

Handbook for Clinician Scientists

Tools for a Successful Academic Career



Robert Bortolussi, MD, FRCPC, Editor



Canadian Child Health Clinician Scientist Program
Programme canadien de cliniciens-chercheurs
en santé de l'enfant

SickKids[®]
FOUNDATION


CIHR IRSC
Canadian Institutes of Health Research / Instituts de recherche en santé du Canada


BC CHILDREN'S HOSPITAL
FOUNDATION

sanofi pasteur
The vaccines division of sanofi-sintelabo Group

The Canadian Child Health Clinician Scientist Program (CCHCSP) is funded by a Strategic Training Initiative in Health Research (STIHR) grant of the Canadian Institutes of Health Research (CIHR), and by SickKids Foundation, and BC Children's Hospital Foundation. Additional funding for this book is made possible by a generous unrestricted grant from Sanofi Pasteur Inc.

Handbook for Clinician Scientists

Tools for a Successful Academic Career

Dedication

This book is dedicated to my first and most important mentors: my parents, Joseph and Bernice Bortolussi

Acknowledgements

We thank the many authors and reviewers from Canada, the United States, and the Netherlands for their advice and comments on the early drafts of this book. Josh Thorpe provided invaluable assistance as copyeditor and Luke Itani as graphics designer. We also thank the many trainees and students we work with every day for their enthusiasm and helpful suggestions to identify issues important to their career needs. This book is for them.

All rights Reserved. No part of this book may be reproduced in any form without written permission of the copyright owners.

© HSC Research and Development Limited Partnership

Designed by SickKids Graphic Centre

ISBN 978-0-9690091-6-0

Foreword

The current revolution in health research is creating unprecedented opportunities to delineate the molecular mechanisms of disease. These new insights are, in turn, opening up novel strategies for the diagnosis, treatment and prevention of disease. What areas of expertise are required to fuel this scientific revolution and ensure that scientific discovery is translated into clinical practice? And how can Canada and other nations with publicly funded health systems, position themselves optimally to both contribute to and benefit from this revolution in science and medicine?

As always, there is an urgent need to attract the very best young minds, individuals capable of integrative thinking in this era of multidisciplinary. Ironically and frustratingly, at a time when clinical research and clinician scientists have never been more central to health research, young people increasingly are choosing not to pursue a career as a clinician scientist. They perceive a career in clinical research as too demanding, too competitive, requiring unacceptably long periods of training, and unappreciated by both their basic and clinical colleagues. The rapid pace of change today also makes it difficult even for fulltime clinicians or scientists to keep current in their fields.

For these reasons, health research organizations around the world are attempting to create new strategies aimed at developing a new generation of clinician researchers able to sustain a career in research. For example, when the Canadian Institutes of Health Research (CIHR) was launched in 2000, one of the very first priorities that was recognized was the need to revitalize and transform the training of the next generation of health researchers creating a cadre of young people comfortable with a problem-based, multidisciplinary approach to research. Accordingly, CIHR and its partners launched the Strategic Training Initiative in Health Research (STIHR) in 2001 to address these and other challenges. This new program places emphasis not on the individual student or mentor but on multidisciplinary groups of investigators who have come together around a common scientific theme or problem.

The creation and development of the Canadian Child Health Clinician Scientist Program (CCHCSP), one of 88 STIHR programs, has transformed the training of clinician scientists in Canada. With nodes at every pediatric teaching and research facility across Canada, and at all 17 academic health science centres, CCHCSP has, for the very first time, brought together in one program trainees and their mentors to focus on child health and launch the careers of the next generation of clinician scientists. Overnight, this national program has created the environment, the critical mass, the visibility, and the resources that are needed.

This timely Handbook, edited by Robert Bortolussi, arises out of the experiences of the CCHCSP since its inception in 2002. It focuses on the challenges facing clinician scientists at the beginning of their professional life, the scientific, technical and people skills that a clinician scientist needs in this post-genomics era, the special ethical issues that arise out of research involving children, the increasingly interdisciplinary nature of research, and the importance of mentoring for clinician scientists.

The importance of training clinician scientists has been recognized by other organizations in Canada and beyond. Indeed, child-focused foundations in Canada have partnered with the CIHR and CCHCSP to support its development. Of course, it will be very important and interesting to examine CCHCSP's success in turning around, in both quantitative and qualitative terms, the training of child health clinician scientists in Canada. Anecdotally, I believe one can already say that the CCHCSP has become a model internationally, and that the students who are now starting to move on from their training, and the young investigators being supported by the CCHCSP, will be the lasting evidence of the success of what CCHCSP has already accomplished. This Handbook is an important contribution to the ongoing dialogue internationally about how best to attract, train and nurture clinician scientists. Without them, we will not reap the full harvest of the potential of the great transformation currently taking place in health research.

Alan Bernstein, OC, PhD, FRSC, (LLD, Hons)

Executive Director

Global HIV Vaccine Enterprise and President Emeritus CIHR

Contents

Introduction 2

Ethics and Integrity

1. Basics in Research Ethics: *History of research ethics and the concept of “risk”*. 4
2. Conflict of Interest and Integrity 12
3. Regulating Research: *Navigating the sea of research ethics regulations* 20
4. Children in Research: *Involvement in research decisions*. 30
5. Culture, Religion and Ethnicity: *Undertaking research in vulnerable populations* . . 38

The Essential Toolkit

6. Research Design:
 A: Quantitative analysis: A general overview. 44
 B: Qualitative research: Basic principles 50
7. Basic Biology: *The ABCs of modern biological technologies* 58
8. Good Clinical Practice: *GCP 101* 66
9. Commercialization: *Welcome to the world of IP, TT, contracts, and licensing* 72
10. Setting Up a Research Program: *Short- and long-term needs* 84

Person to Person

11. Your Academic Home:
 A: How to find your first appointment 90
 B: Mentoring and Navigating your career path 96
12. Person to Person Management: *Tips on hiring and collaborating*. 104
13. Managing Time: *A friend not an enemy*. 110

Communication

14. Presentations: *How to successfully communicate your research story* 118
15. Writing a Manuscript: *Planning, drafting and publishing* 124
16. Writing a Research Grant: *Strategies for a successful outcome* 130
17. Policy Research: *How to communicate your research story to influence health policy*. 136
18. Knowledge Translation and Exchange: *How to ensure your research has impact in practice, policy, and health care* 144

Introduction to the Handbook for Clinician Scientists

The *Handbook for Clinician Scientist* is intended for aspiring clinician scientists who plan to pursue an academic career. Clinician scientists include physicians, surgeons, nurses, psychologists, occupational and physical therapists, and other health professionals who both care for patients and undertake research.

The Handbook arises from the curriculum developed within the Canadian Child Health Clinician Scientist Program (CCHCSP), a program dedicated to training the next generation of clinician scientists in the field of child and youth health. Clinician scientists in other fields will also find the Handbook useful since it contains information useful to all clinician scientists.

A career as a clinician scientist requires in-depth training in both clinical and scientific disciplines, leading to the development of a sustainable and productive program of research. Clinician scientists must also be prepared to meet ethical, interpersonal, and managerial challenges and to cogently communicate ideas in an oral and written form that captivates scientists, clinicians, and the lay public. The goal of this book is to help clinician scientists develop the knowledge and skills to meet these challenges.

The best approach in dealing with any career challenge is to carefully assess the issues and discuss options with peers and senior researchers before committing to a course of action. The chapters of this book are intended to prepare the reader for the day those assessments and discussions arise in the real world. Readers are also encouraged to participate in group discussions of various case scenarios at their own institution (see “Additional Learning Material” located on back cover).

There are four sections to the Handbook for Clinician Scientists.

- **Ethics and Integrity** sets the stage for an ethical research career by presenting a historical background of research ethics and contemporary views on conflict of interest, integrity, regulatory requirements, and the protection of vulnerable populations.
- **The Essential Toolkit** provides basic information on design and analytic methods, molecular biology, good clinical practice, and commercialization. These chapters will allow researchers to understand the added value of working with collaborators with diverse backgrounds.
- **Person to Person** gives insights on how to find a job, negotiate with one’s department head, establish good working habits, and develop good relations with employees and colleagues.
- **Communication** shares experts’ ideas on the best ways to make a presentation, write a paper or grant, and translate research into better practices and policies.

Robert Bortolussi, MD, FRCP(C)

Professor of Pediatrics and
Microbiology & Immunology
IWK Health Centre,
Dalhousie University
Director of Curriculum, CCHCSP

Norman D. Rosenblum, MD, FRCP(C)

Professor of Paediatrics and
Canada Research Chair in
Developmental Nephrology,
The Hospital for Sick Children
and University of Toronto
Principal Investigator, CCHCSP

Basics in Research Ethics:

History of research ethics and the concept of “Risk”

Nuala Kenny, MD, FRCPC

Department of Bioethics

Conrad Fernandez, MD, FRCPC

Department of Pediatrics

Dalhousie University

Halifax, Nova Scotia, Canada

What events come to mind when you think of the modern history of research involving human participants? Are there special considerations for children?

This module summarizes milestones in the history of research ethics, with a particular emphasis on research involving children and vulnerable populations, and provides an introduction to the ethical analysis of “risk.”

The objectives of this chapter are threefold:

- Recognize the centrality of voluntary consent in human research.
- Identify the ethical concerns with third-party (surrogate) decision-making regarding acceptable risk.
- Describe the different conceptions of risk for child participants.

History

The Nuremberg Trials

In 1947, 23 Nazi physicians and medical administrators were found guilty on charges of “murders, tortures and other atrocities committed in the name of medical science.” The tribunal recognized that certain types of medical experiments were ethically justified but, delineated “basic principles that must be observed in order to satisfy moral, ethical and legal concepts.” These points have become known as the Nuremberg Code:

- The voluntary consent of the human subject: the person involved... should be so situated as to be able to exercise free power of choice without the intervention of any element of force, deceit... or any form of coercion.
- Experimental validity: the experiment should be such as to yield fruitful results for the good of society.
- Other principles: avoidance of unnecessary harm and the importance of scientifically qualified researchers.

The trial of physicians at Nuremberg anticipated a major challenge to the Hippocratic tradition, which states that physicians should not inflict “intentional harm or injustice.” As scientific medicine developed, it was clear that new treatments would have to be studied in real patients who may be harmed with no hope for benefit before we would have evidence of the balance of potential benefits and risks. Thus began the ethics of human experimentation.

Tuskegee

In 1972 it was revealed that for 40 years the US Public Health Service had been performing studies on poor black men from Tuskegee, Alabama who had been denied treatment for syphilis. Awareness of these studies created a demand for more stringent regulations regarding informed and voluntary participation in human research.

The Need for Research in Vulnerable Populations

One might suggest that research should only be done on consenting adults who can make choices about risks, harms, and benefits, and that this research information should be then extrapolated to children and other populations. The history of research demonstrates clearly that this course has frequently been dangerous in its misunderstanding of the unique nature of the growing and developing child. The Nuremberg Code in its insistence on voluntary research participation prohibited most research involving children and many vulnerable populations. The Declaration of Helsinki formally disallowed non-therapeutic research on non-consenting subjects. Both of these codes present difficulties for those who work to advance the health of the most vulnerable in society, including children, who have not yet achieved the capacity for consent, and adults who have temporarily or permanently lost this capacity.

An essential and enduring problem for society is how to promote the best interests of children and other vulnerable populations through participation in research advances while protecting their rights and welfare.

It should be clear that while voluntary participation is an essential value, those who are not capable of giving voluntary consent must be studied somehow so they too can benefit from scientific advances. Policy that strictly prohibits children and other vulnerable populations from participation in research may harm both individuals and the populations *en masse* by making them research “orphans.” Overprotection can be harmful.

Ethical Issues Regarding Research Participation

Children are a vulnerable population and so are accorded special protection from research risks. Child-health scientists may encounter conflicts between protecting vulnerable children and developing generalizable knowledge to benefit them.

Special consideration needs to be given to the primary duty of protection from harm. In order for progress to be made, a number of regulatory frameworks have been developed to identify acceptable and unacceptable risks in the kinds of research to which parents and guardians can give permission. This response requires Research Ethics Committees (RECs) [referred to as Research Ethics Boards (REBs), in Canada, and Institutional Review Boards (IRBs) in the US] to determine the balance of harms and benefits. This balancing strategy can be found in the Belmont Report (1979), the US Federal Regulations (454 CFR 46), and the Tri-Council Policy in Canada.

Concept of Risk

The conduct of clinical research is responsible for upholding three central ethical principles: respect for persons, beneficence, and justice. These principles are codified in the US Federal Common Rule and many international research guidelines, including the Canadian Tri-Council Policy Statement. One principle of respect for persons requires that those who are unable to consent have protections, including a surrogate decision-maker. In the case of a child, the parent usually adopts this role as it is assumed that they act in the best interests of the child. In addition, respect requires a promise of confidentiality. The principles of non-maleficence and beneficence follow two complementary tracks: to do no harm and to maximize potential benefits while minimizing risk. Research ethics committees are charged with examining studies to determine whether or not there is an acceptable balance of risk and potential benefit. This is particularly true for participants who are vulnerable, such as children, and others who have a diminished capacity for decision-making. Lastly, the principle of justice requires that the burdens of research participation are distributed equally and, in addition, the potential benefits of research are accessible to all. Thus, there is a tension between offering

protection to potentially vulnerable subjects such as children and ensuring that they have equitable access to advancements in science, which are only available through carefully conducted research.

Definitions of Minimal Risk

The US Federal Common Rule describes minimal risk as meaning that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. Both the Canadian Tri-Council Policy on Research and the US Common Rule provide a limited list of minimal risk procedures and activities. The concept of minimal risk should also be considered in the overall context of the research. For example, a single venipuncture may not constitute more than minimal risk but a protocol that requires multiple venipunctures may well exceed what is considered minimal risk. It is also important to recognize that context may play an important role in interpreting minimal risk. For example, does minimal risk mean a) all the risks normal people encounter, b) the risks all healthy normal people encounter, or c) the minimal risks all healthy normal people encounter? Each of these interpretations has difficulties. Exposure to risk varies depending upon occupation, lifestyle, and habits, from the accountant working from home to the cliff-diving firefighter. Clearly, some of these life experiences constitute significant rather than minimal risk. If we consider what all people may be exposed to, we get into difficulty defining what is likely for whom, as well as how it applies across cultures and geographic locations. The magnitude of risk of exposure in one setting may be quite different from that of another, yet both constitute normal day-to-day exposures.

The US Common Rule further defines minimal risk as that which may be encountered in regular health care interactions. However, there is difficulty in interpreting what is “normally encountered.” While some invasive procedures may be easily ruled out as more than minimal risk, debate continues on what the cutoff should be. In addition, it is important to avoid focusing exclusively on the physical; we must not overlook psychological, social, and economic risks. Each should be included in the wide spectrum that is examined by research ethics committees.

