Postgraduate Medical Education

Introducing the student and trainee to biomedical experimentation – a selective annotated bibliography

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Introduction

The main aim of a student in professional school, e.g. medical school, is to acquire professional skills. That goal is furthered during internship or residency periods. During these periods, research is encouraged, but only a minority of students or residents actually pursue research training or a research project. Many students and trainees, however, would like to understand research principles and procedures, or are simply intrigued by research. Sometimes the initial question is simply: what is research and would I enjoy being involved in experimentation? Many times a student who asks these questions wishes to understand the basics of research and may find her/himself dissatisfied with the rather limited formal education received from undergraduate, graduate and practice-oriented postgraduate schooling. Students interested in research occasionally approach a faculty member at their institution with hopes of being introduced to experimentation. Senior investigators have limited time with which to introduce the neophyte to the fundamental structure and especially the general ideas behind research. It is helpful for a researcher to have a bibliography of worthwhile readings to offer a student who wishes to acquire a basic background.

Furthermore, some students find themselves at institutions where there is little investigation done in their area of interest. Others may be at institutions which are not research centres. They might approach directors of student's education, or directors of residency programmes who are not necessarily researchers but would like to guide the student or trainee. These students might be motivated to do independent reading and would also benefit from a bibliography.

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The following questions are a representative sample which any beginning student or aspiring researcher might find himself asking. Some of these were actually asked by a fourth year medical student (first author) and others were further developed together with a supervisor (second author). What are the underlying schools of thought within which we function and in what ways do they facilitate or interfere with our quest for truth? What is truth? What is a fact? What are the different sorts of research? What is a clinical trial? What is the difference between a clinical trial and an experiment? How necessary is a preliminary literature search? How does one perform it and what should be focused on? Given that research involves answering some sort of question, what are the wise ways in which to ask the question? After a question has been refined, what are the basic elements any research design must have? What are the procedures central to experimentation? What is a research design? What are the basic requirements that a research design must meet to be valid? How much statistics does one need to know? How does one go about writing and publishing the research paper? How can computers help with the data management? How can one ethically experiment on humans? How does one acquire funding for research? What impact has technology had on research? What are the different instruments used by experimenters? Why do some investigators seem to work mainly in the laboratory and others function without one? Where does one look for an investigator to do research with? Does one need a mentor? If yes, how does one choose the most appropriate mentor. The list of questions is potentially almost infinite.

The nature of these inquiries varies from rather broad fundamentals to more specific details, such that they cannot be easily satisfied from one source. Searching for a particular topic within that broad spectrum can be tedious. Students and medical residents may benefit from an abbreviated biblio-

graphy which can help to focus an overwhelming literature search. An effort was made to find an annotated bibliography which addressed experimentation fundamentals. The most recent one found regarding this topic was from 1973. Therefore, a more recent search was undertaken by performing a library computer-assisted search of the keywords: research, research design, experimentation, experimental design and methodology. An extensive list of texts and journal articles was elicited. This annotated bibliography is a selective sample of that list.

One of the textbooks and one of the articles is each a more comprehensive introduction to various aspects of experimentation fundamentals than are the other references. It is suggested that these would be a sound starting point. They are identified with an asterisk.

Bibliography

Federer W., Balaam L.

Bibliography on Experiment and Treatment Design
Hafner Publishing Co., New York, 1973, 769 pgs
A listing of 8,700 citations which focus on the conduct, layout, philosophy, and statistical analyses of experimentation. There are no citations regarding the ethical aspects of research.

Books

*Oyster C., Hanten W., Lorens L.

Introduction to Research: A Guide for the Health Science Professional
J.B. Lippincott, Philadelphia, 1987, 238 pgs
This is possibly the most comprehensive text presented. It describes how to search the literature, the formation of the research problem, various experimental research designs, and the use of the computer in research. It also contains a simplified, but reasonably thorough overview of basic statistics. There is no discussion of how to apply for a research grant.

Campbell M., Machin D.

Medical Statistics: A Commonsense Approach
John Wiley and Sons, Chichester, 1990, 172 pgs
This text covers a broad range of basic topics, but especially includes a section which explains common mistakes that are made when using medical statistics. There is no discussion of the use of computers for statistics.

Dawson-Saunders B., Trapp R.

Basic and Clinical Biostatistics
Appleton and Lange Norwalk, Connecticut, 1990, 329 pgs

Besides a description of basic statistics there are chapters regarding the evaluation of diagnostic procedures and decision making in the clinical setting.

Freeman C., Tyrer P.

Research Methods in Psychiatry. A Beginner's Guide
ISBN 0 902241 29X, 1989, 248 pgs
Contains basic information for the beginner, with special emphasis on rating scales and the process of writing one's first paper. This text will not offer information beyond the social sciences.

Friedman L., Furberg C., DeMets D.

Fundamentals of Clinical Trials
PSG Publishing Company, Littleton, Massachusetts, 1985, 302 pgs
This text introduces basic concepts of clinical trials through examples from the authors' own experience and from the literature. There is no discussion of literature search or ethics.

