create an informative title and abstract, prepare relevant and succinct tables and figures and organise the sections of an interesting and readable original scientific or clinical paper.

Faculty
• Helen Beard, Managing Editor ESHRE Journals
• John Collins, Editor-in-Chief Human Reproduction Update (Course Chair)
• PierGiorgio Crosignani, Deputy Editor Human Reproduction
• Hans Evers, Deputy Editor Human Reproduction
• Steve Hillier, Editor-in-Chief MHR
• Ed Hughes, McMaster University
• André Van Steirteghem, Editor-in-Chief Human Reproduction
• Andy Williams, Managing Editor Human Reproduction

09:00 - 09:15  Introduction to the course - John Collins (Canada)
09:15 - 09:45  Why do we write scientific papers? - Steve Hillier (United Kingdom)
09:45 - 10:15 Eighteen paragraphs can make a paper - Hans Evers (The Netherlands)
10:15 - 10:45 Essentials and inessentials of a materials and methods section – André Van Steirteghem (Belgium)
10:45 - 11:00 Coffee break and assignment
11:00 - 12:30 Assignment 1: Title and abstract - Faculty
12:30 - 13:30 Lunch
13:30 - 14:00 Optimizing the results section of a RCT manuscript - Ed Hughes (Canada)
14:00 - 14:30  What has to be in the results section of a basic science paper? – Steve Hillier (United Kingdom)

14:30 - 15:00  Five components of a good discussion - PierGiorgio Crosignani (Italy)

15:00 - 15:15  Coffee break and assignment

15:15 - 17:00  Assignment 2: Effective tables and figures - Faculty

17:00 - 18:00  Workshop (optional) - Faculty
   Work in progress, bring your questions.
Why do we write scientific papers?

Steve Hillier
The University of Edinburgh
Editor-in-Chief MHR
s.hillier@ed.ac.uk

“Work, Finish, Publish.”

MICHAEL FARADAY

“Why do we write scientific papers?”
• Historical perspective
• Current issues
• Future trends
“Why do we write scientific papers?”

- **Historical perspective**
  - Science history
  - Early ‘scientific’ publication
  - Emergence of the scientific journal

Science History:
From 'Female Testicles' to 'Test-Tube Babies'

- Aristotle
- Galen
- Avicenna
- Leeuwenhoek
- De Graaf
- Steptoe & Edwards
- Von Baer
- Harvey
Early 'Scientific' Publication:
Regnier de Graaf 1672

ERITLE TO COSIMO III, GRAND DUKIE OF TUSCANY, DEDICATING A NEW TREATISE
CONCERNING THE GENERATIVE ORGANS OF WOMEN

Serene Highness
Grand Duke,

"... It is indeed many generations since a man of genius
has created something splendid, or discovered something
abstruse, and not thought it necessary to present it to some
heric member of your family in order to demonstrate his
feelings of gratitude..."

"...I myself have made bold to strip off Nature’s robe to
reveal the first threads of our nativity, the whole workshop
of human manufacture and its tools..."

"...I am now about to publish a quite new discovery
and...earnestly beseech your indulgence to allow me to
make use of your title and your name alone..."

SOURCE: HD Jocelyn, BP Setchell (1972)
J Reprod. Fert. Suppl. 17

Early Scientific Publication:
Antonie Van Leeuwenhoek's

- Discoverer of red blood cells (1673) and sperm (1677)
- Published 375 letters between 1678-1717, most in Philosophical
  Transactions of the Royal Society of London
- First letter to the Royal Society in 1673

SOURCE: WAW MOLL
http://www.euronet.nl/users/warnar/leeuwenhoek.html#sperm

"A specimen of some observations made by a
Microscope contrived by Mr. Leeuwenhoek, lately
communicated by Dr. Regener de Graaf"
The earliest European scientific journals:

5 January 1665
Le Journal des Sçavans

6 March 1665
Philosophical Transactions of the Royal Society of London

The advent of 'science'

"science"
- derived from the Latin word scientia for knowledge

"scientist"
- coined in 1833 by William Whewell
- refers to "a systematically-working natural philosopher (as opposed to an intuitive or empirically-minded one)"

"scientific method"
- the prescriptive part of how to make discoveries in natural philosophy, almost unused during the early part of the 19th century
- introduced in the 1870s - rarely total agreement on what it was

Exponential journal growth

Decline in priority disputes

Derek J. de Solla Price, Science Since Babylon.
New Haven: Yale University Press, 1961
“Why do we write scientific papers?”

- Historical perspective
- **Current issues**
- Future trends
“Why do we write scientific papers?”

• Ideals
  - Priority
  - Scientific progress
  - Quality of life etc.

• Realities
  - What to publish?
  - Where to publish?
  - With whom to publish?

What to publish?
‘Publish or perish’
- Primary article
- Letter
- Review
- Conference proceedings
- Technical report
- Grant application
- Abstract
- Book chapter
- Patent
“Why do we write scientific papers?”

Where to publish?

Impact Factor
- General interest journal
- Society journal
- Specialist journal
- Open access
- Book
- Thesis
“Why do we write scientific papers?”

• Ideals
  - Priority
  - Scientific progress
  - Quality of life etc.

• Realities
  - What to publish?
  - Where to publish?
  - With whom to publish?

The ‘Matthew Effect’

Merton RK (1968) Science 159:56-63

“...For unto every one that hath shall be given, and he shall have abundance: but from him that hath not shall be taken away even that which he hath.”