Risk in Therapeutic Procedures

Risks involved in therapeutic procedures should be evaluated separately from the risks of non-therapeutic procedures since treatment itself may constitute considerable risk of harm. Therapeutic risks could be regarded as falling within the range of minimal risks for research participants as they are an inherent part of the patient's treatment. The test in this situation is the principle of clinical equipoise. This exists when there is a state of uncertainty within the expert clinical community as to the relative superiority of two strategies of treatment. This is based on the premise that, regarding the anticipated balance between harms and benefits, the intervention being tested is standard. Therefore, exposure to therapeutic risk even in vulnerable subjects is acceptable as long as a situation of clinical equipoise exists. Thus, ethicists have argued that an ethical analysis of risk would set no limit on the therapeutic risk to which children may be exposed. Indeed, this is the case in which children with cancer are exposed to chemotherapy agents in which death, secondary to toxicity of treatment, is a real and not infrequent event. This would only be acceptable in a research context if clinical equipoise existed.

Non-therapeutic Procedures

Non-therapeutic risks are those actions that go beyond the needs of the subject and occur only for the benefit of the research project. Thus, it is important for a research ethics committee to distinguish therapeutic from non-therapeutic research in determining the overall acceptability of the research. Research ethics committees should total up the accumulative additional research risk that a given study poses to children in determining where it stands in the minimal risk to potential benefits ratio.

Two main ethical requirements underline the acceptability of non-therapeutic procedures, that risk should be minimized and that risks posed by non-therapeutic procedures should be proportional to the knowledge that may be reasonably expected to be gained. Thus there is a limit to the magnitude of non-therapeutic risk to which the subject may be exposed. The research ethics committee has several important roles. One is to disallow a procedure if there is a less invasive alternative. A second is to question the inclusion of procedures that do not lead to creation of important new knowledge when there may be potential harm.

Third-party Decision-making

When an individual is incapable of providing his or her own consent, we must obtain consent from a third party decision-maker. In general, this is the responsibility of parents or guardians who are generally regarded to have the best interest of the individual child in mind.

There are, however, a variety of vulnerabilities when adults make decisions for children, in particular where significant disease is present in a child. Potential conflict of interest in determining the competence of an adolescent to make a research decision may be present for the parent. There may also be significant influence by health care professionals who are also investigators or recruiters for research protocols, especially if the disease is rare and the parent has no other choice for medical care. A third-party decision-maker who is under pressure may allow greater risk in defining acceptable minimal risk than would an impartial observer. This must be considered by the researcher in designing research projects and by the research ethics committees in assessing for acceptability. This applies for children, as well as for other vulnerable populations such as adults with dementia. It would be unethical for a legal proxy to authorize a patient's participation in research that represented more than a minor increment over minimal risk, unless there was anticipated potential direct benefit for that individual. The proxy must also withdraw the subject's participation if unacceptable or unforeseen harms or discomforts begin to accrue. A simple example of this is an immunization study with regular blood monitoring where a child becomes increasingly distraught with follow-up blood work for serology. In this situation, it would be appropriate for the parent to withdraw the child from the study.

Placebo-controlled Trials

As placebo-controlled trials are widely regarded as a gold standard for testing, this methodology may well be applied to children's research. The ethics of placebo controlled trials remains controversial. Miller et al. have outlined an approach to considering the acceptability of placebo-controlled trials by stating that placebo controls and active treatment should be evaluated as separate interventions. As such, the risk/benefit profiles should be assessed independently for each arm of a study involving placebos. They argue that the clinical trials may only be approved

when the placebo intervention satisfies one of three conditions: 1) minimal risk, 2) greater than minimal risk but with the prospect of direct benefit from the placebo intervention (and at least as favourable as the available alternatives), or 3) a minor increase over minimal risk if direct benefit from the placebo is unlikely but the study is deemed likely to produce knowledge of vital importance to the subject's own condition or disease. In addition, the placebo control should be approved only if there are convincing methodological reasons to use them rather than an active control.

The concept of minimal risk has two main functions. The first is to help focus a research ethics committee's attention on studies that involve more than minimal, non-therapeutic risk. It thus allows an expedited review of minimal risk protocols – the foundation of proportionate review. In this function, it also allows that risk is more than just physical and that, for example, secondary use of data may represent more than minimal risk and require informed consent, either of the original participants or a community representative. The second major function of defining minimal risk is to guide the acceptability of studying or exposing persons incapable of giving consent, including children. Risk analysis underpins these two crucial functions.

Key Points

- Research involving infants and children and adolescents must be undertaken to provide them the same potential benefits as adults.
- The concept of risk in this population must include a consideration of minimal risk for non-therapeutic research.
- There is no moral reason to exclude high risks in therapeutic research as long as there is clinical equipoise.
- The definition of minimal risk is contextual.

Links

Integrity Advisory Panel on Research Ethics (Canada) <http://www.pre.ethics.gc.ca/english/index.cfm>

The Canadian Tri-Council Policy Statement on Research Ethics. Section on Minimal Risk, Section 1, C1 <http://www.pre.ethics.gc.ca/english/policystatement/section1.cfm#1C1>

The Interactive Research Training Curriculum, Web Version <http://www.fhi.org/en/topics/ethics/curriculum/default.htm>

The Belmont Report. Ethical Principles and Guidelines for the Protection of Human Subjects of Research <http://ohsr.od.nih.gov/guidelines/belmont.html>

References

National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research, Report and Recommendations: Research Involving Children. DHEW publication #(OS)77-0004, 1997.

Annas G and M Grodin (eds). The Nazi Doctors and The Nuremberg Code: Human Rights in Experimentation. New York: Oxford University Press, 1992.

Freedman B, A Fuks, and C Weijer. In loco parentis: minimal risks as an ethical threshold for research upon children. Hastings Center Report 1993 March/April:13–19.

Freedman B. On the rights of the voiceless. J Med Philos. 1978 3:196–210.

Kodish E. Pediatric ethics in early phase childhood cancer research: conflicted goals and the prospect of benefit. Accountability in Research 2003 10:17–25.

McCormick R. Proxy consent in the experimental situation. Perspectives in Biology and Medicine 1974 18:2–20.

McCormick RA. Experimenting in children: sharing in society. Hastings Report 1976 6(6):41–46.

Miller SG, D Wendler, and D Wilfond. When did the federal regulations allow placebo-controlled trials in children? J. Pediatrics 2003 142:102–107.

Weijer C. The ethical analysis of risk. Journal of Law, Medicine and Ethics 2000 28:344–361.

Conflict of Interest and Integrity

Robert Bortolussi, MD, FRCPC

Department of Pediatrics
Dalhousie University
Halifax, Nova Scotia, Canada

In consultation with:

Kathleen Glass DCL
McGill University
Montreal, Quebec, Canada

Jocelyn Downie LLD PhD
Dalhousie University
Halifax, Nova Scotia, Canada

All actions involving choices on how one should, or should not, act have moral implications. While moral integrity is certainly not unique to a clinician scientist, the special value placed on health, and the special trust placed on health professionals make clinician researchers particularly accountable. As health professionals, we are in a fiduciary (trust) relationship with our patients and must follow their wishes. If we do not, we may be sanctioned by the courts or by our own licensing and regulatory bodies. Some types of research generate unique concerns. Principal among these is research (either basic or clinical) undertaken to develop or evaluate products that potentially have both clinical and commercial value. Such research highlights the importance of avoiding situations of conflict of interest or even the perception of such a conflict.

The objective of this chapter is to help you recognize situations that may pose a conflict of interest and to develop strategies to avoid or manage such conflicts. You will also gain a better understanding of the legal principles in dealing with conflict of interest and the need to demonstrate integrity in your research and in the mentoring of others.

Overview of Conflict of Interest

One of the best definitions of conflict of interest was proposed by Denis Thompson. According to him, “a conflict of interest is a set of conditions in which professional judgment concerning a primary interest (such as a patient’s welfare or the validity of research) tends to be unduly influenced by a secondary interest (such as financial gain)” (Thompson, 1993).

The “primary interests” Thompson talks about are determined “...by the professional duties of a physician, scholar or teacher”; and “...they should be the primary considerations of any professional decision that a physician, scholar or teacher makes. The secondary interest is usually not illegitimate in itself, and indeed it may even be a necessary and desirable part of professional practice. Only its weight in professional decisions is problematic.” In other words, health professionals engaged in research may be viewed as being in conflict if their own interests or their interest in research may affect their judgment in making management decisions for their patients.

The purpose of rules on conflict of interest in the research context is: 1) to maintain the integrity of professional judgment and 2) to maintain confidence in such judgment. To fulfill the latter purpose, the appearance of conflict of interest should be avoided where possible.

There is no comprehensive legislation governing human subject research in most countries. Regulations that do exist are often based on policies or guidelines developed by national or international panels of experts. The “Good Clinical Practice: Consolidated Guideline,” or GCP, is an example of an international regulation while the Canadian Tri-council Policy Statement on research involving humans is an example of a national regulation (see Chapter 3). The GCP sets out what is expected of investigators and institutions who receive industry funding for clinical trials. It is detailed with respect to investigators’ obligations but largely silent on the issue of conflicts of interest. On the other hand, some professional organizations, such as the Canadian Medical Association (CMA), and the American Medical Association (AMA), have developed codes of ethics and policies to inform their members of what is expected of them when they are confronted with actual or potential conflicts of interest. For example, the CMA Code of Ethics states that the “well-being of the patient” is the physician’s first concern and the patient must never be exploited for personal advantage. Physicians are also advised to “enter into associations only if [they] ... can maintain ... [their] professional integrity by doing so.”

With the increased involvement of “for-profit” enterprises in research, there is heightened potential for conflict of interest in the conduct of clinician scientists. Concerns about the maintenance of scientific independence and

integrity in commercially supported research have grown as commercial support and practical applications of scientific research have increased.

Specific Conflicts of Interest

Role Confusion (Caregiver vs. Researcher)

When health professionals conduct research, they are acting with two different goals, 1) to provide individual care that may be offered in the patient's best interests, and 2) to acquire generalizable knowledge. The two goals are not the same and can present a conflict for a person doing research. To be ethical, researchers cannot disadvantage research subjects, particularly when they are patients who come to them for care. This is the nature of their fiduciary duty. Clinical researchers under the Helsinki Declaration, the AMA, the CMA guidelines, and common and civil law must act in the patient or subject's interest when the patient seeks or requires care. There is no principle, law, or regulation that allows a physician to opt out of giving patients what would be considered the standard of care. This is the objective of equipoise in clinical trials – genuine uncertainty about the merits of new treatment vs. old means no one will be disadvantaged. There is no ethical or legal principle that allows a caregiver to sacrifice current patients for future ones. Patients should not be recruited into trials that do not serve their best interests.

It is crucial for patients to understand that when their health care provider is conducting research, he or she is also acting for the benefit of others (future patients, sponsors) and not solely for the patient, even though they may hope their patient receives a benefit. Canada's Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS) attempts to alleviate these problems. First, the TCPS recommends that researchers "separate their role as researcher from their roles as therapists, caregivers, teachers, advisors, consultants...." If it is difficult or impossible for the researcher to do so, this fact must be disclosed and the researcher should dissociate their role as researcher from other roles throughout the project.

Financial Conflicts of Interest

Clinicians may be in a conflict of interest if they or their family have investment interests in a company funding their research since this may affect how the researcher enrolls research subjects, identifies adverse events, and interprets research data and results. Such a person has an

interest which is in conflict with the mandate to produce unbiased results especially if they may negatively impact the investment. While the majority of researchers may not succumb to unethical or fraudulent practices, in the face of these conflicting interests incidents do, unfortunately, occur from time to time.

Authorship Conflicts

To communicate the results of one's research is a fundamental principle of the scientific process. Publication of a research article provides recognition for one's efforts and paves the way to academic advancement. As such, situations can arise creating conflicts between authors or conflict of interest between scientific and personal gain. The International Committee of Medical Journal Editors (ICMJE) developed guidelines in 1997 and updated them in 2004 to help authors and editors in their mutual task of creating and distributing accurate, clear, easily accessible reports of biomedical studies. The guidelines describe ethical principles related to the process of publishing manuscripts in biomedical journals and the relationships between editors and authors, peer reviewers, and the media. Each author has to participate sufficiently to take responsibility for all or part of the work. This requires:

- a meaningful contribution to the conception and design, or acquisition of data, or analysis and interpretation of data;
- drafting the article or revising it critically for important intellectual content; and
- approval of the final version of the manuscript to be submitted.

Research Sponsorship and Compensation

Most research requires funding of some sort or other. Some funds come from local institutions, universities, or governments. Investment in research is also made by the pharmaceutical industry. It costs money to conduct research and individuals undertaking it and the institutions in which it takes place need to be compensated for their work and expenses. For example, investigators who forego seeing patients to be involved in a clinical trial need compensation for lost income. Research also puts financial burdens on institutions for administration, staff time, and use of research facilities. But compensation over-and-above the usual can tempt some individuals and institutions away from doing good research.

Concerns about scientific independence and integrity has grown as commercial interest and support has increased. In order to avoid such conflicts of interest, a number of professional organizations have developed guidelines or issued statements on the interaction between health care professionals and the pharmaceutical industry (CMA 1994, American College of Physicians 1990, American Academy of Neurology, 1998).

Institutional Conflicts

Researchers should also be aware of conflicts of interest institutions may be exposed to. Institutions compete for industry money to generate overhead income to fund research. They may form commercial partnerships with industry to share in the profits of research. The concern is that these close ties may conflict with the institution's other goals and responsibilities. Very few guidelines are available regarding institutional conflicts, but it is generally accepted that institutions should maintain an arm's length to decisions of research ethics committees. Many institutions also reserve the right to refuse projects that it deems unacceptable because of their controversial nature or for other reasons.

Remuneration for Enrolling Patients in Research Trials

So-called finder's fees – payment for recruiting or enrolling patients in research studies – has been criticized by many as representing a conflict of interest for a treating physician. The AMA's Council on Ethical and Judicial Affairs has stated that payment by or to a physician solely for the referral of a patient is unethical. Although the Canadian TCPS does not prohibit finder's fees, it notes that participation in a clinical trial may compromise a clinician's professional integrity because of the potential conflict between financial remuneration and duty to serve the best interests of a participant. For this reason, the TCPS recommends that research ethics committees examine the budgets of clinical trials to ensure that ethical concerns are respected.

In general, enrolling patients in approved research studies should not exceed the normal practice pattern of the health care clinician and the remuneration should not constitute enticement. Subjects participating in research should be informed of the source of funding for the study. Any fee should be approved by the relevant review board.

Additional ethical issues exist when the participants are children. Parents may unconsciously minimize the risks or inflate the clinical benefits of the research with the possibility of financial reward. While the European Union has prohibited all "incentives or financial inducements" for pediatric research, the American Academy of Pediatrics argues that the practice of paying children or their parents is consistent with the "traditions and ethics of [American] society." Even so, the AAP advocates two safeguards:

- parents should receive no more than a "token gesture of appreciation," and
- payments to children should not be disclosed until the end of the study.