Heaney R., Dougherty C.

Research for Health Professionals
Iowa State University Press, Ames, 1988, 268 pgs
This text directs attention to the collection and analysis of data, taking into account the variable nature of the data source. There is significant discussion of the ethical aspects of using humans for research. It offers little on the formulation of the research problem.

Meinert C., Tonascia S.

Clinical Trials: Design, Conduct and Analysis
Oxford University Press, New York, 1986, 469 pgs
This text covers seven basic topics: the current status of clinical trials, the principles behind and the execution of the trial, managing and analysing the trial, reporting the trial, and finally an appendix regarding these six topics. There is no discussion of ethics.

Royeen C.

Clinical Research Handbook
Slack Incorporated, Thorofare, New Jersey, 1989, 216 pgs
A rather focused text that concentrates solely on data analysis.

Spilker B.

Guide to Clinical Studies and Developing Protocols
Raven Press, New York, 1984, 302 pgs
A description of how to develop study designs and clinical protocols, and then how to conduct clinical studies. This text does not offer fundamental philosophy or theory behind research.

Stein F.

Anatomy of Clinical Research

Slack Inc., Thorofare, New Jersey, 1989, 269 pgs
A discussion of the scientific method, research problem, model, design, methodology and statistics. Somewhat unique to this text is the inclusion of a section on literature search. There is no discussion of ethics.

Thomas L.

The Lives of a Cell: Notes of a Biology Watcher
Bantam Books, New York, 1975, 192 pgs

A collection of essays which ruminate on the connections between science and the surrounding world. For example, one essay makes an analogy between a cell and a local community. This text does not present experiments or case studies.

Journal articles

General background

*Rogers B.

The question and the answer. Part 1: Levels of research questions.

Am Assoc Occupat Health Nurs J **38**(10): 502–3, 1990 Oct

This two-part article contains the broadest, most simplified introduction to various aspects of experimentation fundamentals. Part 1 suggests that questions are posed at three levels, with each level lending itself to certain types of research design, method and analysis. There is little discussion of 'how' each of the levels lends itself to appropriate methodology.

*Rogers B.

The question and the answer. Part 2: Planning for data analysis.

Am Assoc Occupat Health Nurs J **39**(1): 42–4, 1991 Jan

Appropriate statistical analysis is easily derived from the level of research question posed. Various statistical analyses are referred to, but there is little beyond basic introduction. For example, there is an explanation of the function of the chi square, but no actual presentation of a formula or of examples of how to use it.

Durant J.

Overview. Current status of clinical trials.

Cancer **65**(10): 2371–5, 1990 May 15

Needed advances in clinical oncology are dependent upon overcoming various problems interfering with the advancement of science. This paper will not teach one how to do a clinical trial.

Genest J.

Clinical research.

Can Med Assoc J **143**(5): 383–7, 1990 Sep

A description of the long history of clinical research as it has grown from the project of an isolated individual to become a huge effort supported by national governments. Because of the growth of molecular biology, clinical scientists are essential for linking biologists to clinicians. This paper also has some introductory information regarding the various paradigms of biomedical research, but no information about how to design research or analyse data.

Irby D.

Shifting paradigms of research in medical education.

Academic Med **65**(10): 622–3, 1990 Oct

As underlying scientific philosophies evolve, medicine also approaches the disease process in a different manner. This paper does not include information about methodology, or how to actually do an experiment.

Loeb V.

Reflections on clinical trials – and tribulations.

Cancer **65**(3 Suppl): 845–6, 1990 Feb 1

A discussion of how clinical trials have made significant contributions to medicine, but could make an even greater impact if patient entry into trials and funding were minimized as problems. This article does not attend to any of the theory, methodology, or format behind research.

Smith F.O.

Practice-based research: opportunities for the clinician.

South Med J **84**(4): 479–82, 1991 Apr

The performance of clinical trials in the physician's office can benefit both the physician and the discipline of medical research.

Steckler A., McLeroy K., Goodman R., Bird S., McCormick L.

Toward integrating qualitative and quantitative methods: an introduction.

Health Education Q **19**(1): 1–8, 1992 Spring

A comparison of the qualitative and quantitative approaches to research and a proposed means of combining the two.

Research funding

Koopman W.

Expressing our inner thoughts: how to organize and write a clinical research project grant application.

J Rheumatol **19**(Suppl 33): 16–9, 1992 Apr

Each component of the grant application is discussed as being a potential source of grant rejection. This paper states what an application requires and encourages the reader to attend to detail in each of these sections, but it does this with little elaboration. For example, there are no case presentations of poor writing followed by a corrected version.

Literature search

Wagner J., Wagner S.
Keeping abreast of the medical/dental literature: a simplified approach.

J Oral Maxillofacial Surg 50(2): 163–8, 1992 Feb
Clinicians have been found to prefer journal reading in order to continue their education. This paper presents algorithms and basic methods which can enhance one's ability to read the scientific literature.