Matthew 25:29, King James Version.

The ‘Matthew Effect’ in Scientific Publishing:

• “[...irrespective of the order of authors on a paper, it is referred to informally and sometimes formally by the name of the best-known author.”

• “[...in laboratory libraries papers are filed under the name of the "senior" author and remembered and discussed under his or her name.”

• “[...A graduate student in my laboratory had published a seminal paper, without my name on it, on an enzyme called alcohol dehydrogenase that everyone agrees has revolutionized the experimental study of population genetics. Shortly afterward I gave a lecture on a different subject, at the end of which a colleague came up from the audience and said, "That was very interesting but what I really admire is your paper on alcohol dehydrogenase.”

• “[...There is some justice in the world, however, and the misappropriation of intellectual property occasionally means that one may try to pass a bad check. The Matthew Effect then does its work. The fraud attributed to Imashiki-Kari becomes known as the "Baltimore Affair." To them that hath it shall be given.”

COPE Guidelines on Authorship

1. The award of authorship should balance intellectual contributions to the conception, design, analysis and writing of the study against the collection of data and other routine work. If there is no task that can reasonably be attributed to a particular individual, then that individual should not be credited with authorship.

2. To avoid disputes over attribution of academic credit, it is helpful to decide early on in the planning of a research project who will be credited as authors, as contributors, and who will be acknowledged.

3. All authors must take public responsibility for the content of their paper. The multidisciplinary nature of much research can make this difficult, but this can be resolved by the disclosure of individual contributions.

4. Careful reading of the target journal’s “Advice to Authors” is advised, in the light of current uncertainties.

“Why do we write scientific papers?”

• Historical perspective
• Current issues
• Future trends
“Why do we write scientific papers?”

• Future trends

Number of internet hosts per country, 2005

http://en.wikipedia.org/wiki/Internet_hosting

“Why do we write scientific papers?”

e-research

1. Digitisation of analogue information: journals/books/libraries/artefacts
2. The ’Data Deluge’ – explosion of ’born digital’ information
3. Availability of bandwidth, computation power
4. Increasing use of visualisation and modelling for data analysis
5. Text-and data-mining
6. The realisation of the collaborative potential of the Web (Web 2.0, network effects, collective intelligence)
7. The extension of ’collaboration’ from humans to machines – “from a web of documents to a web of data” (Semantic Web)

Eighteen paragraphs can make a paper.

Human Reproduction Precongress course Amsterdam

JLH Evers
Center for Reproductive Medicine
Maastricht University Medical Center
Maastricht, The Netherlands

At the end of this lecture the participant should be able to:

- Describe the historical developments in the composition of a scientific article
- Describe the IMRAD system
- Name the 18 essential paragraphs that together constitute a scientific article
- Summarize the several ways in which clinicians read journals
- Know how to get technical assistance from the CONSORT site, and for which types of articles

Writing up biomedical research

- Think of yourself as a reader for a moment.
- What kind of papers do you like to read?
- Short, substantial and clear most likely.
- Well, then, write short, substantial and clear papers yourself.

Mimi Zeiger
2 questions before deciding to write

☐ So what?

☐ Who cares?

Scholarly journals

5 January 1665

Denis de Sallo, France

Le Journal des Scavans

Le Journal de Scavans 1665

☐ Catalogue and short description of books
☐ Obituaries of famous men
☐ Experiments in physics and chemistry
☐ Astrological phenomena
☐ Anatomical findings
☐ Useful machines
☐ Decisions of tribunals and universities
☐ Current events in academia
Scholarly journals

1665 Journal de scavans France
1665 Philosophical transact Royal Society U.K.
1668 Giornale dei litterati di Roma Italy
1670 Miscellanea curiosa medico-physica Germany
1673 Acta medica et philosophica Denmark
1680 Collectanea medico-physica Netherlands

The organization of articles

1665 Letter  "First I saw this, then I saw that"
1750 Report  Narrative
1850 TED  Theory
            Experiment
            Discussion
1972 IMRAD  Introduction
            Material & Methods
            Results
            Discussion

![Graph showing the evolution of article formats from 1925 to 1995]
There are 3 ways in which clinicians read journals

1. Grazing
How do clinicians read journals?

1. Grazing  80%
2. Hunting   15%
3. Gorging  5%, and falling
What do grazers read?

I had my six good serving men
They taught me all I know
Their names were
What and Why and When
And Who and Where and How

Rudyard Kipling

6 Questions before starting

<table>
<thead>
<tr>
<th>Introduction</th>
<th>Why did you study this problem?</th>
</tr>
</thead>
<tbody>
<tr>
<td>M&amp;M</td>
<td>What did you do?</td>
</tr>
<tr>
<td></td>
<td>How did you do it?</td>
</tr>
<tr>
<td>Results</td>
<td>What did you find?</td>
</tr>
<tr>
<td>Discussion</td>
<td>What does it mean?</td>
</tr>
<tr>
<td></td>
<td>How does it relate to previous work in the field?</td>
</tr>
</tbody>
</table>
Reporting clinical studies effectively in 18 thoughtful paragraphs

Introduction

<table>
<thead>
<tr>
<th>Paragraph</th>
<th>Text</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Start</td>
<td>The first sentence should pick up some or most of the words from the title</td>
</tr>
<tr>
<td>2. Why</td>
<td>Provide a context and motivation for the investigation</td>
</tr>
<tr>
<td>3. What</td>
<td>The last sentence should begin: “The purpose of this study is to ...”</td>
</tr>
</tbody>
</table>

Oral contraceptives and GnRH-agonists show similar outcomes in endometriosis.