Informed Consent

The law regarding informed consent for treatment has established that patients have the right to be informed about the range of treatment options available, the risks associated with each treatment, the risks associated with refusing treatment, and the prognosis associated with each treatment option. The courts usually require a study to disclose all risks that a reasonable person would want to know about in making an informed treatment decision. Physicians are also required to give patients an opportunity to ask questions and have those questions answered.

Thus, prospective research subjects must be told as much or more information as patients in the treatment context. They are entitled to a full and frank disclosure of all the facts, probabilities, and opinions that a reasonable person (in that patient's situation) would be expected to consider before giving his or her consent. Research subjects should also be informed about new information acquired throughout the course of research that changes the potential harms and benefits. This disclosure requirement is set out explicitly in the GCP Guideline:

"The written informed consent form and any other written information to be provided to subjects should be revised whenever important new information becomes available that may be relevant to the subject's consent... The subject or the subject's legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the trial." (GCP Guidelines, 4.8.2)

Confidentiality Agreements

One function of a confidentiality agreement is to protect a company's commercial and intellectual property interests by restricting the release of study results until the company can prevent the information from being used by competitors. The legal system recognizes this right unless the contractual provision violates other laws or public policy.

The Nancy Olivieri case (Baylis, 2004) highlights difficulties that a confidentiality agreement can pose for a researcher. In this case, the research sponsor threatened to sue Dr. Olivieri for revealing her concerns about potential harms of a drug. The company planned to use the confidentiality agreement, fearing the information might jeopardize their ongoing multinational trial with the drug. Dr. Olivieri, on the other hand, believed she had an ethical and legal duty to provide the research subjects with the new information. She took her concerns to the research ethics committee, which agreed. This case points out the fact that researchers must inform research subjects of potential harms on an ongoing basis. This obligation cannot be compromised.

Key Points

- Researchers, research ethics committees, and institutions can all experience conflicts of interest in the research enterprise.
- All research must be approved by an appropriate ethics review body in accordance with the standards and procedures of the country.
- Researchers should disclose actual, perceived, or potential conflicts of interest to the research ethics committee.
- The research ethics committee should assess the likelihood that the researcher's judgment may be influenced and the seriousness of any harm that may result, and thus determine what action needs to be taken.
- Researchers should never sign a contract that may place them in violation of ethical and legal duties to their research subjects.

Links

Food and Drug Administration. Modernization Act of 1997 (FDAMA 1997): <http://www.fda.gov/cdrh/devadvice/371.html>

Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans: <http://www.pre.ethics.gc.ca/english/>

European Guideline on clinical research: <http://www.emea.europa.eu/>

ICH Guidance: Good Clinical Practice: Consolidated guideline: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/ich/efficac/e6_e.html

The following link provides publicly accessible (free) information on Conflict of Interest issues: <http://www.cojm.org/toc/COI.htm>

CMA Policy "Physicians and the Pharmaceutical Industry": www.cma.ca

International Committee of Medical Journal Editors. Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication: <http://www.icmje.org/index.html>

Dean H and MacDonald N. Who is an "Author" in Medical Publishing? *Can. J. Diabetes March*: 14–15, 2007: http://www.diabetes.ca/section_professionals/cjdmar07.asp

References

- American Academy of Neurology. Policy on Conflicts of Interest. *Neurology* 1998 50:332–334.
- American Academy of Pediatrics. Guidelines for the ethical conduct of studies to evaluate drugs in pediatric populations (RE 9503). *Pediatrics* 1995 95:286–294.
- American College of Physicians. Physicians and the Pharmaceutical Industry. *Annals of Internal Medicine* 1990 Vol. 112(8):624–626.
- Baylis F. The Olivieri debacle: where were the heroes of bioethics? *J Med Ethics* 2004 30:44–49.
- Campbell EG, Gruen RL, et al. A national survey of physician-industry relationships. *N Engl J Med* 2007 356:1742–50.
- Thompson D. Understanding Financial Conflicts of Interest. *N Engl J Med* 1993 329:573–576.

Regulating Research:

Navigating the sea of research ethics regulations

Michael R Hadskis, BSc (Hons), LLB, LLM

Faculty of Law

Dalhousie University

Halifax, Nova Scotia, Canada

Clinical research must be undertaken in a manner that is consistent with ethical and legal standards that apply to human research. It is important, therefore, to be knowledgeable about the standards and processes involved in the ethical review of research. Standards can come from a wide variety of sources, including:

- formal legal rules;
- policies created by governments, research funding agencies, and professional bodies; and
- guidelines published by institutions that carry out research. (This chapter uses the term “regulatory instruments” to refer to these documents.)

In order to ensure that these standards are met and that the rights, safety, and welfare of research subjects are protected, an ethics panel conducts reviews of proposed and ongoing studies. These panels have been given various names, including institutional review boards (IRBs) and research ethics boards (REBs). In this module, they will be referred to as research ethics committees (RECs).

Since there are many regulatory instruments that can directly or indirectly apply to a particular research project, researchers are often unclear about what specific standards apply to their study and what procedural requirements the REC will expect them to follow. In light of this, the objectives of this chapter are to:

- provide a guide for clinical researchers regarding some of the main ethical and legal standards, and
- outline the review process that RECs follow.

Regulatory Instruments for Research Involving Humans

Biomedical research may be directly regulated by formal legal standards in some countries (e.g., the *Code of Federal Regulations* [CFR] in the United States) and/or by non-legal instruments created by governmental bodies, research funding agencies, professional organizations, and local

research institutions such as hospitals and universities. In Canada, the principal regulatory instrument for biomedical research that is followed by academic centres is the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (TCPS). The TCPS sets out the standards and procedures applicable to the review of research undertaken by researchers or institutions receiving financial support from national funding agencies, including the Canadian Institutes of Health Research (CIHR). Although the TCPS is not a formal legal instrument, there are factors which mandate or encourage compliance with its standards.

Canada and most other countries use statutes/legislation to regulate clinical drug trial research and significant penalties can be imposed on individuals who breach their provisions. They require that clinical drug trials be conducted in accordance with “good clinical practices” (GCP), which are generally accepted clinical practices that are designed to ensure the protection of the rights, safety, and well-being of clinical trial subjects.

There are other instruments that impact the conduct of biomedical research activities. Professional codes of conduct and judge-made law on matters such as informed consent can also exert direct or indirect regulatory control. Also critical is the growing body of legislation that many countries are enacting that has implications for the collection, use, and disclosure of personal information in the research context. Legislative instruments also exist that apply to specific research activities, such as those related to human reproduction, medical devices, and post-mortem gifts of bodies or body parts for research.

Researchers are increasingly involved in multi-national health research and, therefore, they are frequently being confronted with the regulatory frameworks adopted by other countries. For example, as noted above, the CFR in the United States contains legal standards for the protection of human research participants and is applicable to all human research funded by the US Department of Health and Human Services (which includes the National Institutes of Health), regardless of where it is conducted.

As covered in Chapter 1, two international instruments, the *Nuremberg Code* and the *Declaration of Helsinki*, have played an important role in the evolution of mechanisms devised by many countries for the protection of human research subjects. Readers are referred to that chapter for a discussion of those fundamental instruments.

Research Ethics Committees

Composition and Function of RECs

The primary mandate of RECs is to review research projects with the aim of protecting research subjects' rights, safety, and well-being. Most teaching hospitals and universities have their own RECs to review studies being proposed or conducted by their affiliated researchers. Although private (for profit) RECs can review research carried out by private sector organizations, such as pharmaceutical companies, most academic institutions require their affiliated researchers to submit their research proposals to the institution's REC.

The relevant regulatory instruments in most countries impose a number of requirements regarding the composition of RECs. Typically, committees must consist of no fewer than five people and must possess diversity in terms of experiences, expertise, and gender. To achieve diversity, RECs are made up of individuals with expertise in science as well as persons knowledgeable in the pertinent ethical and legal norms. In the interests of independence and community representation, individuals from the local community who are not affiliated with the REC's host institution are included within the committee's membership.

REC Jurisdiction

Many countries have regulatory instruments that require all research involving humans to be approved by an REC before it can begin. Thus, a preliminary question you should ask is, Does my project fit within the meaning given to the term "research" under the relevant regulatory instrument? The TCPS, for instance, defines research as "a systematic investigation to establish facts, principles or generalizable knowledge." It is critical to note that just because a project may offer potential therapeutic benefits for research subjects, does not mean that it is excluded from REC review. If the project possesses an element of "research," it must be reviewed.

Examples of the kinds of activities that must be reviewed by an REC include research involving:

- human remains, cadavers, tissues, biological fluids, and embryos;
- identifiable personal data collected by interviews and questionnaires; and
- secondary use of data when the data can be linked to individuals.

You must also identify the specific REC(s) from which you will need to seek approval for your project. Since each institution is accountable for the research carried out under its auspices, multi-centred research projects may need to be approved at each institution, a daunting task for a new researcher. Fortunately, some research institutions have signed inter-institutional agreements that authorize their RECs to accept the review of other RECs if certain conditions are met.

REC Application Materials

The submission materials that must be provided to RECs can vary according to the demands of the particular institution and the type of research being proposed. The required documentation may include:

- checklists developed by the institution,
- research summaries that follow a prescribed format,
- subject consent forms,
- subject recruitment tools (e.g., draft advertisements and telephone recruitment scripts),
- questionnaires,
- interview guidelines,
- contracts entered into with sponsors (including confidentiality agreements), and
- the curriculum vitae of those involved.

You should always obtain the REC's application guidelines and adhere to the submission format they set. This will invariably make for a smoother ride through the REC process.

REC Decision-Making Process

The type of REC review that is carried out is, in part, determined by the nature of the risk that the proposed research presents. Research that involves more than "minimal risk" (discussed in Chapter 1) is reviewed at one of the REC's regular meetings, in which REC members with the necessary backgrounds and expertise are present. If the minimal risk threshold is not exceeded, the study may qualify for an expedited review (e.g., research that entails the review of patient records by hospital personnel). Expedited reviews often take the form of a designated REC member or a small subgroup of the REC being given the task of conducting the review on behalf of the committee as a whole.

After reviewing the research proposal, the REC will decide whether to approve, reject, or propose modifications to the study. The most common outcome of an REC's initial review of a study is a request for modification and/or clarification. You should promptly, thoroughly, and respectfully reply to these requests.

REC Decision-Making Considerations

REC members are guided by a number of ethical principles when deliberating on a proposed research project. These considerations include:

- whether the research proposal provides for free (i.e., voluntary) and informed consent of subjects or, where applicable, their substitute decision-makers (e.g., the parents or legal guardians of a young child);
- whether anticipated benefits outweigh the foreseeable harms to participants;
- whether adequate safeguards are in place to protect subjects' privacy and confidentiality;
- whether the potential for harm to subjects has been minimized;
- whether the potential benefits of the research have been maximized;
- whether any actual, perceived, or potential conflicts of interest have been adequately addressed (see Chapter 2);
- whether there is a fair distribution of the benefits and burdens of the research (i.e., disadvantaged persons should neither bear an unfair share of the burdens nor be unfairly excluded from potential benefits associated with participation);
- whether the design of a research project is sound; and
- whether an adequate continuing review mechanism will be put in place.

You should be mindful of these considerations when formulating your research protocol as well as your submissions to the REC. This will demonstrate to the REC that you are sensitive to the ethical implications of your project.

REC Considerations on Use of Databases

Given the growing prevalence of electronic databases and the strong interest in using them for research purposes, a few words are in order regarding the REC's role in ensuring that respect for privacy and confidentiality is maintained in the context of database research. Of course, the other considerations noted above are also in play for this form of research.

Health records or other patient information constitutes a source of data that may have research value. Identifiable personal information will usually be present on such documents, making it critical for researchers and RECs to adhere to the requirements set out in relevant regulatory instruments (such as privacy legislation, privacy policies published by funding agencies, and any relevant guidelines created by the researcher's host institution). These regulations may contain provisions that apply to the collection, use, and disclosure of personal information for research purposes.

Since privacy is a fundamental value of human dignity, it is your ethical responsibility to ensure that personal information does not reach others without the research subject's consent. Misuse of confidential information could result in legal action being taken against you. For these reasons, you must seek REC approval for all research projects involving the use of information about an identifiable individual. The REC will indicate what security measures must be taken regarding the collection, analysis, and storage of such information. For example, the REC may require that access to the database be restricted to people on the research team who sign an appropriate confidentiality agreement.

The definition of identifiable personal information may differ between regulatory instruments (e.g., the privacy policy adopted by one hospital may not be the same as that of another). Researchers and REC members should inform themselves of the definitions and requirements contained in the instruments that apply to them. Typically, identifiable personal information includes any information pertaining to a reasonably identifiable person, such as an individual's name, hospital number, address, and date of birth.

Information collected, used or disclosed for a purpose that the subject has explicitly or implicitly agreed to is referred to as primary use of data. For example: the use of information contained in a hospital's health record for the purpose of delivering health services to the patient concerned.

Secondary use of data refers to the use of primary data for a different purpose than originally intended; for example, using a patient's health record for research purposes. This becomes a significant concern when the data can be linked to individuals. Both primary and secondary use of data for research must be approved by an REC.

In some cases, data from one database may be linked to another database using one or more linking identifiers (e.g., name and hospital unit number). However, if the information from two or more data sets may be linked for research purposes, the researcher must obtain REC approval for the project.

One way to protect confidentiality is by "anonymizing" the data (i.e., permanently stripping the data of all identifiers such that the information has no reasonable potential for any organization or person to identify a specific individual). In situations where data for analysis does not contain identifying information, RECs can often review the request using an expedited process.

The REC will usually conduct a full review (as opposed to an expedited review) of the research proposal if identifiable information will be used. The committee will ask why identifiers are necessary. If identifiers are required, the researcher will need to show how confidentiality will be safeguarded. Personal information from a database should never be released to a third party without the consent of the subject, unless such disclosure is required by law. Research subjects have a right to know the nature of the information that will be stored on the database and who may access it. In particular, the researcher must inform the subject if information may be provided to the government or any other third party.

Data must be secured in a manner that is acceptable to the REC. Data transferred to an analysis file must also be properly secured. Usually, "linking identifiers" are stripped from the file and replaced by a study number unique to each individual in the research data set. Files with identifiers (or information on linkers) must be destroyed by the date specified by the REC.

Ongoing Ethics Review

A specific risk, unknown at the time of REC approval, may come to light once a project is underway. As well, changes made to the research design or research documents (e.g., consent forms) may generate ethical concerns. Thus, it is important to ensure that ongoing review mechanisms

exist which are commensurate with the risks that the study presents. Researchers should, at the very least, submit an annual status report to the REC. Research that exceeds the minimal risk threshold may need further scrutiny, such as random REC audits of the free and informed consent process.

The need for ongoing review is particularly important in clinical drug trials where serious (unexpected) adverse drug reactions can occur. Safety monitoring committees (also referred to as "data safety monitoring boards") are often established to oversee this form of research. These committees usually comprise biostatisticians, scientists, ethicists, and clinicians who are knowledgeable about the research project. Their responsibilities typically include analyzing adverse event reports in an effort to determine the likelihood that a relationship exists between this event and the relevant subject's participation in the drug trial. Safety Monitoring Committees may also conduct interim analysis of clinical outcome data in order to determine if there is sufficient evidence that one treatment is more efficacious or harmful than another. Additionally, they may ask you to provide them with further information, require informed consent forms to be revised, or recommend that a research project be terminated (Hadsakis, 2007).