Critical assessment of research papers

Easterbrook P., Berlin J., Gopalan R., Matthews D.
Publication bias in clinical research.

Lancet 337(8746): 867–72, 1991 Apr 13
An assessment of whether the presence of significant findings in a project determines whether or not the paper is published and where it is published.

Fowkes F., Fulton P.
Critical appraisal of published research: introductory guidelines.

Br Med J 302(6785): 1136–40, 1991
How to assess the hard facts of a paper. There is no review of statistics.

Rabeneck L., Viscoli C., Horwitz R.
Problems in the conduct and analysis of randomized clinical trials. Are we getting the right answers to the wrong questions?

Arch Intern Med 152(3): 507–12, 1992 Mar
Problems generated by performing clinical trials can result in directing the research focus away from its original intent. There is no basic description of what a randomized clinical trial is.

Ryan-Wenger N.
Guidelines for critique of a research report.
Heart Lung 21(4): 394–401, 1992 Jul–Aug
A guide to analysing research papers as based upon the scientific method, measurement theory, research ethics, and basic statistics.

Ethics

Dickens B., Gostin L., Levine R.
Research on human populations: national and international guidelines.

Law, Med Health Care 19(3–4): 157–161, 1991
A review of various papers and the current legal and political aspects of ethical positions as held by the WHO, CIOMS, and PHS. This paper does not compare the philosophical aspect of different positions.

Forrester J.
Using oneself as one's only experimental subject.
Lancet 336: 798–9, 1990 Sep 29
The allocation of subjects is a difficult aspect of scientific research so various investigators have turned to using themselves.

Halbreich U., Carson S.
Drug studies in women of childbearing age: ethical and methodological considerations.

J Clin Psychopharmacol 9(5): 328–32, 1989 Oct
Drug research in women of reproductive age has been rather restricted because of ethical concerns. A proposed drug study, which considers the use of lithium in women, is discussed to present the ethical and methodological problems of such a study.

Hellman S., Hellman D.
Of mice but not men. Problems of the randomized clinical trial.

N Engl J Med 324(22): 1585–9, 1991 May 30
Discussion of the moral dilemma for the physician-scientist, who as a physician has an obligation to each individual patient, and the scientist who has an obligation to society as a whole, possibly at the cost of the individual.

Passamani E.
Clinical trials – are they ethical?
N Engl J Med 324(22): 1589–92, 1991 May 30
This article offers support for the clinical trial as being ethical.

Structuring research design

Durrleman S., Simon R.
When to randomize?
J Clin Oncol 9(1): 116–22, 1991
Contends the classic notion that it is important to randomize as late as possible. Discusses how the timing of randomization can influence certain factors and how to decide which time is desirable and feasible. This paper does not discuss the fundamentals of which randomization is, or the theory behind it.

Fingerhut M.A., Halperin W., Okin A.
Enhancing the quality of epidemiologic studies.
J Occupational Med 33(12): 1233–5, 1991 Dec
Three suggestions are offered to improve epidemiological studies. They include the research protocols, dissemination of study results, and utilizing expertise from other disciplines. There are no suggestions regarding improvement of data analysis.

Gurr M.
Whatever happened to the notion of controlled experiments?
Br J Nutrition 63(2): 143–44, 1990 Mar
A general criticism of how various investigators have been generating inadequate studies with provision of examples within the nutritional field.

Halbreich U., Bakhai Y., Bacon K., Goldstein S., Asnis G., Endicott J., Lesser J.
The normalcy of self-proclaimed 'normal volunteers'.
Am J Psychiatry 146(8): 1052–5, 1989 August
Persons without physical or mental diagnoses as determined by brief structured interview were assessed more extensively for current and past diagnoses.

Jacobsen B.
Seeing the importance of blindness.
Nursing Res 39(1): 54–7, 1990 Jan
Discusses how nurses consciously omit blinding from their research, despite the need for it.

Ott M.
Importance of the study protocol in epidemiologic research.
J Occupational Med 33(12): 1236–9, 1991 Dec
Study protocol is assessed as being an essential quality link between research design and execution.

Overall J.
Design issues in clinical trials.
Prog Clin Biol Res 317: 1291–9, 1989
Different phases of clinical drug development require different types of experimental design.

Statistics

Arkin C.
How many patients are necessary to assess test performance?
JAMA 263(2): 275–8, 1990 Jan 12
Text, various tables, and example problems are presented which state sample size requirements necessary to elicit significant results.

Chanter D.
Why do we need statistics?
Br J Nutrition 62(3): 527–8, 1989 Nov
Written by a statistician who assesses submitted journal articles for statistical quality, this editorial addresses the fundamental role of statistics in experimentation, the need for researchers to have background in experimental design and the disenchantment of scientists with statisticians. There is no information about how to use statistical tests.

Clark V.
Sample size determination.
Plastic Reconstruct Surg 87(3): 569–73, 1991 Mar
Discusses the importance of sample size for research quality and how to determine the necessary sample size to ascertain results. The paper will give one a functional, but not very theoretical understanding of sample size determination.