It has been suggested that the treatment outcome of GnRH-agonists in endometriosis is superior to any other medical treatment.

Hum Reprod 2006;22, 112-118
Introduction

1. Start: The first sentence should pick up some or most of the words from the title.
2. Why: Provide a context and motivation for the investigation.
3. What: The last sentence should begin: “The purpose of this study is to ...”

Motivation Example

<table>
<thead>
<tr>
<th>Purpose</th>
<th>This paper presents an evidence-based approach to diagnosing PID.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scope</td>
<td>This paper discusses 5 causes of fertilization failure after ICSI.</td>
</tr>
<tr>
<td>Viewpoint</td>
<td>Calling ART clinicians ‘providers’ insults our professionalism.</td>
</tr>
<tr>
<td>Quotation</td>
<td>Recently, in Human Reproduction, Van Steirteghem reported ...</td>
</tr>
<tr>
<td>Question</td>
<td>Which is the safest way to perform a laparoscopy?</td>
</tr>
<tr>
<td>Argument</td>
<td>The diagnosis of PCOS is not based on ultrasound findings. Is this logical?</td>
</tr>
<tr>
<td>Action</td>
<td>Now is the time to reconsider blastocyst transfer.</td>
</tr>
<tr>
<td>Case report</td>
<td>The next patient you see may have porphyria. Will you recognize it?</td>
</tr>
<tr>
<td>Statistic</td>
<td>1 in 6 high school girls is chlamydia positive.</td>
</tr>
</tbody>
</table>

Introduction

1. Start: The first sentence should pick up some or most of the words from the title.
2. Why: Provide a context and motivation for the investigation.
3. What: The last sentence should begin: “The purpose of this study is to ...”
Material & Methods

<table>
<thead>
<tr>
<th>Paragraph</th>
<th>Text</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. Subjects Study design</td>
<td>Inclusion/exclusion criteria, participants Informed consent, IRB approval Demographics (if retrospective): table 1</td>
</tr>
<tr>
<td>5. Procedures Detail experiment, drugs, equipment</td>
<td></td>
</tr>
<tr>
<td>6. Definitions &amp; criteria Disease criteria, ranking system (give criteria), staging of disease, (in)dependent variables</td>
<td></td>
</tr>
<tr>
<td>7. Data collection Prospective/retrospective Validation of data, data quality Blinding, intra/interobserver variability Gold standard</td>
<td></td>
</tr>
<tr>
<td>8. Statistics Statistical tests in order in which applied Sample size, power calculation</td>
<td></td>
</tr>
</tbody>
</table>

Results

<table>
<thead>
<tr>
<th>Paragraph</th>
<th>Text</th>
</tr>
</thead>
<tbody>
<tr>
<td>9. Subjects Demographics (if prospective): table 1</td>
<td></td>
</tr>
<tr>
<td>10. Results Facts &amp; numbers, no editorializing</td>
<td></td>
</tr>
<tr>
<td>11. Presentation Tables &amp; figures (do not repeat text)</td>
<td></td>
</tr>
<tr>
<td>12. Correlations How well did independent variable (predictor) lead to dependent variable (outcome)? Effect sizes of variables Comparison to gold standard Statistical significance (statement of strength of evidence, not of clinical importance)</td>
<td></td>
</tr>
</tbody>
</table>

Discussion

<table>
<thead>
<tr>
<th>Paragraph</th>
<th>Text</th>
</tr>
</thead>
<tbody>
<tr>
<td>13. Summarize results Principal findings, i.e. those that address questions posed in Introduction Do not reiterate Results Never, never introduce new data</td>
<td></td>
</tr>
<tr>
<td>14. Interpretation of results Principal findings of paragraph 13 become substrate on which principal conclusions are based Too many conclusions dilute the impact of any one</td>
<td></td>
</tr>
<tr>
<td>15. Interpretation in context of the literature Consistent with or departure from current thinking Give reasons No literature review, focus on relating studies</td>
<td></td>
</tr>
<tr>
<td>16. Clinical implications Clinical study: discuss new insight in disease Basic study: discuss pathophysiology</td>
<td></td>
</tr>
<tr>
<td>17. Limitations Be thoughtful &amp; self-critical, discuss validity of findings, practical limits, interpretations</td>
<td></td>
</tr>
</tbody>
</table>
Conclusion

Paragraph Text

18. So what
Restate principal findings and conclusions
Emphasize clinical and basic science implications of principal findings
Indicate logical next step (if any)

Introduction

Results
9. Descriptive statistics, baseline population comparisons
10. Results, outcome
11. Measures of data validity
12. Statistical analysis

Discussion & Conclusion
13. Principal results
14. Interpretation of principal results
15. Interpretation in context of literature
16. Clinical/pathophysiol. implications
17. Limitations
18. Conclusion, future directions

M&M
4. Subjects
5. Procedures & techniques
6. Definitions & criteria
7. Data collection & validation
8. Statistical tests

What IMRAD does not address
☐ The title
☐ The authors
☐ The abstract
☐ The acknowledgements
☐ The references
SET in IVF

In unselected patients, elective single embryo transfer prevents all multiples, but results in significantly lower pregnancy rates compared with double embryo transfer: a randomized controlled trial.