Key Points

- Obtain, review, and comply with REC's ethics review application guidelines and consult with REC for guidance as needed, particularly if you are unsure if an activity must be approved by an REC (e.g., Does the activity constitute "research"?).
- Carefully consider the ethical principles that the REC will apply to your research project and provide it with the documentation need to conduct the review (e.g., set out all foreseeable risks involved in the study).
- Provide a full, timely, and respectful response to any queries or requests for modifications that the REC may make following its review of your application.
- Most importantly, always respectfully engage with research subjects.

Links and References

Assisted Human Reproduction Act, SC 2004, c.2 (Canadian):
<http://laws.justice.gc.ca/en/A-13.4/index.html>

Code of Federal Regulations, Title 45 CFR Part 46 (American):
<http://ohsr.od.nih.gov/guidelines/45cfr46.html>

Declaration of Helsinki (International): <http://www.cirp.org/library/ethics/helsinki/>

Food and Drugs Act, RSC, 1985, c.F-27 (Canadian):
<http://laws.justice.gc.ca/en/f-27/61279.html?noCookie>

Food and Drug Regulations, CRC, c.870, Part C, Division 5: Drugs for Clinical Trials Involving Human Subjects (Clinical Trial Regulations)(Canadian):
http://laws.justice.gc.ca/en/showdoc/cr/C.R.C.-c.870/bo-ga:l_C-gb:l_5//en#anchorbo-ga:l_C-gb:l_5

Good Clinical Practice: Consolidated Guidelines (International):
<http://www.fda.gov/cder/guidance/959fml.pdf>

Hadskis M. "The Regulation of Human Biomedical Research in Canada" in Downie J, T Caulfield, and C Flood, eds., Canadian Health Law and Policy (3rd ed.). Markham: Lexis Nexis, 2007.

International Committee of Medical Journal Editors. Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication:
<http://www.icmje.org/>

Lemmens T, and A Thompson. Non-institutional Commercial Review Boards in North America: A Critical Appraisal and Comparison with IRBs (2001) 13:2 IRB: A Review of Human Subjects Research 1.

Nuremburg Code (International): <http://www.hhs.gov/ohrp/references/nurcode.htm>

Personal Information Protection and Electronic Documents Act, SC 2000, c.5 (Canadian):
http://www.privcom.gc.ca/legislation/02_06_01_01_e.asp

Tri-Council Policy Statement on the Ethical Conduct of Research Involving Humans (Canadian):
<http://pre.ethics.gc.ca/english/policystatement/policystatement.cfm>

Children in Research: Involvement in research decisions

Christy Simpson, PhD

Dalhousie University
Halifax, Nova Scotia, Canada

Are you comfortable with a five-year-old being involved in the decision-making process about research participation? How about a thirteen-year-old? What role should children play in decision-making about research participation?

Historically, parents made the decision about whether their child would participate in research. This approach is now seen as insufficient since it is felt that those with developing decisional capacity should be involved in some way. In spite of this, the involvement of children in decision-making about research participation is often neither routine nor standardized. In this chapter, I will discuss issues on the respectful involvement of children in the decision-making process.

The objective of this chapter is to understand the concepts of assent and dissent in children's decision-making process about research participation and appreciate how your responsibilities may change depending on the child's decisional capacity.

Background

Involving children in the decision-making process about research participation requires a balance between two key obligations or responsibilities:

- Protection of the vulnerable. Due to their developing decision-making capacity, children are vulnerable to harm.
- Respect for persons. This responsibility grounds respect for autonomy and respect for those with diminished or developing autonomy.

Children can benefit from participation in decision-making both by gaining experience with making decisions (as their abilities allow) and/or by gaining information about the research they will be participating in (even if a young girl cannot make a decision, she can be harmed by not knowing what is happening to her). Finding the appropriate balance between demonstrating respect by involving children in decision-making about research participation and ensuring they are afforded proper protection in this process has been the focus of much debate. The requirement of

permission by a legally recognized surrogate decision-maker – typically the child's parent(s) - and, recently, the agreement by a child to research participation in order to proceed has been the standard approach to ensuring these responsibilities are balanced.

In establishing a place for children in the decision-making process about research participation, two concepts have come into play to both create this role for children and distinguish this role from that of persons with full decisional capacity. These concepts are *assent* and *dissent*.

- *Assent* is typically understood to be the agreement by a child to participate in research. This assent does not replace nor forgo the requirement for a legal authorization to proceed.
- *Dissent* is the child's expressed unwillingness to participate and is often taken to preclude participation in research.

These concepts can be found in research guidelines around the world (Baylis, 1999). It is worth noting that neither assent nor dissent are defined in many of the guidelines. As such, current practice is often to request verbal assent, and respect the dissent of children whether expressed verbally or physically.

Does this approach work in practice? As mentioned above, the involvement of children in decision-making about possible participation in research is neither routine nor standardized (Simpson, 2003). This is due, in part, to confusion about the moral and legal weight of these concepts. Consider, for example, the following two claims:

The lack of clarity in law and morality on the decision-making authority of children with respect to research seems to be mutually reinforcing. Inconsistent and arbitrary age-related legal thresholds of legal competence reflect the difficulty in practice of making moral judgments of the weight to be assigned choices made by children with developing decision-making capacities. (Kenny, 2000)

...if a parent's legal and morally valid authorization can be overridden by a child's dissent, then it appears that a dissent by a person with developing decision-making capacities has the same moral force as a refusal by a person with decision-making capacities. This is perplexing, for while it is undeniably important to heed a child's objections, it is not clear that these

objections should be authoritative in the same way and for the same reasons that a refusal by a person with decision-making capacity is generally regarded as authoritative. (Baylis, 1999)

One approach to help resolve the confusion about dissent has been to use the language of protest for a child's verbal or behavioural objections. It is understood that a child's protest is not authoritative, and thereby distinct from a refusal by a fully competent individual. However, parents must consider their child's protest in their assessment of whether to enroll or proceed with research.

Developing Decisional Capacity

While the use of assent and dissent promotes the goal of protecting children's interests (that is, protecting them from research harm), it is not clear that this approach fosters a suitable balance with recognizing and perhaps even nurturing children's decision-making abilities. If we focus on whether and in what ways each child is capable of participating in decision-making about research participation, what are some of the factors we should consider? Attending to the context of each possible child participant in research is important, we must consider the following:

- The child's capacity for involvement in decision-making – for example, the child's physical, emotional, and cognitive capacities could influence how well a child can make decisions. The perceptions by others of a child's capacity for such involvement. What might be appropriate involvement of children in this decision-making – involvement of healthy versus chronically ill children could influence what one attends to for a child's participation in decision-making.

If children are involved in decision-making about research participation, the ways we set-up the process become important. We must assess:

- what the child wants to know,
- what the child can understand,
- what the child's decision-making capacity is, and
- what the child *needs* to know to participate appropriately.

In addition, this process must be iterative and interactive. Without engaging with each child, listening and responding to her concerns,

repeating information, etc., it will be unclear to what extent the child can participate in the process and to what degree the child understands what is going on with a particular research project.

Categories of Decisional Capacity

Five categories of children can be described to help understand the developing decisional capacities of children. These categories are not defined by specific age ranges and recognize that children will develop their decision-making skills over time, at different rates, and will be able to be involved in decision-making in some contexts but not others. As you read over these descriptions, it is worth noting the implicit transition from greater protection of the child (less involvement in, and authority of, decision-making) to a greater recognition of the child's developing decision-making skills (gains full decision-making authority). Children may have:

- no language and no decisional capacity,
- some language comprehension and limited decisional capacity,
- good language comprehension and developing decisional capacity,
- good language comprehension and sufficient decisional capacity (mature, non-emancipated minors) or
- good language comprehension and sufficient decisional capacity (mature, emancipated minors).

Changing Roles of the Child, Parent, Researcher, and Ethics Committee

As the role of children in decision-making about research participation changes, so do the ethical requirements of parents, researchers, and research ethics committees (RECs).

Table 1: Decision-Making Roles of Children in Research Participation

Category of Children	Child's Role	Parent's Role	Researcher's Role	REC's Role
No language comprehension, no decisional capacity	No decision-making authority, may protest, but protest does not preclude research	Full decision-making authority, present during research, withdraw child if benefit-harm ratio is unfavourable	Ensure full disclosure to parents and should withdraw child if benefit-harm ratio becomes unfavourable	Protect children's interests, require full disclosure to parents and their documented authorization

Table 1: Decision-Making Roles of Children in Research Participation (continued)

Category of Children	Child's Role	Parent's Role	Researcher's Role	REC's Role
Some language comprehension, limited decisional capacity	Receptive role in decision process, may ask questions, may protest, protest does not necessarily preclude research participation	Full decision-making authority, share information with child and address questions, heed child's protest, withdraw child if benefit-harm unfavourable	Ensure full disclosure to parent and relevant disclosure to child and address child's questions, must heed child's protest.	Protect children's interests as above and require relevant info. is shared with child, require documentation of authorization and discussion with child
Good language comprehension, and developing decisional capacity	Increased role includes some decision authority, agreement needed but not sufficient, protest authoritative unless parent judges potential benefit outweighs harm and additional harm if overriding child's preference(s)	Agreement required but child's protest may override, share information with child and address questions, allow child to express wishes and take them into account, withdraw child if benefit-harm ratio unfavourable	Ensure full disclosure to parent and relevant info to child and address child's questions, allow child to express wishes, ensure parents take child's wishes into account, withdraw child if benefit-harm ratio unfavourable.	Recognize decision-making skills of child and require relevant info is shared with child, require documented agreement of parents and child, respect and defend child's protest as authoritative in some cases
Good language comprehension, and sufficient/substantial decisional capacity: mature but not emancipated minors	Significant decision-making authority, child's consent necessary and may be sufficient, parental agreement may be needed, child's refusal always authoritative	Limited decision-making authority, parental agreement may be needed but it is never sufficient	Disclosure to child, address child's questions, determine if child's consent sufficient or parent's is needed too, discuss withdrawal with child	Recognize children's decision-making ability, ensure full disclosure to child, require documentation of consent of child and, if necessary, parent agreement
Good language comprehension, and sufficient/substantial decisional capacity: mature emancipated minors	Full decision-making authority (consent/refusal), no obligation to share information with parents re: research participation	No decision-making authority	Same obligations as for any legally competent adult research participant	Same obligations as for research involving legally competent adults

Emancipated Minors

If a child is deemed to be mature and capable of making her own decisions, is it right to deny her this choice in some cases? The distinction between category four and category five described above suggests that mature minors who are not emancipated are different from those who are emancipated with respect to decisional authority. The child who is mature, but not emancipated, is still in a parent-child relationship or guardianship context. However, mature minors may well have the same decisional capacities as adults and therefore, it is argued, should have and be able to make the same choices about research participation as any fully competent adult. This is held to be true regardless of whether the minor lives at home. If this argument holds, categories four and five would collapse into one category.

Influence of Parents, Health Care Providers, and/or Researchers

One concern about involving children in the decision-making process is the possibility that they will be unduly influenced by parents or researchers. Discussing research and participation in such a way that children understand that they can protest or refuse is essential. Indeed, acutely and chronically ill children are not only willing to dialog about their ongoing healthcare, but about their involvement in research as well.

Key Points

- Researchers are responsible to:
 - Discuss research so participants understand they can protest and refuse.
 - Respect and protect vulnerable people with diminished decision-making capacity,
- Expectations of parents, researchers, and research ethics committees change as a child's understanding develops.
- Assent to participate in research is the agreement by persons with diminished or developing autonomy.
- Dissent to participate in research is the person's expressed unwillingness to participate.

References

Baylis F and J Downie. An Ethical and Criminal Law Framework for Research Involving Children in Canada. *Health Law Journal* 1 1993:42–64.

Baylis F, J Downie, and Kenny. Children and Decisionmaking in Health Research. *IRB: A Review of Human Subjects Research* 1999 21(4):5–10.

Committee on Drugs. Guidelines for the Ethical Conduct of Studies to Evaluate Drugs in Pediatric Populations. *Pediatrics* 1995 95(2):286–294.

Downie J. Information/Consent/Authorization for Minors' Participation in Research. *Health Law Review* 1999 8(2):10–12.

Kenny N and P Miller. Comment: Research Involving Children: Clarifying Roles and Authority. *Journal of Clinical Ethics* 2000 11(2):151–156.

Lynch A. Research Involving Adolescents: Are They Ethically Competent to Consent/Refuse on Their Own? In Gideon Koren (ed.). *Textbook of Ethics in Paediatric Research*. Malabar, Florida: Krieger Publishing Company, 1993; 125–136.

Simpson C. Children and Research Participation: Who Makes What Decisions. *Health Law Review* 2003 11(2):20–29.

Culture, Religion and Ethnicity: Undertaking research in vulnerable populations

Fern Brunger, PhD

Memorial University
St. John's, Newfoundland, Canada

Although much attention is paid to cultural sensitivity in a clinical care setting, less attention has been given to this issue in research. Yet, it is critical for the ethical conduct of research to understand when and how cultural values or beliefs may play a role. This chapter focuses on that role to discuss people's decisions about participating in research.

The learning objectives are threefold:

1. To understand the importance of culture, religion, and ethnicity in clinical research.
2. To understand the cultural basis of our assumptions and practices in clinical research
3. To identify and manage cross-cultural ethical dilemmas.

Culture, Religion, and Ethnicity in the Ethics of Research

All values and beliefs – including those of medicine, science, and research – are shaped by culture. Cultural and religious values can permeate all aspects of a research project, which will be shaped by the subject's values as well as your own. Cultural sensitivity requires that you appreciate that the values, beliefs, and practices of research subjects may be different from those of medical research.

Culture may be defined as the web of meaning systems that shape the lives of groups and individuals. Culture helps to provide people with the world view that gives meaning to their personal and collective experience through shared social institutions, beliefs, and values.

While culture shapes the understanding and use of clinical services, it is not possible to determine an individual's understanding by knowing their cultural affiliation (ethnicity). The differences within any community are likely to be as significant as the differences between them. For instance, although refusal of blood transfusion is part of a system of beliefs for Jehovah's Witnesses, this general knowledge does not relieve the clinician from the duty to seek specific consent (or refusal) from patients who are known to be Jehovah's Witnesses.

Bioethical issues related to culture usually arise when culture appears to be affecting the choices of patients and families about a patient's best interests. Culture or religion may influence parents' decisions when a child cannot evaluate due to limited maturity. Some researchers may be concerned that children are harmed when they are deprived of the benefits of experimental interventions, or enrolled into risky research, apparently because of the cultural beliefs of their parents.

Patients, parents, subjects, and scientists all have values and beliefs, practices, and norms that are culturally shaped. At times when values of subjects do not mesh with those of a scientist, both sets of values must be scrutinized and considered to ensure that the research is being conducted in the best interests of the subject. Culture cannot be removed to get to a valid understanding of risks and benefits; culture shapes our understanding of risks and benefits themselves.

Ethnicity may be defined as the feeling of group solidarity based on shared characteristics such as language, ancestry, shared history, and unique cultural traditions and symbols.

Ethnic categories ("Jewish," "African American," "Greek") are statements about identity based on cultural or other shared features. Ethnic categories are not decisive factors influencing decision-making in health research. Cultural features do impact decision-making, but as a complex web of shared meaning systems that shape one's life experiences in complex and individual ways. The cultural sensitivity and multiculturalism movements, while founded on a genuine interest in improving health care, have blurred the distinction between culture and ethnicity, a distinction which is essential to a more complex and appropriate understanding of culture. Categorizing people on the basis of ethnic affiliation may be useful for uniting and empowering members of ethnic groups, but when done for the purposes of explaining culturally shaped beliefs and values, this categorization may be misleading.

Culture should be understood in a manner that is qualitatively different from the standard epidemiological approach in medicine; culture is not just another variable to add next to smoking, alcohol, age, and profession in understanding the health care needs of the patient.

The concept of race emerged in the eighteenth and nineteenth centuries, in the context of, and to support, European colonialism. However, this concept has no scientific validity, since the human species can not be divided into different populations based on genetic make up. Although scientific opinion thoroughly discredited race as a classificatory tool, the term is commonly used in health research as if it were a valid category to explain differences between populations.

Ethnicity, and its associated concept “race,” sometimes arises in health research when ethnicity is a factor to be controlled for in the research design. In research that uses ethnicity as a variable, it is important to ensure that attention to genetic difference does not end up inadvertently characterizing cultural or social differences as genetic differences and vice versa.

Culture and Ethnicity in the Ethical Conduct of Research

There is now a large body of knowledge that questions the assumption that modern health science and health care are value-free. Culturally shaped beliefs are not limited to members of ethnic communities. The values and beliefs of practitioners, no less than those of patients, are shaped by culture. The concept of individual autonomy is at the core of the ethical concerns in research involving vulnerable subjects such as children. These concerns are particularly pronounced when a proxy decision-maker is asked to act in the best interests of their child or ward.

Autonomy, one of the cornerstone principles of informed consent in research, gives priority to the values and wishes of the individual research subject. The importance of self-determination is supported by various culturally-shaped norms and practices in western society. Like the notion of individual consent, individual autonomy is reinforced by the legal system and is thought to be indispensable for patient rights. Informed consent in western bioethics emerged as a legal and ethical consensus on the right of individuals to make decisions about their medical treatment in reaction to medical paternalism (where physicians made decisions about health care on behalf of patients, without fully informing them). In research, the importance of informed consent was magnified by atrocities that occurred in the Nazi era. In the past three decades, the principle of autonomy, the right of individuals to make their own decisions, has become sacred to western research ethics.

This understanding, however, of the person as an independent individual, is not shared by every culture. In much of the world, boundaries within the body and between the body and its surrounding social and spiritual environment are fluid. Decisions about medical treatment may be a collective responsibility or one of an authority figure representing the group

Informed consent is a legal doctrine that asserts a patient’s right to know the potential risks and benefits of research participation. But informed consent is also increasingly a risk management strategy; it protects the institution from liability by showing that the potential harms of research were known and accepted by the research subject. That the individual patient’s voice is given primacy echoes western culture’s valuation of the individual over the community. When patients or research subjects adhere to values that support a communally based ethic, conflicts may occur between families and caregivers when it comes to deciding the best interests of the patient.

Therefore, a clear distinction must be drawn between the ethic of informed consent (which is an ongoing relationship) and the regulatory requirement for documentation. The moral validity of informed consent rests upon a process in which needed information is disclosed to the potential subject, this information is understood, there is the opportunity to ask questions, and a clear decision is expressed. Regulatory requirements to document consent have a legalistic basis, mainly to protect institutions from legal liability. Informed consent does not require that patients’ decisions be uninfluenced by their cultural, social, or familial context. People from any cultural background will draw on their cultural and social context and need to be able to trust health care professionals to support their decisions. This is not a violation of autonomy.

Subject Selection in Research

The principle of justice requires us to include children and vulnerable populations in research, where the research may have benefits for them. That is, the benefits and burdens of research participation are to be distributed fairly. There is a fine line, however, between seeking to ensure diverse representation in subject selection and inadvertently perpetuating harms of the past – where vulnerable persons were recruited into risky research because they were powerless to refuse. A good general rule is to include all who could benefit directly or indirectly from research and attempt to involve the least vulnerable of the vulnerable.

The meanings of *risk*, *well-being*, *illness*, and *disease* are shaped by culture. Considering the harms and benefits of research is not straightforward. Even if the statistical probabilities are understood from a mathematical perspective, the meaning or relevance of that potential outcome is never static, and is always shaped by everyday life. For example, working-class mothers who smoke opt to smoke after assessing the risks of smoking compared with the risks of stress. Behaviour cannot be understood outside of its cultural context. Calculations of harms and benefits in decisions around participating in research will always be context-dependent, whether or not obviously religious or cultural values shape the decision.

Confidentiality

Confidentiality can be a major concern when health care professionals or translators are from the same community as the patient and the family. While some families may prefer to be seen by a clinician or translator with a similar cultural background, others may worry that this will compromise their privacy. Concerns may be strong in small communities, especially with research that may reveal the presence of stigmatizing health conditions. For example, stigma around certain conditions may make a child unsuitable for a good marriage where marriages are arranged. Even the mere participation in research could impact in stigmatizing ways.

Refugees

Special consideration must be given to refugee families. Signing a consent form may itself be a dangerous act in some contexts. In repressive political regimes, citizens may associate signed documents with oppressive arms of the state. Researchers should know that patients who have been tortured may not make the fact known, and that those who have performed any acts of torture may have been medical staff. Given the impact of exposure to organized violence, war, and violent authority figures, refugees should not be invited to participate in research studies except in circumstances where there is a high potential of benefit.

Communication

Linguistic, cultural, and religious differences can pose barriers to effective communication. Communication is even more complex if translation is needed. Translation is not simply a matter of interpreting words and meanings. It involves communicating the meanings of concepts that may not even exist in the cultural context of the second language. It is important to realize, however, that poverty, education, class, and other

social and historical factors can also lead to poor communication even if no cultural differences exist. For example, differentials in social status (rank, caste, class) may create a reluctance to disclose health information. The possibility of inaccurate information as a result of the translation process is a significant concern.

Key Points

- You do *not* have to be familiar with all other cultural beliefs and values in relation to health care decisions and practices; in fact, believing that you understand a patient's beliefs can be detrimental if it leads to stereotyping.
- Remember, all health care decisions and practices are cultural; even where a patient's culture appears to be the same as yours, you need to ask the patient about their values and beliefs in relation to a decision in order to ensure fully informed consent.
- The quickest and most effective route to cross-cultural sensitivity is to continually reflect on, and hold up for examination, the cultural values, beliefs, and practices of western biomedicine.

Recommended Links and Readings

Marshall PA. Informed Consent in International Health Research. *Journal of Empirical Research on Human Research Ethics* March 2006 1(1):25–42.

A code of ethics for health care interpreters: A working paper for discussion. The National Council on Interpreting in Health Care Working Paper Series. July 2002: <http://www.ncihc.org>

Adelson N. *Being Alive Well: Health and the Politics of Cree Wellbeing*. Toronto: University of Toronto Press, 2000.

Tan Alora A and JM Lumitao, eds. *Beyond a Western Bioethics: Voices from the Developing World*. Washington: Georgetown University Press, 2001.

Fadiman A. *The Spirit Catches You and You Fall Down: A Hmong Child, Her American Doctors, and The Collision of Two Cultures*. NY: Farrar, Straus and Giroux. 1997.

Research Design:

A: Quantitative analysis: A general overview

Suzanne Tough, PhD

University of Calgary
Calgary, Alberta, Canada

Epidemiology is a study of diseases in populations undertaken by collecting and analyzing statistical data. In this chapter, we will explore quantitative methods of study design and analysis used in epidemiological studies. The chapter will give readers who are not familiar with quantitative analytic methods a very basic understanding of research designs including their strengths and weaknesses. Readers should use textbooks or the references cited at the end of the chapter to learn more.

Preliminaries

A key determining factor for successful interventional research trials is the study design. The study design is the plan of investigation assessing the relationship between one or more interventions. The study design should allow you to transform the conceptual hypothesis into an operational hypothesis that can be tested. Since all study designs have potential flaws, you should understand the weaknesses and strengths of study designs to avoid flaws and ensure success of your project. Most flaws in the initial design cannot be corrected in subsequent stages.

A good research design will perform the following functions:

- enable the comparison of a variable (such as disease frequency) between two or more groups, or in one group before and after the intervention;
- allow the contrast to be quantified;
- establish the temporal sequence by permitting investigators to determine when the risk factor occurred and when the disease occurred; and
- minimize bias, confounding variables and other problems that may complicate the interpretation of data.

Directionality

Directionality answers the question, “When did you observe the exposure variable relative to when you observed the health outcome?”

- Directionality can be forward, backward, or non-directional.
- Directionality also affects whether or not a study will have selection bias.

Timing

Timing answers the question, “Has the health outcome of interest occurred before the study actually began?”

- If it occurs before the study is initiated, the timing is retrospective.
- If it occurs after the onset of the study, the timing is prospective.
- Timing affects whether or not a study will have measurement error and information bias.

Randomization

Randomization is an allocation procedure that assigns subjects into groups so that each subject has the same probability of being in one group as in any other. Randomization attempts to equalize demographic, behavioural, genetic, and other characteristics of the comparison groups to isolate exposure status as the primary differentiating factor. If the study finds a difference between comparison groups, that difference may be attributable to the difference in exposure status. Randomization offers insurance, though no guarantee, that outside variables are evenly distributed among different groups. If distribution is found to be different, the investigator should take this into account in the analysis, for example, by stratifying on age.

Types of Studies

Epidemiological research studies can be broken down into two large groups: experimental and observational.

In experimental studies, the investigator proactively determines the exposure. For example, in a clinical trial to assess the effect of a treatment, the drug or other intervention is predetermined. Randomization is generally used in experimental studies to minimize bias and error. Community intervention trials can also be studied in an experimental model (for example, to assess the effectiveness of a community lunch program).

In observational studies, the subject determines his or her exposure or treatment. Observational studies can be either descriptive or analytic. Descriptive studies, such as case reports or case series, may look at the natural history of disease to help decide on funding allocation or to suggest a hypothesis. Analytic observational studies can test hypotheses or may be used to assess causation. Observational analytic study designs include case-control and cohort studies.

Choosing the Study Design

Because some research questions can be answered by more than one research design, the choice of design depends on a variety of considerations, including:

- speed,
- cost, and
- availability of data.

Controlled Clinical Trials

The randomized controlled clinical trial is the design that most closely resembles a laboratory experiment and has become the “gold standard” for evaluating treatment interventions. The major objective is to test the efficacy of a therapeutic or preventive intervention. Key features of such a clinical trial include:

- Randomization: to make study groups comparable on all factors except for exposure status.
- Blinding: patient and/or investigator should be unaware of the treatment assigned.
- Ethical concerns: “first, do no harm,” stopping rules.
- Intention to treat analysis: “analyze what you randomize.”

Advantage of clinical trials:

- allows the investigator to control the research process

Disadvantages of clinical trials:

- time-consuming and usually costly
- only interventions or exposures that are controlled by investigator can be studied,
- problems related to therapy changes and dropouts
- may be limited in generalizability

Cohort Studies

The cohort study is a basic observational study design most similar to a clinical trial. Characteristics include:

- must follow-up study with forward directionality
- study can be prospective or retrospective

Advantages of cohort studies:

- least prone to bias when compared to other observational study designs
- forward directionality looks at cause before effect
- can be used to study several diseases

Disadvantages of cohort studies:

- often costly and time-consuming, particularly if prospective
- loss-to-follow-up may lead to bias
- poor design for studying rare diseases or diseases with long latencies

Case-control Studies

The case-control study is a basic observational study design that is usually retrospective. It is often inexpensive and quick to carry out, but is prone to bias when compared with a cohort design.

Selection of a control group is an important issue in any case-control study. The ideal control group should be representative of the population from which the cases are derived (the *source population*). Controls can be population- or hospital-based. In population-based case-control studies, cases and controls come from the same source population. In hospital-based studies controls are accessed through the hospital database. However, hospital controls are not usually representative of the source population.

Advantages of case-control studies:

- inexpensive and less time-consuming compared to cohort studies
- provides sufficient numbers of cases for rare diseases with long latencies
- allows several exposures to be evaluated

Disadvantages of case-control studies:

- susceptible to both selection and information bias
- does not allow estimation of risk
- does not consider more than one disease
- not feasible for rare exposures.

Cross-sectional Studies

A study of a population at a single point in time, cross-sectional studies are useful for determining the prevalence of risk factors and the frequency of prevalent cases of a disease for a defined population. They are also useful for measuring current health status and planning for some health services.

Advantages of a cross-sectional study:

- fairly quick and easy to perform
- useful for hypothesis generation

Disadvantages of a cross-sectional study:

- can't provide temporal relationship between risk factors and disease
- not good for testing hypotheses

Case Reports and Case Series

Case reports and case series describe the experience of a single patient or a group of patients with a similar diagnosis. The collection of a case series rather than reliance on a single case can mean the difference between formulating a useful hypothesis and merely documenting an interesting medical oddity.

Advantages of a case report and case series:

- recognition of new diseases
- formulation of hypotheses

Disadvantages of a case report and case series:

- based on the experience of one person, or just a few people
- the presence of any risk factor may be coincidental
- lack of an appropriate comparison group

Key Points

- A good research design will enable quantitative comparison of variables between groups, show temporal relationships and have minimal bias.
- Directionality, timing and randomization are important considerations in designing a study.
- Each type of study has advantages and disadvantages:
 - Clinical trials: gold standard for studies but costly and time consuming
 - Cohort study: useful for study of common diseases but time consuming and open to bias
 - Case-control study: inexpensive and less time consuming but susceptible to bias
 - Cross sectional study: relatively quick and easy but will not allow hypothesis testing or development
 - Case report and case series: good for study of new or rare diseases but lack ability to generalize results to other situations.

References and Links

Creswell, JW. *Research Design: Qualitative, Quantitative, and Mixed Methods Approaches*. Thousand Oaks, CA: Sage Publications, 2003. Note: Some topics in this module are available as a free preview at <http://books.google.com>.

Hennekens CH and JE Buring. *Epidemiology in Medicine*. Toronto: Little Brown and Company, 1987.

Active Epi. <http://www.sph.emory.edu/~dkleinb/activepi.htm>. Excellent resource for this module.

Shapiro ED. Case-control studies. *Pediatric Infectious Diseases Journal*. 22(1):85–7, 2003.