About titles

NEJM: Concise and descriptive, not declarative
Lancet: Concise but informative
Ann Int Med: As brief as possible while conveying essential features of the article's content
BMJ: Keep them concise
HR: Specific and informative, should not exceed 25 words
Auricular electro-acupuncture as an additional perioperative analgesic method during oocyte aspiration in IVF treatment
Essential for titles
☐ Concise and precise
☐ Informative and descriptive
☐ Not misleading or unrepresentative
☐ Specific: type of study (RCT) and numbers (if large)
☐ Words appropriate for classification
☐ Interesting, not dull, lure grazer into reading

G.M. Hall, How to write a paper, 2008

Describe paper in 1 or 2 sentences
A epidemiological geographically based study of the quantity and effects of ionising radiation received by male employees of a nuclear reprocessing plant and male residents working elsewhere in the same vicinity shows an increased risk of infertility in nuclear workers only. (41 words)

Remove waste words
A epidemiological geographically based study of the quantity and effects of ionising radiation received by male employees of a nuclear reprocessing plant and male residents working elsewhere in the same vicinity shows an increased risk of infertility in nuclear workers only. (41 words)
A epidemiological geographically based study of the quantity and effects of ionising radiation received by male employees of a nuclear reprocessing plant and male residents working elsewhere in the same vicinity shows an increased risk of infertility in nuclear workers only. (41 words)

Write draft title Epidemiological study of the effect of ionising radiation on fertility in male employees of nuclear reprocessing plants. (17 words)

Reduce it Nuclear reprocessing, radiation exposure, and male infertility: an epidemiological study. (10 words)
Search for Charged Higgs Bosons from Top Quark Decays in $p$ Collisions


HR structured abstract

Background  
Background and objective

Methods  
Design, setting, patients, interventions, main outcome measures

Results  
Main results

Conclusions  
Conclusion
Single most important limitation
The CONSORT statement is an important research tool that takes an evidence-based approach to improve the quality of reports of randomized trials.
Technical assistance

CONSORT  Treatment study, RCT
STARD    Diagnostic test study
STROBE   Observational study
QUOROM   Systematic review, meta-analysis of RCT’s
MOOSE    Systematic review, meta-analysis of observational studies

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

Wager, Godlee, Jefferson:
How to survive peer review? 2002

How to survive peer review?

Further reading

Björn Gustavii
Robert A Day
George M Hall
Further reading

Jennifer Peat  Vernon Booth  Robert Taylor
Introduction

- The Methods should be reported in sufficient detail to permit a competent researcher to repeat the study and reproduce the results.
- As part of the outline of the manuscript one has to briefly state the population in which you worked, the sampling method you used, and most importantly, the methods you used to carry out the study.
- The technical details of an article are essential to the science but not to the narrative of the article; these technical details should be in Methods section.
- In the Materials and Methods section one has to answer the previously posed questions: What did you do? How did you do it?
- Each Journal may have specific requirements for M&M which are mentioned in the Information for Authors (IFAs).

What do Human Reproduction's IFAs mention?

- In Methods section the design, setting, patients, interventions and main outcome measures should be described.
- Names, town and country of origin of all suppliers.
- Randomized controlled trials (RCT) should be reported in accordance with CONSORT statement: 1) flow chart showing progress of participants through the trial; 2) check list for editors and reviewers showing that 22 key points are in the report.
- For ESHRE journals all RCTs are reviewed by a team of journal-appointed statisticians.
- Systematic reviews with or without meta-analysis should be reported in accordance with QUOROM (Quality of Reporting of Meta-analyses): flow chart and checklist are needed.
General requirements for M&M section

• Order of procedures can be chronological or by type of procedure
• Use sub-headings
• Use the past tense and the third person to describe what was done. Instead of “I incubate the sample at 37°C for 3 days” it should be “The sample was incubated at 37°C for 3 days.”
• Describe experimental design clearly, including the hypotheses you tested, variables measured, how many replicates you had, controls, treatments, etc.
• Explain why each procedure was done. Provide reference to published paper instead of lengthy description.

General requirements for M&M section

• Identify equipment, reagents, medications used
• Only modifications to already published equipment or procedures must be described. For example “controlled ovarian stimulation was done as described in detail in – reference;” should not be followed by a lengthy repetition of the protocol sometimes reported as “in brief the protocol includes ……” and then the stimulation protocol is repeated in detail.
• Measurements should be correctly quantified including errors of measurement
• Approval of the study by local or national ethics committee and informed consent of the subjects must be clearly mentioned.

General requirements for M&M section

• A section of M&M will include statistics: which tests were used
• Ordinary statistical methods can be used without comments
• Advanced or unusual methods may require brief description and literature citation
• When the M&M section is written, show the text to a colleague and ask whether they would have difficulty in repeating the study
• Do not mix Results with M&M
• Avoid irrelevant information for the reader for instance the colour of the ice bucket used.
Purpose of M&M section

- Cornerstone of scientific method implies that experiment can be repeated
- It is irrelevant that experiments will, most likely, not be repeated
- Were correct methods used? If this is not the case, the findings are not valid
- Most readers skip this section; general reader has no interest in details
- Good reviewer will read M&M carefully and in case of doubt, rejection of manuscript will be recommended