Research Design:

B: Qualitative research: Basic principles

Lorelei Lingard, PhD

Department of Pediatrics
University of Toronto
Toronto, Ontario, Canada

The qualitative research paradigm seeks to describe and understand the nature of social, relational, and experiential phenomena in their natural setting. For instance, a qualitative approach is appropriate when we wish to understand how a social group works, what people think or feel about an experience, or how a social process unfolds. The objective of this chapter is to outline the principles of qualitative research using examples to critically assess how it may be used effectively. The chapter will provide an overview of the qualitative research approaches, methods and the three key principles for its use.

The qualitative paradigm is broad and varied, drawing from a range of disciplines including anthropology, sociology, and the humanities. The paradigm can be conceptualized on two levels: research approaches (how your study is framed) and methodological tools (how your data are collected).

Research Approaches

There are several ways to approach a research question in the qualitative paradigm. The approach will depend upon the research question, the nature of the research setting, and the objective of the research. The principle of “best fit” is used to decide how best to approach or frame research questions, since there is no approach that is inherently “better” than another. This is a key difference from the quantitative research, where the randomized controlled trial is widely accepted as the “gold standard.”

A detailed review of qualitative approaches is beyond the scope of this module, but it is important to recognize that research design is shaped by the selection of the approach. Qualitative research approaches include:

- case study – the in-depth analysis of a “bounded system”;
- grounded theory – the development of theoretical explanations that are derived from participants’ experience of a social phenomenon;

- phenomenology – the exploration of individuals’ experience of a phenomenon;
- ethnography – the study of the meanings inherent in a culture’s or group’s everyday activities and routines and
- critical theory – the description and analysis of power dynamics

Each approach has its strengths and weaknesses. For instance, consider the question, How do pediatricians advocate for patients experiencing chronic conditions? This could be investigated using several approaches. If case study is selected, the boundaries of the case need to be defined, and sampling decisions are made on the basis of elaborating the case appropriately. If grounded theory is selected, theoretical sampling will govern the sampling process because the grounded theory approach requires the researcher to pursue evolving thematic trends throughout an iterative data collection and analysis process, towards the goal of building an explanatory theory of the studied experience, process, or phenomenon.

Research Methods

Methodological tools used in qualitative research include the individual interview, the focus group (group interview), participant and non-participant observations, open-ended survey questions, the creation and review of documents (e.g., participant journals, video diaries), and the review of existing documents (e.g., In-Training Evaluation Reports or ITERs). The selection of tools depends upon the research question and data collection will generally be considered in more detail below, under the heading “Authenticity.” What is important to note is that any research method can be used within any research approach. The methods are the “toolbox” of available resources, which are selected and arranged according to the research question, the research site, the participants, and the approach or framework guiding the work.

Principles Determining Quality

This module boils qualitative research down to three principles of quality or rigour. These principles are drawn from an extensive literature outlining guidelines for excellence in qualitative research. You can use these principles either as a framework for critical appraisal of qualitative

research studies in the literature, or as a starting point for considering how to design a qualitative project.

The three principles are:

- sampling and saturation
- authenticity (data collection)
- trustworthiness (data analysis)

Sampling and Saturation

Because qualitative research explores social and experiential phenomena, deciding whom to include and exclude is a critical step in the sampling logic. Social phenomena, such as human relationships or group processes, often engage a wide variety of participants. The researcher must justify their decisions about who to observe or interview and who to exclude. The researcher must determine what contexts are appropriate to a full exploration of the study questions. The following key points must be addressed:

- Who are the participants, and can they provide data relevant to the research question?
- If the sample does not represent all relevant participants in the research setting, how are inclusion and exclusion justified?

Sampling in qualitative research is not just about how many subjects to include in the study. In qualitative research, sufficiency of sample is a matter of thorough exploration of a culture or phenomenon. Often such thoroughness is referred to as saturation, meaning that the collection of new data is not revealing new issues. For instance, if after 20 observation sessions, the researcher is not seeing any new patterns of interaction and recurrent themes are similar across field notes, saturation is said to be reached and data collection may be stopped. Sample estimations may also be explained by referencing method-based estimates, or specific sampling strategies, such as theoretical sampling. Of course, in this case the method of data collection needs to reflect the sampling strategy. For instance, theoretical sampling requires data analysis to proceed alongside data collection.

Example:

All final year medical students were invited by e-mail to participate in a study. The e-mail message indicated that the study was investigating students' experiences of stress in medical school, and that participants would be asked to discuss their perceptions of how medical school impacts their physical and mental health. Confidentiality was assured. Thirty medical students volunteered to participate, and were individually interviewed using the in-depth interview technique. Interviews were audio-recorded and transcribed.

Appraisal:

Overall, this study does a poor job of observing the criteria for sampling.

If the study is investigating "students' experiences of stress in medical school," final year medical students are not the only relevant sample. Justification of why students from other years are excluded from sample is required. Further, students who reach the final year may represent only part of the "experiences of stress in medical school," since they will be the stress survivors. Those who dropped out before final year due to stress are not part of this sample, so their perspectives will not be part of the data collected.

The sample size of 30 also requires justification. How did researchers determine that was a sufficient sample to explore the phenomenon?

Authenticity: the Quality of Data Collection

Because qualitative researchers must engage with their research participants, their relation to the participants, and the ways in which that relationship may shape the data being collected, requires careful thought both when deciding how to collect the data and when considering constraints on its interpretation. An important strategy used by qualitative researchers to improve the quality of their data set is triangulation. Triangulation is a term from cartography, which refers to the process of finding one's position on a map with reference to other mapped positions. In qualitative research, triangulation involves collecting data from several "positions" in order for the researcher to gain insight from

multiple perspectives, thus realizing a more refined and comprehensive understanding by the end of the research. Triangulation requires that the researcher select the most relevant data sources and ensure their integrated analysis to explore how the data sources confirm or disconfirm one another.

There are other considerations that may influence authenticity. Researchers must consider their relation to study setting and subjects, and to any potential coercive influence that may arise from that relation. In the case of interview research, the interview script and process must be non-leading. That is, do questions suggest a “right” answer? Will the interview location reinforce particular values? Was the script piloted appropriately?

In observational research, has the researcher considered the Hawthorne effect (in which observed participants act differently than they would if the observer were not present)? Has the team discussed mechanisms to minimize the Hawthorne effect, such as prolonged engagement in the field and rapport-building? Was there a process for recording or reflecting on the Hawthorne effect? Field notes should record any references to observer presence, such as comments about the study or questions directed to the observer.

Is there an effort to triangulate data for maximal richness by collecting complementary data sets or accessing different subject populations?

Example:

A web-based survey consisting of 25 open-ended questions was distributed by e-mail to all female emergency medicine residents at three US medical schools. The purpose is to collect data regarding educational, personal, and social experiences in an emergency medicine postgraduate program. The survey was developed in a two-stage process. First, the literature was reviewed to identify key issues such as maternity leave, mentoring, and sexual harassment. These issues were then presented to a focus group of female residents in medicine and surgery for elaboration, discussion, and refinement. The resulting core issues were crafted into 25 questions for open-ended, text-based responses by participants. A three-time e-mail reminder system, sent by the departmental postgraduate office, was implemented to maximize the response rate.

Appraisal:

This study exhibits some weaknesses regarding the quality of the data arising from the collection methods. While female residents in a high-pressure residency program are an appropriate and relevant sample for exploring the issues under study, the use of a survey with 25 open-ended questions seems in conflict with the context of these participants. Also, no mechanism for triangulation is incorporated: interviews might yield more insight into areas less amenable to written response. Finally, the potentially coercive nature of an e-mail reminder from the post-graduate office requires consideration.

Trustworthiness: the Quality of Data Analysis

The process used in analysis in qualitative research should be clear, with little or no “mystique” surrounding how the researchers proceeded from a pile of transcripts to a list of thematic categories. Thus the steps involved in the analysis process should be explicit and described in the researcher’s own notes to provide an “audit trail” to review their analytical journey.

How did the analysis process explore participants’ perceptions of the developing interpretation? Were participants engaged in reflecting on the results of the analysis? Were insider experts used to verify coding samples? Was “return of findings” conducted? If an analysis process is well described, researchers will be able to tell who participated in analysis, what their roles were, and how they integrated their different perspectives. What steps did they take to resolve discrepancies? Was computer software employed in the categorization process? Did researchers exhibit “constant comparison”? (This involves comparing new instances from the data set to existing instances in developing categories to elaborate the categorical definition and/or reconsider the previous assignment of instances.)

Example:

All 18 interviews were audio-taped and fully transcribed. Themes were identified and developed by three authors reading and re-reading transcripts, both independently and in joint discussions of emerging patterns. These themes were further refined and clarified through focused attention to participants’ original accounts and researchers’ observations

of the study setting, towards the development of theoretical explanations of core phenomena. Interviews and analysis were conducted concurrently and continued until themes were saturated. Trustworthiness was enhanced by the transparent process of analysis, the involvement of three researchers who read and compared ideas on the transcripts, and the careful treatment of discrepant instances. Analytical memos documented ongoing analytical decisions and reflections on discrepancies. Four representative interviewees were sent a copy of the primary analysis and asked to comment.

Appraisal:

The analytical process makes clear who conducted the analysis, the steps involved, the iterative process of data collection and analysis, the strategy in place for keeping an audit trail, and the effort to engage participants in refining the analytical concepts.

Key Points

- There are many qualitative approaches. Deciding which one to use for a particular research project depends upon “best fit.” The approach shapes the framing of the question and the selection of methods.
- These three principles of rigour can be applied to qualitative research to determine the quality. This is not a “recipe” for qualitative research, but rather key areas for consideration.
 - sampling and saturation
 - authenticity (data collection)
 - trustworthiness (data analysis)

References and Links

Creswell J. Five Qualitative Traditions of Inquiry. *Qualitative Inquiry and Research Design: Choosing Among Five Traditions*, pp 47–72. Thousand Oaks, CA: Sage Publications, 1998.

Denzin N and Y Lincoln. Introduction: The Discipline and Practice of Qualitative Research. In Denzin N, Lincoln Y, eds. *The Sage Handbook of Qualitative Research*, pp 1–32. Thousand Oaks, CA: Sage Publications, 2005.

Lingard L, and TJT Kennedy. *Qualitative Research in Medical Education*. Monograph booklet, published by the Association for the Study of Medical Education. In press.

Mays N and C Pope. Qualitative research in health care. Assessing quality in qualitative research. *BMJ* 2000 320:50–52.

Tesch R. *Qualitative Research: Analysis Types and Software Tools*. UK: Falmer Press, 1990. This book is free and available online at <http://books.google.com>.

Basic Biology:

The ABCs of modern biological technologies

David Speert, MD, FRCPC

Department of Pediatrics
University of British Columbia
Vancouver, British Columbia, Canada

Andrew Stadnyk, PhD

Department of Pediatrics, Microbiology and Immunology
Dalhousie University
Halifax, Nova Scotia, Canada

The tools of modern biology have revolutionized the way scientific questions are asked and solved. Clinician scientists today have the opportunity to pose important questions and solve them using exciting new technologies to provide answers. There are many examples of how the modern tools of research have provided new avenues to diagnose, treat, and prevent diseases in children. But the quality of the question depends on how well we understand the limits as well as the power of the new technologies. The objective of this chapter is to inform non-biologists on principles of biology and provide an overview of key tools that are now used in research. The information should permit a more informed dialogue between basic researchers and clinician scientists.

Introduction to Molecular Biology

One Gene, One Protein

Deoxyribonucleic acid (DNA) contains the genetic instructions used in all known living organisms. DNA is often compared to a set of blueprints, since it provides the instructions needed to construct components of cells. Arrangements of four nucleotides bases (adenine, A; cytosine, C; guanine, G; and thymine, T) provide the genetic code. It is quite remarkable that arrangements of only four nucleotides create the rich diversity that exists. The four nucleotides are linked together into a gigantic string of DNA called a chromosome. The 46 chromosomes in a cell contain the entire human genome, consisting of about 30,000 genes.

A protein is a molecule in a cell; it is composed of various chains of the 21 amino acids. Each amino acid is encoded by a codon – a set of three nucleotides. For instance, the amino acid *proline* is encoded by the

nucleotide sequence “CCG.” A series of these nucleotide triplets produce a string of amino acids called a protein.

A gene is a segment of DNA that controls the production of a specific protein. Since genes are strung together end-to-end on chromosomes, a mechanism must exist for instructing the cell when to start and when to stop making a protein. The start site is called a start codon and the stop site a stop codon. Thus genes are like a string of three-letter words, each string with a beginning and an end, between which are the tri-nucleotides that encode instructions for assembling the next amino acid.

DNA, RNA, and Proteins

Forty-six pairs of chromosomes constitute the “volumes of the book” that contain the instructions for how to create what we know as living beings. But how does the translation from DNA to a whole human being take place? As described above, genes provide the instructions for making individual proteins, but there are many steps involved in translating genes into properly functioning proteins.

If all genes in the body were active in making protein in every cell in the body, each of us would be a blob of a single cell type; clearly this is not the case! There must be a method for rendering some genes active in some cells and different ones active in others. Thus muscle cells will be different from brain cells and liver cells. There are a number of regulatory mechanisms that turn genes on or off under certain situations. An example of this is inflammation, during which immune cells are instructed to make certain disease-fighting molecules. These molecules are useful in fighting disease but can also be toxic, so their production must be turned off as soon as they are no longer needed.

For a gene to make a protein, it must be “turned on.” This process of gene activation is very complex and will not be explained here, but it can be influenced by many different environmental signals or cues. Once a gene is turned on, it makes a mirror image of itself in the form of ribonucleic acid (RNA). Several different forms of RNA are responsible for such tasks as providing the “message” for protein production (messenger RNA, or mRNA) or for transporting the amino acid (transfer RNA) to the nascent protein that is assembled one amino acid at a time in the order coded by nucleotide triplets of the master DNA. The protein is assembled following the code laid down by the RNA and is then released for further processing.

Table 1: Glossary of Terms used in molecular biology

- **Nucleus:** the part of a cell holding genetic instructions for the cell's function.
- **Cytoplasm:** the part of a cell surrounding the nucleus.
- **Chromosome:** a major part of the nucleus made of a large string of DNA. There are 46 chromosomes in the human cell that contain the entire human genome, consisting of 30,000 genes.
- **Gene:** segment of DNA that controls the production of a specific protein.
- **DNA:** (Deoxyribonucleic acid) a molecule holding the coded genetic instructions used in all living organisms.
- **RNA:** (Ribonucleic acid) a mirror image of an activated DNA segment that allows the DNA instructions to be made into a protein.
- **Nucleotides bases:** these are the molecules that are strung together to make a gigantic string of DNA.
- **Codone:** set of three nucleoside (a triplet) that codes for a specific amino acid in a sequence of amino acids that form a protein

Cell Biology

To understand disease, one must appreciate how individual components of the cell function in health. The advent of powerful technologies in molecular biology has allowed the entire human genome to be sequenced and has provided extraordinary opportunities to determine how each of the 30,000 genes influences the function of normal cellular architecture and function. Powerful new technologies can probe the transcription (i.e. the conversion of DNA into RNA) of every human gene in individual cells. This analysis allows us to deduce the environmental signals that affect expression of specific host adaptations. This has provided exciting ways to clarify mechanisms of disease and identify targets for new therapies. Clinician-scientists can collaborate in such studies since they can identify disease states and suggest environmental signals for investigation.

Components of the Cell

Cells have unique characteristics as well as common characteristics responsible for general cellular function. With rare exceptions, all human cells contain cytoplasm and a nucleus. The nucleus contains the chromosomes that dictate the ultimate function. The cytoplasm contains specialized structures called organelles. The membrane that contains the cytoplasm is rich in fats that form a barrier to penetration for most proteins.

Manipulation of Cells for Investigation

With the rapid advance in knowledge of human molecular biology, questions about the function of genes can be addressed. Cells can be:

- “immortalized” so that they can be studied indefinitely,
- “transfected” to introduce foreign (mutated or normal) genes,
- cultured to model the conditions occurring in disease, and
- manipulated to deduce what effects different conditions have in human health and disease.

Specific genes can even be “knocked out” (permanently inactivated) or knocked down (temporarily silenced) to clarify their role in the functioning of the cell.

Laboratory Techniques in Cellular and Molecular Biology

Flow Cytometry

In order to conduct analyses it is often necessary use flow cytometry to isolate specific cell types in a mixed population of cells. With this method, an antibody to a unique antigen on a cell can help to identify one cell type from others. For example, if you wish to know the percentage of cells called lymphocytes in blood, you would incubate a sample of blood with a lymphocyte-specific antibody (CD3 antigen, for example) labeled with fluorescent dye. The flow cytometer is a machine capable of counting cells containing the antibody labeled fluorescent dye. The machine detects the fluorescence as a flash of light thus allowing it to count the numbers of cells with antibody compared to cells without antibody. From this the percent of cells emitting light (and with the antibody marker) is determined. Up to five different colored dyes can be used simultaneously in the same

sample to provide information for about five unique markers on each cell. If a particular color is detected, the instrument can be programmed to apply a small electrical pulse to the cell that causes it to separate from the mainstream flow of cells. Such cells can be culled for additional study.

More information on the operating principles can be found at:
<http://www.meds.com/leukemia/flow/flow0.html>

In Situ Hybridization

A variation on antigen detection in tissue section is based on detecting the messenger RNA (mRNA) responsible for translating the proteins, using complementary nucleic acid sequences in a technique called in situ hybridization. The tissue section is flooded with short specific nucleic acid sequences that are complementary to the mRNA of interest. This “probe” is bound to a reporter molecule. Following washing, the section is flooded with the substrate for the reporter molecule to produce a signal that indicates the nucleic acid probe has bound to its target mRNA. This approach enables the detection of the cell source of specific molecules defined by their mRNA. Some issues include choosing a suitable fixative that preserves the mRNA and difficulty in achieving suitable hybridization conditions to have the two nucleic acid strands bind.

Enzyme Linked Immunosorbent Assay (ELISA)

With the ELISA technique, an antibody is used to coat the 96 wells of a plastic dish. When the plate is flooded with fluid containing the antigen for the specific antibody, it binds to the plate. After washing the plate to remove non-adherent antigen, a second antibody – to a different binding site on the antigen – is applied and used to detect the same antigen. This second antibody will be labelled with an enzyme or a fluorescent dye. After more washing to remove unbound secondary antibody, the substrate for the enzyme is added and a color reaction ensues. The color change can be detected in a spectrophotometer or a fluorescence detector.

ELISA detection of antigens can be highly sensitive and specific but, there are many potential pitfalls. See the following link on ELISA:
<http://www.edvotek.com/269.html>

Western Blotting

One approach that overcomes some shortcoming of ELISA is Western blotting, which is based on polyacrylamide gel electrophoretic (PAGE) separation of proteins. Proteins from a mix can be separated by molecular weight using their respective electrical charges. The PAGE gels are then transferred to a nitrocellulose membrane for further handling. The membrane is flooded with an antibody specific for the antigen in question. The antibody is often conjugated to an enzyme that becomes activated when substrate for the enzyme is added. A substrate reaction is seen where the antibody has bound the protein. The result is a “band” identifying the antigen of interest and at the same time providing an indication of the molecular weight of that antigen. This technique allows you to confirm that the antigen being detected is indeed of the suitable size. Although Western blotting is less sensitive than ELISA, it is preferred for detecting molecules in small samples. Comprehensive descriptions of Western blotting can be found at <http://www.edvotek.com/317.html>

Polymerase Chain Reaction (PCR)

PCR is a quick and simple technique to amplify a gene or a specific region of DNA present in a sample to bring it to a detectable quantity. PCR can be used to detect DNA or RNA sequences from any organism, from humans to bacteria and viruses, which makes it a useful clinical tool for evaluating the presence of, or exposure to, infectious disease. It is also useful for detection of genes that encode for genetic disorders and for forensics (as shown on the popular TV series CSI).

To perform PCR, primers must be selected to target the sequence in question, for example, a mutation in a gene that leads to a genetic disorder such as cystic fibrosis. Primers are nucleotide sequences about 20 nucleotides in length that flank the targeted sequence and allow it to be copied. They are designed in such a fashion that they target only that sequence. Before PCR begins, primers and other reagents must be added to the mixture. Other reagents include nucleotides, the building blocks for new DNA synthesis, and Taq polymerase, an enzyme that polymerizes new DNA.

PCR reactions begin with denaturation, which is done by heating the sample so that the two strands of DNA separate and are exposed and accessible to the primer. Next the mixture is cooled so that the primers can anneal to the denatured strands of DNA. Two sets of primers are added to the mixture: one that binds to the front end of the target sequence and one that binds to the tail. After the primers have annealed, the mixture is heated back up to a temperature that is optimal for the functioning of Taq polymerase. Taq polymerase moves along the single strand of DNA, creating a new complementary strand. Next, the sample is reheated to deactivate the Taq polymerase. This begins the cycle again. In one PCR cycle, the number of DNA molecules is doubled. The cycles can be repeated up to 40 times, during which DNA polymerization favors the targeted sequence. After PCR is performed, the results can be visualized using gel electrophoresis and other techniques. A useful link describing the principles of PCR is available: <http://allserv.rug.ac.be/~avierstr/principles/pcr.html>

Key Points

- With developments in molecular biology, powerful new techniques can unravel many new secrets of biology.
- These new tools can be exploited best if biologists and non biologists work together toward common objectives.
- This chapter describes several of the most commonly used techniques:
 - Flow cytometry allows us to separate distinct cells for further investigation.
 - InSitu hybridization is used to identify the source of specific molecules,
 - Enzyme linked immunosorbant assay (ELISA) and Western blotting techniques allow us to detect minute amounts of specific proteins,
 - Polymerase Chain Reaction (PCR) can be used to detect specific DNA or RNA sequences to identify genetic disorders or disease triggered changes in the cell.

Links

For an excellent image of cellular anatomy visit <http://micro.magnet.fsu.edu/cells/animalcell.html>

For a comprehensive web-based tutorial on biological methods visit:

<http://www.edvotek.com/about.html> and

http://www.rndsystems.com/western_blot.aspx

Good Clinical Practice: GCP 101

Darlene Baxendale, BScN, RN, CCRP

Canadian Centre for Vaccinology
Halifax, Nova Scotia, Canada

Robert Bortolussi, MD, FRCPC

Department of Pediatrics
Dalhousie University
Halifax, Nova Scotia, Canada

Good Clinical Practice (GCP) is the accepted international ethical and scientific standard for designing, conducting, recording, and reporting clinical trials. It protects the rights and safety of research subjects while ensuring that the clinical research process and data are valid and accurate. GCP also describes the responsibility to:

- strictly conduct the clinical trial according to the protocol,
- ensure that all ethical requirements are met,
- document and maintain records and procedures, and
- comply with regulatory requirements.

This chapter will summarize the GCP guideline to help you understand what is expected when you undertake clinical research using GCP.

The objectives of this chapter are threefold: to help you learn the principles for GCP, understand your responsibilities under GCP, and identify GCP resources to guide your clinical research practice.

Where did Good Clinical Practice come from?

The first attempt to develop standards for GCP was made in the mid-1970s by the US Federal Drug Administration as a means to improve the quality of information and data submitted to regulatory authorities for licensing of new drugs. Shortly thereafter, the European Union and Japan created GCPs for their own regulatory agencies. In 1996, an international agreement involving the USA, Europe, Canada, Scandinavia, Australia, and the World Health Organization was signed that provided one common standard for GCP. This agreement, known as the International Conference on Harmonization (ICH GCP) is now the accepted standard to conduct clinical trials of new drugs in the developed world.

In order to protect the rights, safety, and confidentiality of participants, GCP has embraced the cardinal principles of human ethics:

- Respect for the dignity of the person.
- Beneficence. Research must never be placed above the health, well-being, and care of the research subject.
- Justice. The benefits and risks of the research must be distributed equitably among all groups and social classes, taking age, sex, economic status, culture, and ethnicity into account.

Table 1: Principles of GCP

- Conduct of the trial must remain in compliance with the protocol.
- Each individual involved should be qualified by education, training, and experience to perform his or her tasks.
- Informed consent of trial subjects must be obtained before participation.
- Information must be recorded, handled, and stored to allow accurate reporting, interpretation, and verification.
- Participant records must be protected to respect privacy and confidentiality.
- Systems must be in place to assure the quality of every aspect of the trial.

What are the researcher's responsibilities?

Whether it is today, tomorrow, or next year, anyone who looks at your research should be able to find all of the essential documentation. This will be your responsibility. To accomplish this, you must:

- understand and accept all aspects of the protocol,
- personally conduct or supervise the study according to the protocol,
- make changes only with approval of the sponsor and the research ethics committee,
- ensure that the requirements for obtaining informed consent are met,
- report adverse events to the sponsor and the research ethics committee,
- inform study staff about their responsibilities,

- provide necessary documents to the research ethics committee for the initial and continuing review and approval of the study,
- promptly report all changes in the research activity and all unanticipated problems involving risks to participants,
- maintain adequate and accurate records and make them available for inspection, and
- comply with all regulatory requirements regarding the obligations of a clinical investigator.

Compliance with GCP and ethical standards is a joint responsibility of the sponsor (i.e. the principal investigator [PI] or industry) and you, the clinical researcher. Clinical research trials may be developed (sponsored) by industry or by clinical researchers, acting alone or in collaboration with others. The sponsor is responsible for implementing and ensuring quality assurance and quality control. In industry-sponsored research, industry provides resources for trial management, data handling, and record keeping to the investigators. In investigator-initiated research, the PI, acting as both sponsor and investigator must ensure that all documentation is complete and that the protocol will be adhered to at all sites involved in the trial.

Monitoring to ensure rights, safety, and confidentiality of research subjects is required in all drug trials. You must ensure that you meet all the requirements of your institution's research ethics committee. This will include documenting procedures to collect, store, and analyze confidential information. Although the degree of the monitoring will depend on level of risk, all research protocols must include a plan to collect and analyze adverse events (graded by severity). You will be responsible to report adverse events to the research ethics committee (and sponsor) in a timely manner. If data and records are stored electronically (for example on a personal computer) procedures must be in place to control access to the data. This may include using encryption of personal identifiers, passwords, and other measures specified by your research ethics committee. You must also ensure accuracy of the data, and prevent unauthorized access, alteration, or removal. Compliance with GCP requires a team effort with your research assistants.

Essential Elements

Essential documents are those documents that individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. These documents serve to demonstrate the

compliance with GCP and with all applicable regulatory requirements (ICH GCP). Essential documents include source document, study record, case report forms, and study files. Essential documents must be retained according to regulations.

Investigators are required to collect and maintain adequate and accurate records of all observations and other data pertinent to the study for each participant. ICH GCP states that "All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation, and verification."

What is a source document?

Source documentation is where the information is first recorded. These are the original documents and supporting data including the dated consent forms, clinic notes, lab results, medical records, etc.

What is a study record?

A study record is the unique record which contains the source documents for each step of the research protocol. You will need to keep a full record of data required in the protocol for each subject. The record should contain:

- documentation of informed consent;
- documents showing that inclusion and/or exclusion criteria have been met;
- data forms, audiotapes, and videotapes of the subject;
- laboratory and diagnostic reports;
- written records of study procedures;
- all communication with participant (phone calls, diaries, questionnaires, correspondence); and
- reports on any protocol deviations or violations.

What is a case report form?

The case report form (CRF) is defined as a printed, optical, or electronic document designed to record all of the protocol-required information to be reported to the sponsor on each trial subject (ICH GCP). Any data reported on the CRF that is derived from source documents must be consistent with the source documents themselves. The CRF is the official documentation of the study for both sponsors and regulatory authorities and together with the source documents will be closely examined. The CRF may be designed for paper or electronic data collection.

What are the study files?

The study files include all essential documents needed to properly conduct the trial. A rigid system of file organization is critical to the daily activities of clinical research. An organized system ensures adherence to the regulations and maintenance of the rights and welfare of the human participants. This will provide an auditable trail to show that the principles of GCP were respected. This documentation includes:

- investigator agreement, protocol, and amendments;
- case report forms;
- current CV and licenses of study team;
- research ethics committee approvals and correspondence;
- original signed consents;
- safety reports sent to the research ethics committee;
- laboratory normal values;
- recruiting material;
- drug or device accountability records (if applicable);
- screening log or subject log;
- financial records; and
- delegation-of-responsibility log.

The minimum list of essential documents is documented in the ICH GCP Guideline.

How do you make corrections to essential study documentation?

Corrections to study records may occur during any study protocol. GCP has defined appropriate procedures for recording such changes. The responsible person must always be prepared to justify each correction. A line should be made through the entry, with the corrected entry and date written beside it. The identity of the person making the correction should be indicated with their initials. The original, incorrect entry should still be visible. Corrections should never obscure or conceal the original entry through “white outs” or erasure.

What about standard operating procedures?

In clinical research, standard operating procedures (SOPs) are defined by the ICH GCP as “detailed, written instructions to achieve uniformity of the

performance of a specific function.” The purpose of an SOP is to document a predefined procedure. SOPs are written instructions, necessary to achieve a consistent approach to a process. They are designed to ensure that clinical research, and its supporting activities, is conducted according to the principle of GCP.

It is, therefore, essential that all people and sites involved in clinical studies (both at the sponsor site and at the investigative sites) have appropriate SOPs in place in order to conduct clinical research and to assure compliance with the current regulations.

Key Points

Adhering to GCP requires education, training, and experience. GCP provides a unified standard for conducting clinical trials and facilitates mutual acceptance of clinical data.

To guarantee a successful trial, you must:

- employ qualified support staff,
- obtain proper informed consent,
- record information appropriately,
- protect confidentiality,
- handle investigational products appropriately, and
- Implement quality systems.