Materials

- Provide exact technical specifications and quantities and source or method of preparation
- Avoid use of trade names (advertising), use generic or chemical names which are likely to be known worldwide
- For experimental animals include genus, species and strain and special characteristics (age, sex, genetic and physiological status)
- For human subjects describe in detail all inclusion and exclusion criteria
- The Journal’s IFAs may have specific requirements regarding for instance cell lines and reagent data – ensure you’ve read them

Methods

- The usual order for presentation is chronological
- Related methods should be described together precluding sometimes following straight chronological order
- If a particular assay was not done until late in research, the assay method should be described along with the other assay methods
Headings

• M&M section often has subheadings. Consult analogous papers in the selected journal to see whether subheadings are appropriate

• If possible construct subheadings that will “match” the subheadings in the Results section

• Writing of the manuscript will be easier if you strive for internal consistency; the reader will grasp quickly the relationship of a particular methodology to the related results

Measurements and analysis

• Be precise. Methods are similar to cookbook recipes. If a reaction mixture was heated, give the temperature. Questions such as “how” and “how much” should be precisely answered by the author and not left to be found out by reviewer or reader

• Statistical analyses are usually necessary, but feature and data should be discussed, not the statistics. Ordinary statistics should be used without comment; advanced or unusual methods may require a literature quotation

• Be careful with your syntax.

Are references needed in M&M?

• All methodological details are required if the technique is new and unpublished

• If a method has been published in a journal the literature reference should be given. A few words of description may be necessary for a method with which readers may not be familiar

• If several alternative methods are commonly employed it is essential to identify your method and the reference. It is better to state: “cells were broken down by ultrasonic treatment as previously described (ref)” than to state “cells were broken down as previously described (ref)”
Tables and figures

- For certain methods it may be better to present the information in tabular form. Typical examples are the probes used in PCR for different gene fragments.
- A diagram can sometimes make it easier to understand a procedure.
- A flow chart of experimental protocols and diagrams of experimental apparatus can be useful.

Grammar and correct form

- Do not make the common error of mixing some of the Results in this section.
- A good test is to provide a copy to a colleague and ask whether he or she can follow the methodology. Glaring errors are sometimes picked up.
- Correct use of English grammar and punctuation should be strived for. Something as simple as a missing comma could lead to serious misunderstandings.
- In contrast to other sections of the manuscript the passive voice can be used validly. What was done must be specified, who did it is irrelevant.

Grammar and correct form

- Section provides short, discrete bits of information but the writing becomes sometimes telescopic.
- Most common error is to state the action without, when necessary, stating the agent of the action.
  - "Having completed the study, the bacteria were of no further interest".
  - "Blood samples were taken from 48 informed and consenting patients...the subjects ranged in age from 6 months to 22 years" (Pediatric Research 6:26,1972). There is no grammatical error with that sentence but what about 6 months old children, can they give informed consent?
- Always watch for spelling errors both in manuscripts and PDF proofs.
### Reporting Randomized Trials

- **CONSORT statement:** Consolidated Standards of Reporting Trials
- **Who, what, when and where are good reminders for the methods section of trials and cohort studies**
- **Primary outcome and sample size assumptions should be part of the statistics session**

### Table 1: Original CONSORT Checklist

<table>
<thead>
<tr>
<th>Item Number</th>
<th>Descriptor</th>
</tr>
</thead>
</table>
| 1           | The primary aim was allocated to interventions e.g., 
             randomization, assignment. |
| 2           | Surnames and organisation of animals. |
| 3           | Inclusion and exclusion of animals (e.g., randomization, assignment) |
| 4           | The inclusion and exclusion of studies (e.g., randomization, assignment) |
| 5           | The inclusion and exclusion of studies (e.g., randomization, assignment) |
| 6           | The inclusion and exclusion of studies (e.g., randomization, assignment) |
| 7           | The inclusion and exclusion of studies (e.g., randomization, assignment) |
| 8           | The inclusion and exclusion of studies (e.g., randomization, assignment) |
| 9           | The inclusion and exclusion of studies (e.g., randomization, assignment) |
| 10          | The inclusion and exclusion of studies (e.g., randomization, assignment) |
| 11          | The inclusion and exclusion of studies (e.g., randomization, assignment) |
| 12          | The inclusion and exclusion of studies (e.g., randomization, assignment) |

### Improving the quality of reports of meta-analyses of randomized controlled trials: the QUOROM statement checklist - METHODS

- **Subheading**
  - **Search:** The information sources, in detail (e.g., databases, registers, personal files, expert informants, agencies, hand-searching), and any restrictions (e.g., language, publication status, publication dates, language of publication).
- **Selection:** The inclusion and exclusion criteria (e.g., population, intervention, principal outcomes, and study design).
- **Validity assessment:** The criteria and process used (e.g., masked assessment, quality assessment, and their findings).
- **Data abstraction:** The process or processes used (e.g., completed independently, in duplicate).
- **Study characteristics:** The type of study design, participants' characteristics, details of intervention, outcome definitions and how clinical heterogeneity was assessed.
- **Quantitative data synthesis:** The principal measures of effect (e.g., relative risk), method of combining results (statistical pooling and confidence intervals), handling of missing data, how statistical heterogeneity was assessed, a rationale for any a priori sensitivity and subgroup analyses; and any assessment of publication bias.
Potentially relevant RCTs identified and screened for retrieval (n=…)

RCTs excluded, with reasons (n=…)

RCTs retrieved for more detailed evaluation (n=…)

RCTs excluded, with reasons (n=…)

Potentially appropriate RCTs to be included in the meta-analysis (n=…)

RCTs excluded from meta-analysis, with reasons (n=…)

RCTs included in meta-analysis (n=…)

RCTs withdrawn, by outcome, with reasons (n=…)

RCTs with usable information, by outcome (n=…)

38 of 76
Optimizing the Results
Section of an RCT Manuscript

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Disclosures

• Consulting work for EMD Serono,
  Schering-Plough and Ferring
• Commissioned and voluntary work for
  Agency for Human Reproduction Canada

Why bother?

“The whole of medicine depends
on the transparent reporting of
clinical trials”

Drummond Rennie
Objectives

• The art of medical writing
• Key elements of Results section
  • In Vitro Fertilization with Preimplantation Genetic Screening. Mastenbroek et al, NEJM July 2007; 357 (1) 9-17
• Using medical statistics

Medical writing as an art

“Improving the quality of writing actually improves the quality of thought”

“Readers do not simply read, they interpret”

George Copen and Judith Swan, American Scientist 1990, 78, 550-558

Good writing has “shape”...

• Information is interpreted best if it appears where expected
• Moderate violation of this concept may lead to major misinterpretation
• Conscious control of locations improves the degree of recognition
### Basic principles

- In correct order
- Clear
- Simple
- Concise
- Combining text, tables and figures to **condense** data and **highlight** trends

### Make grammar (and the reviewer) your friend…

- The grammatical subject should be quickly followed by its verb
- Each unit of discourse should make a single point

### The topic position first?

- “As the assumption behind using telephone follow-up was that couples would prefer this approach to traveling a long distance for a short appointment, the responses of the 75 couples who lived > 50 miles from the unit were considered specifically”
• “Data from couples who lived > 50 miles from the unit were analyzed separately, because those patients might consider telephone follow-up more convenient than long distance travel.”

• Couples who were randomized on to the study and returned questionnaires were broadly similar to all couples undergoing embryo transfers at the unit over the study period (Table 1).

• “Study patients were similar to others undergoing IVF/ET at the unit during the same time period (table 1).”
If you don’t love English…

- Get someone who does love it, to read and edit your manuscript before submission

Objectives

- Medical writing as an art
- Key elements of Results section
  - In Vitro Fertilization with Preimplantation Genetic Screening. Mastenbroek et al, NEJM July 2007; 357 (1)
- Using medical statistics

Job description for “Results”

1. Present of data condensed and organized, highlighting key findings and trends
2. Use appropriate statistical tools to help judge significance of findings
3. State them with “qualification” but not with “interpretation”
### Presenting Results

*In Vitro Fertilization with Preimplantation Genetic Screening. Mastenbroek et al, NEJM July 2007; 357 (1) 9-17*

- (Sites for study in Methods section)
- Identify the time frame for study - dates of enrollment, treatment and data collection periods (with reasons) May 2003-Jan 2007

### Presenting Results

*In Vitro Fertilization with Preimplantation Genetic Screening. Mastenbroek et al, NEJM July 2007; 357 (1) 9-17*

- Deviations from protocol: withdrawal of consent, unwillingness to accept blinding
- 408 randomized, brief summary of who received what, then referred to flow chart

### Trial Flow Chart

- Big
- Simple
- Linear
- Use tabs to indent below main numbers
Flow Chart Based on CONSORT Model

Number of patients assessed for eligibility
- Number of patients excluded
  - Didn't meet criteria
  - Declined enrollment
- Number of patients randomly assigned
- Number of patients assigned to intervention
  - Received intervention
  - Didn't receive intervention (give reasons)
- Number of patients assigned to control
  - Received control
  - Didn't receive control (give reasons)
- Number of patients lost to follow-up (give reasons)
- Number of patients discontinued intervention (give reasons)
- Number of patients excluded from analysis (give reasons)

Number of patients analyzed
- Number excluded from analysis (give reasons)
- Number lost to follow-up (give reasons)
- Number discontinued intervention (give reasons)

Tables and Figures

- Table 1: age, gravidity, duration, BMI, primary diagnosis. (No p values)
- If an important prognostic factor is unbalanced between groups:
  - Highlight
  - Explain if possible
  - Later in Results, consider an adjusted analysis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Women Who Underwent Pregnancy Interventions (N = 28)</th>
<th>Controls (N = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age — yr</td>
<td>30 (28.3)</td>
<td>37 (30.4)</td>
</tr>
<tr>
<td>Nulliparous — no. (%)</td>
<td>98 (94)</td>
<td>92 (93)</td>
</tr>
<tr>
<td>Nulliparous — no. (%)</td>
<td>133 (45)</td>
<td>139 (45)</td>
</tr>
<tr>
<td>Duration of infertility — yr</td>
<td>4.1 (2.3)</td>
<td>3.8 (2.5)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>24.6 (4.6)</td>
<td>24.6 (6.7)</td>
</tr>
<tr>
<td>Cases of infertility — no. (%)</td>
<td>9 (32)</td>
<td>8 (27)</td>
</tr>
<tr>
<td>Lower segment cesarean section — no. (%)</td>
<td>7 (15)</td>
<td>7 (37)</td>
</tr>
<tr>
<td>Tocolytic — no. (%)</td>
<td>6 (12)</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Amniocentesis — no. (%)</td>
<td>14 (5)</td>
<td>15 (5)</td>
</tr>
<tr>
<td>Endometriosis — no. (%)</td>
<td>15 (5)</td>
<td>7 (2)</td>
</tr>
<tr>
<td>Cesarean — no. (%)</td>
<td>6 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other factors — no. (%)</td>
<td>2 (1)</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

* P-values are reported as p < 0.05.

† The body mass index is the weight in kilograms divided by the square of the height in meters. The body mass index is calculated for all women (98%).
‡ More than one diagnosis per couple was possible. 169 couples had one diagnosis, and 31 couples had two diagnoses.
§ Donors were from women of advanced maternal age were used in these cases.
Presenting Results: primary outcome first

In Vitro Fertilization with Preimplantation Genetic Screening. Mastenbroek et al, NEJM July 2007; 357 (1) 9-17

- PGS resulted in lower live birth rate*
  24% [49 of 206] vs. 35% [71 of 202]
  Rate ratio 0.68; 95% CI, 0.50 to 0.92
  p=0.01 (absolute diff 11%, NNH 10)
- Simple presentation of distilled information

Principles for Tables, Figures

- Data summarized, not raw
- Use text to describe data and table to show them
- Use figures only when data lend themselves to visual representation

Principles of Table structure

- Format to help reader find, read understand and remember information
- Values compared, placed side by side
- Data should not be duplicated elsewhere in text
- Title and table should be freestanding
Principles of Figure construction

- Charts for categorical data and graphs for continuous data
- Include only necessary elements
- Emphasize data
- Identify all elements in the data field
- Caption and figure should be free-standing

Tables and Figures

- Table 2: key results, rate ratios with 95% CI and exact p value
- Table 3: clinical characteristics by treatment cycle 1-3, further details
- Table 4: embryology data

Presenting Results

- Then sub-group analyses for cycle
- Then embryology / implantation rates
- Finally details of abnormal pregnancies - termination for trisomy, preterm twins, stillbirth
Summary: Results presentation

- Key results up front
- Present all primary data, positive or negative
- 95% CI, NNT (or harm), exact p value
- Be concise, clear
- Use tables/figs to compliment text

Objectives

- Medical writing as an art
- Key elements, Results section
- Using medical statistics

Using medical statistics

- *Inferring* from "sample" to "population"
- *Defining* the effect
- *Testing* the effect
Statistical inference: key questions to consider

- Is the sample representative of the population?
- Are groups within sample similar to each other?
- Are effects seen due to intervention, bias or chance?

Defining the effect with confidence intervals (CI)

- Study measurements are “sample estimates” of “population truth”
- CI’s show the range of values believed to encompass the “true” population value (95 samples out of 100)
- CI’s shift focus from qualitative estimate of chance to quantitative measure of effect

Example of CI use

- 400 obese women with PCO randomized to a partial meal replacement protocol vs dietary advice
- Mean wt loss 5.5kg vs 0.9kg, p 0.02
- Absolute difference 4.6kg (95% CI 1.8, 7.4kg, p 0.02)
### Statistical inference: CI’s

- CI’s give a sense of estimate precision
- Give a sense of clinical significance
- Have units!
- …report absolute differences and CI’s around all primary comparisons
  - whether results are statistically significant (positive) or not (negative)

### Testing an observed effect

The effect of IUI on pregnancy rate:
- “was statistically significant”
- “was statistically significant (p<0.05)”
- “8/200 (4%) with timed IC and 18/200 (9%) with IUI (p = 0.02)”
- “8/200 (4%) with timed IC and 18/200 (9%) with IUI (absolute difference 5%, [NNT 20], 95% CI 2.8%)”

### Testing the effect

- P<0.05 doesn’t prove anything….
- It defines the likelihood that the observed effect is real
- P values don’t “trend towards significance”
Using p values

- For a clinically important difference that isn’t statistically significant, report the effect size and the 95% confidence intervals.

Abuse of p-values

- “Absence of proof” is not “proof of absence”
- Failure to disprove the null hypothesis (p > 0.05) may be due to low power
- If a difference wasn’t detected, state the power of the study to demonstrate a clinically significant difference, had it been present.

Clinical and statistical significance

- A difference, to be a difference, must make a difference
  
  Gertrude Stein

- Specify the clinically important difference in advance (in Methods as key for power calculation)
Reporting statistics

- Consistent use of decimal places
- Use exact p values unless in a table showing large groups of data
- Use standard deviation as a measure of spread, not standard errors
- Use 95% confidence intervals for effect stats like correlation coefficient or difference between means

Medical statistics: red flags

- Multiple testing
  - should be adjusted for
- Post - hoc testing
  - should be plausible reason and reasonable conclusions
- Sub-group analysis
  - as above

Conclusions: medical writing as an art

- Each unit of discourse makes a single point
- Put subject, verb and object in correct order
- Use words judiciously
- If you don’t love the English language, find someone who does, pre-submission
Conclusions for key elements of Results section

- Inference from sample to population
- Define measured effect
- Test measured effect
- Highlight key trends but don’t discuss / evaluate them

Conclusions: medical statistics

- Goal is to infer from “sample measurement” to “population truth”
- Present 95% CI, exact p value for all primary outcomes, positive or negative (plus NNT where appropriate)
- “Absence of proof” does not equal “proof of absence”

Why bother (with medical statistics)?

“If medicine had not neglected this instrument, this means of progress, it would possess a greater number of positive truths and stand less liable to the accusation of being a science of unfixed principles, vague and conjectural”

Jean-Etienne Esquirol, the Lancet, 1838
“What has to be in the results section of a basic science paper?”

Steve Hillier
The University of Edinburgh
Editor-in-Chief MHR
s.hillier@ed.ac.uk

- The scientific paper: its conventions
- Results: their importance
- Data presentation: best practice
Proposed definition of a primary publication
Council of Biology Editors (1968)
An acceptable primary scientific publication must be the first disclosure containing sufficient information to enable peers to assess observation, to report experiments, and to evaluate intellectual processes; moreover, it must be susceptible to sensory perception, essentially permanent, available to the scientific community without restriction, and available for regular screening by one or more of major recognized secondary services (e.g., currently Biological Abstracts, Chemical Abstracts, Index Medicus, Excerpta Medica, Bibliography of Agriculture, etc., in the United States and similar services in other countries).

The sensory perception of follicles
The sensory perception of follicles

“... If they [the ova of women] are boiled... the liquor contained in them acquires upon cooking the same colour, the same taste and the same consistency as the albumen contained in the eggs of birds.”


Reliable Methods = Reproducible Results

The goal of Methods should be to:
• Facilitate the independent verification of results
• Minimize the influence of individual bias
• Produce results that others can more easily reproduce
• Promote the acceptance of results into the scientific consensus

But no method is infallible!

On Being A Scientist: Responsible Conduct In Research
COMMITTEE ON SCIENCE, ENGINEERING, AND PUBLIC POLICY
NATIONAL ACADEMY OF SCIENCES
NATIONAL ACADEMY OF ENGINEERING
INSTITUTE OF MEDICINE
NATIONAL ACADEMY PRESS
Washington, D.C. 1995

A good scientist never blames his methods

Andrews Vesalius. De humani corporis fabrica (1543) (On the Workings of the Human Body)
Vesalius on female testicles

The 'modern' scientific paper

- Title
- Abstract
- Introduction
- Methods
- Results
- Discussion
- Acknowledgements
- References
The ‘modern’ scientific paper

- Title
- Abstract
- Introduction
- Methods
- Results
- And
- Discussion
- Acknowledgements
- References

“What has to be in the results section of a basic science paper?”

- The scientific paper: its conventions
- Results: their importance
- Data presentation: best practice

“What has to be in the results section of a basic science paper?”

Answer: **EVIDENCE**

- Qualitative
  - Diagrammes
  - Images
- Quantitative
  - Tables
  - Graphs

“The fool collects facts, the wise man selects them”

*John Wesley Powell, 1888*
A 19th century result:

"Chromatolysis" = "Apoptosis"

A 20th century result:

"It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."


A 21st century result:

"A core network module in humans and mice was identified that is enriched for genes involved in the inflammatory and immune response and has been found to be causally associated to obesity-related traits."


Contains 2 tables, 3 figures, Supplementary Results (additional references, 7 Tables, and 7 figures with legends) and Supplementary Methods.
“What has to be in the results section of a basic science paper?”

- The scientific paper: its conventions
- Results: their importance
- Data presentation: best practice

Playfair graph: 200 years of wages and the price of wheat.

Recommended reads
Aim of the discussion

• Is NOT to “sell” the paper
• Is NOT to convince readers that the authors are right in their interpretation of data

Discussion: frequent pitfalls

• Emphasis only on strengths of the study
• Polemic instead of explanatory
• Authors go beyond the evidence and draw unjustified conclusions
First component of a good discussion

Must be “focused” on:

• the originality
  and
• the specific contribution of the study

Originality and specific contribution

Research area

• New area
• New findings in an old area
• Original contribution in a controversial issue

Originality and specific contribution

Study design

• Randomization
• Large population
• Long term observation
Originality and specific contribution

Material and methods
• Reliability
• Practicability
• Costs

Second component of a good discussion

Must be comprehensive
• All significant contributions quoted
• Priorities acknowledged
• Fair comparison for data produced by others

Third component of a good discussion

Must be essential
• Not too long
• Avoid repetitions
• Unjustified theories are not welcomed......
Fourth component of a good discussion

Must be self critical

The study limitations must be identified and explained

Different kind of study limitations

• Originality
• Design
• Biases
• Statistics

Fifth component of a good discussion

Must be open

Suggestions on the lines for future investigation are welcomed
Special types of reports have specific requirements that should appear in the discussion

- CONSORT = Consolidated Standards of Reporting Trials
- QUOROM = Quality of Reporting of Meta-analyses
- STARD = Standards in Accurate Reporting of Diagnostic

Suggested structure for discussion of scientific papers – 1 (R. Smith, BMJ, 18, 1224, 1999)

1. Begin with statement of principal finding: one or two sentences.
2. Honest examination of strengths and weaknesses. Editors and readers are mostly interested in weaknesses.
3. Relate the study to the previous ones. Not just mentioning that your study is better: compare strengths and weaknesses. Discuss why you might have reached different conclusions from others. Do not assume that your results are right if you do not know why your results are different.

Suggested structure for discussion of scientific papers – 2 (R. Smith, BMJ, 18, 1224, 1999)

4. What is the meaning of your findings?
   Be cautious, do not go beyond often “limited” evidence and emphasize sometimes what your study does not mean
5. What questions remain unanswered?
   What further work is needed?
   Do not corrupt evidence with speculation
<table>
<thead>
<tr>
<th>Key points of a good discussion</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Discussion should not be longer than results</td>
</tr>
<tr>
<td>• Avoid unjustified extrapolation and selective reduction.</td>
</tr>
</tbody>
</table>