Links

ICH Harmonized: Guideline for Good Clinical Practice. J Postgrad Med 2001 47:45–50. <http://www.jpgmonline.com/text.asp?2001/47/1/45/235>

World Health Organization: Registry of Clinical Trials. <http://www.who.int/trialsearch/Default.aspx>

US Department of Health and Human Services. FDA. Guidance for Clinical Trial Sponsors. On the Establishment and Operation of Clinical Trial Data Monitoring Committees. <http://www.fda.gov/cber/gdlns/clindatmon.htm>

Murff H. GCRC, Vanderbilt University Medical Center. Data and Safety Monitoring in Clinical Trials. http://www.mc.vanderbilt.edu/gcrc/workshop_files/2004-10-08.ppt

Good Clinical Practice: Consolidated Guidelines (International). <http://www.fda.gov/cder/guidance/959fnl.pdf> and <http://www.ich.org/LOB/media/MEDIA482.pdf>

Commercialization:

Welcome to the world of IP, TT, contracts and licensing

Stuart Howe, PhD

Director, Corporate Ventures
The Hospital for Sick Children
Toronto, Ontario, Canada

Heidi Falckh, BSc

Director, Knowledge Partnerships
The Hospital for Sick Children
Toronto, Ontario, Canada

Whether requesting biological materials from a colleague or funding from industry, any clinician scientist's career will involve legal contracts. Your research may also lead to the invention of new technologies, products, or processes. To become commercially viable, such inventions require investment beyond your ability or the university's mandate. Thus, you may need to transfer such new knowledge to a third party who can undertake such commercial development. Contract and technology transfer laws are complex, and require knowledge beyond the expertise of most researchers. Thus, as you start your career, it is important to understand the principles upon which contract and technology transfer agreements rest. Fortunately, most universities have written policies on these matters and employ staff familiar with the law to assist you.

The objective of this chapter is to convey a basic understanding of contract law as well as the principles governing technology transfer, commercialization of patented inventions, and knowledge transfer of non-patented intellectual property. Although such principles are important, to best prepare for the career ahead of you, you will also need to become familiar with your own institution's specific policies.

Contracts

A contract is an agreement that is enforceable by law. The parties to a contract are the named individuals, companies, or institutions that sign the contract, are legally responsible to perform the contract terms, and can be sued if they fail to meet their obligations. Depending on your institution's policies, you, the investigator, may or may not be a party to the contract. If you are not, performance of many of the contract terms may still be delegated to you. Accordingly, you are responsible for compliance to the contract terms on behalf of the institution.

Contract terms and conditions specify the details of the research to be done. These terms will also determine your rights and obligations and assign responsibility if something goes wrong. Although oral contracts may be enforceable by law, disputes tend to revert to "he said, she said" arguments. Thus, whenever possible, contracts should be made in writing. In most countries, a legally enforceable contract exists where an offer has been made and accepted with consideration. Every contract must include "consideration," which is defined in English case law as "...some right, interest, profit or benefit accruing to the one party or some forbearance, detriment, loss suffered or undertaken by the other."

A consideration must be reciprocal, although not necessarily equal, and does not need to be monetary. For example, provision of a biological sample may constitute one party's obligation.

Contract Management

When do you need a written contract?

This depends on the policies of your institution, the party with whom you are collaborating, and the nature of the relationship between the parties. Generally, institutions require written contracts for activities such as:

- exchange of confidential information,
- exchange of biological samples,
- clinical and basic research agreements with industry,
- grants and sub-grants,
- formal institutional collaborations, and
- technology transfer.

Who reviews contracts?

Contracts should be reviewed by all parties and departments affected by the contract terms. Since the subject matter of the contract is your research, you should review it, whether or not you are a signator, to ensure that you can fulfill the obligations delegated to you by your institution. For example, you should confirm that the research milestones are achievable, that the budget is sufficient to cover the full cost, that you have adequate staff and expertise to do the work, and that the reporting requirements and publishing terms are acceptable.

Who negotiates contracts?

Most institutions have an office that is responsible for negotiating the terms and conditions of contracts to which they are a party. Although you may not be directly negotiating the contract, your input is critical for implementation of the contract terms and to ensure your rights are protected. For instance, the other party may have a very different position from you and your institution on publication rights and indemnification. The goal is to find an acceptable compromise so that all parties can work within existing policies and needs. Negotiating language that satisfies all parties, the so-called “win-win” scenario, often takes a great deal of time and skill on behalf of the negotiators. The process can be frustrating, but have patience – an ounce of prevention is worth a pound of cure, especially when the cure involves litigation!

Who signs contracts?

All parties to a contract are required to sign it. The authorized signing authority of the institution is usually designated by its policy. Generally, executives of the institution are the only individuals vested with the authority to legally bind the institution. Do not assume you are authorized to sign on behalf of your institution. If you are a party to the contract, make sure you completely understand and agree with all the terms and conditions before you sign it. It is wise to seek the advice of a trained professional before you sign anything. Your institution can help you with this.

Who is responsible for the performance of the contract?

The contract will specify who is responsible to complete each aspect of the work. The named party will have ultimate legal responsibility. Remember, however, that although you may not be a party, as the principal investigator you will be held responsible for meeting most of its obligations.

Types of Contracts

The following is an overview of confidentiality agreements and industrial sponsored research agreements, two important types of contracts for researchers. Your institution can help interpret the terms and legal clauses contained in your contracts.

Table 1: Types of Contract Agreements

Confidentiality agreement	an agreement to divulge information to another party for a specific time and purpose, with the receiving party agreeing to keep that information secret.
Industrial sponsored research agreement	an agreement between a researcher who will receive consideration (benefit) from a for-profit organization for their research.

Confidentiality Agreement

A confidentiality agreement (sometimes referred to as a non-disclosure agreement) is a contract whereby one party (the “disclosing party”) agrees to divulge certain information to another party (the “receiving party”) for a specific purpose, and the receiving party agrees not to reveal that information to anyone else. It is often used as a prelude to discussions between two parties exploring the possibility of transacting business. It is used when you wish to share an idea or information with others without having it passed on to anyone else. It allows you to preserve, among other things, unprotected patent rights, business plans, trade secrets, and other confidential and proprietary information.

Terms and Conditions of Confidentiality Agreement

The contract will begin by setting out who the parties are and who, therefore, will sign it. The contract will clearly define what information is to be kept confidential, including information generated by the receiving party based on or arising out of any disclosure of the confidential information. The contract will also place restrictions on the use of the information by the receiving party, particularly the ability of the receiving party to discuss the information with others, including colleagues within your own institution.

There will be exceptions to the definition of confidential information, which may include information independently created by the receiving party, information that the receiving party had prior to receipt of the disclosure, information that was public knowledge, and information that must be disclosed by a court order.

The contract will also specify a period of time during which the information will be transferred between the parties and a separate time limit on your obligation to maintain confidentiality. This time limit will vary but usually extends three to five years beyond the term of the contract.

Industry Sponsored Research Agreement

An industry sponsored research agreement (ISRA) is required when you work with, or are receiving consideration (benefit) from, a for-profit organization during your research. The one exception is when the for-profit organization is providing support for your research by way of an unencumbered grant, i.e., it is not seeking any rights to the results of your research and places no limitations on your actions. In this case, a letter to that effect may be sufficient. You should consult the appropriate grants/contracts office at your institution; most universities and health care institutions have strict policies regarding the terms and conditions of ISRAs.

There are several benefits for collaborating with industry: financial support, in-kind support, access to product or biological materials, and combinations of all of these. We do well to remember, however, that while a not-for-profit institution seeks knowledge and a for-profit seeks viable commercial products, the purpose of the collaboration should be to benefit the public and improve patient care.

Terms and Conditions of ISR Agreement

The following summary of terms and conditions are found in most ISRAs. But, you may request additional rights and/or obligations. Again, always consult with a trained professional in your institution who can answer any questions you have.

Intellectual Property Rights

This article will specify ownership and use of intellectual property (IP) developed during your performance of the research study. Depending on the circumstances, you, your institution, or the industry partner will own the IP of the project. In sponsor-initiated clinical research studies, ownership of IP is often assigned to the sponsor, whereas in investigator initiated studies, it usually remains with the investigator or institution, depending on your institution's policies.

You and your institution may assign all IP rights to the industry sponsor, while retaining a license or reserving your right to use any IP for clinical, academic, or research purposes. You may also be required to give participating patients their own data and to report on adverse events to your research ethics board and regulatory authorities if the industry partner does not. You may also wish to have access to multi-site raw data arising from a multi-center study, especially if you are the lead site or investigator. You may want to analyze the data yourself before authoring a paper based on it.

Be careful to determine if there are other, pre-existing contracts that affect the research project – a material transfer agreement, for example. You must ensure that the rights you are granting in the ISRA have not already been granted to someone else, and that you are free to grant the rights requested by the sponsor. You must carefully consider how the rights you grant in the contract will affect your immediate and future research plans.

Confidentiality

This section is similar to standard confidentiality agreements, with similar but abbreviated terms and conditions. The section will define what information must be kept confidential, and who must keep the information, for how long. It may also deal with obligations to comply with privacy laws, and to maintain the confidentiality of patient information. You must become aware of your obligations under the relevant privacy laws.

In a clinical research study, in addition to the standard exceptions to confidential information, you should include:

- a) information to be disclosed to research subjects in order to obtain informed consent or for the sake of their health, safety, or diagnosis;
- b) information that must be disclosed to the research ethics boards of participating sites;
- c) information that is published in accordance with the contract; and
- d) information that is released to regulatory authorities in accordance with the contract.

Confidentiality obligations should extend to both parties, not just to you and your institution. Most journals require that authors do not publicly disclose the details of their research or findings before their work

undergoes peer review and is published. Accordingly, where you are obligated to provide reports and data to your sponsor prior to publication, you should ensure that your sponsor agrees to keep your results confidential until they are published. Therefore, in order to determine the acceptability of the clause, you must consider whom you may need to share information with and what information you may need to share.

Public Disclosure

The terms governing public disclosure of information may appear in a number of sections of an agreement: the confidentiality, publication, and publicity sections to name a few. Accordingly, it is important to have a thorough understanding of the contract language, how the contract clauses are associated and qualify each other, and how this relates to your project.

While the confidentiality terms of the contract define what information is to be kept confidential, public disclosure terms clarify what steps a party must take in order to disclose information, and to what extent and in what context you may disclose information. For example, the contract may specify that you must provide a copy of a manuscript or presentation prior to submission in order for the company to seek patent protection. In multi-centre studies, the sponsor may seek to delay your public disclosure until the multi-centre data has been published. Many institutions allow delays of up to ninety days for public disclosure of data arising from a single site research study, and up to one year for public disclosure of data resulting from multi-centre research studies.

The sponsor may seek the right to approve or edit your manuscript, both of which are unacceptable. The contract should clearly state that final analysis and interpretation of your data remains with you and your institution.

The contract may also stipulate that information on adverse events must be disclosed to your research ethics board and the sponsor. The sponsor will usually be required to report the problem to regulatory authorities.

Public disclosure terms may limit the ability of either party to publicly recognize the existence of the agreement or the collaboration. On the other hand it may obligate you to give your sponsor credit for its role in your research, as well as specifying the form that credit takes. It may be a policy of your institution that it must be able to publicly acknowledge all sponsors

of its research activities. Hence the importance of anticipating your need to share or disclose information as it relates to the circumstances of your particular research project (in addition to publication of the results), and of clearly setting these requirements out in the contract.

Indemnification/Insurance

To indemnify someone is to secure or protect them from loss or damage. The question you need to consider is, Who will pay for your defense and any associated or resulting costs in the event you are sued as a result of your participation in a particular research study?

The answer to this question depends upon several factors including the cause of action (i.e., facts that give a person the right to sue) and any insurance coverage you may have through your institution (which in turn may depend upon your legal status in the institution) or any professional body with which you are associated. You should fully appreciate the policies of your institution and professional body to be satisfied that you are covered for all of the activities you will perform.

Your institution will analyze the facts of your study to determine the type of indemnification your research requires. The indemnification will identify the individuals to be indemnified, set out the scope of coverage, state any conditions and what is not covered, and state that you will follow the protocol, laws, and regulations relevant to the research. Issues of negligence or willful misconduct are not indemnified. Other “carve-outs” may include the sponsor’s negligence, product liability, or patent infringement, for which you or your institution should not have to indemnify the sponsor. The clause may also address notice periods, defense of claims issues, and minimum insurance requirements.

Budget

The budget may be a fixed sum, where a specified amount is given for the research study, or may be on a cost-reimbursement basis, where any money not used in the performance of the research study is returned to the sponsor – or a combination of the two. The budget defines the total amount to be paid by each party toward the cost of the research study, and when the payments are to be made. The degree of detail within the budget depends on the financial reporting requirements of the institution and the sponsor, as well as the policies of your institution’s research ethics board.

It is important that the budget cover the true cost of the research, and that the payments are scheduled in a timely fashion. It is easy to overlook “hidden costs” such as pharmacy costs, administrative support, and technician and nurse time. You, rather than your institution, will likely be responsible for determining the appropriate budget in discussion with the sponsor.

Most institutions apply an “overhead” cost in addition to the direct costs of the research. Overhead comprises costs of a project that cannot be directly attributed to it. Examples of overhead items include building use; equipment depreciation; physical plant and maintenance (including utilities, hazardous waste disposal, and security); insurance; financial and contract administration (including purchasing and accounting); and the use of core facilities and libraries. The overhead is usually a percentage of the total direct costs. The sponsor should be made aware of this institutional overhead at the start of budget negotiations.

The importance of accurate budgeting cannot be overemphasized. You do not want to be required to terminate a research study because you failed to properly anticipate its costs.

Completion and Termination

Most contracts will have a predetermined end date upon which the parties’ obligation to perform most of the contract terms will expire. The termination of a clinical research agreement that depends on patient enrollment may, however, be defined by completion of the protocol and subsequent data analysis and reporting. In most agreements, any party can terminate the agreement before the end date for specific reasons with or without prior notice to the other party(ies). In either case (expiration or early termination), the steps each party must take and each party’s ongoing or surviving responsibilities are defined.

Technology Transfer, Intellectual Property, and Commercialization

Technology transfer refers to the conveyance of new technologies from one entity to another, generally under a license agreement for the purpose of commercialization. Knowledge transfer is the conveyance of new knowledge to a third party for the purpose of dissemination of that knowledge by a license agreement or, more usually, simply by publication. Commercialization is the process by which new technology is developed

into salable products, processes or services by a commercial enterprise. The new technology and knowledge is defined as intellectual property (IP), the locus of potential commercial value.

Many academic institutions have established technology or IP transfer offices to develop new technologies or to locate a commercial partner to achieve commercialization. Except for inventors who have formed a “start-up” company to exploit their new invention, institutions usually rely on licensing or sale of inventions to commercial entities to realize the market potential of an invention. Beneficiaries in this process include the inventors, the institutions that support the inventions, and the businesses that commercialize the invention.

Commercial partners reward the owners of the inventions (generally the institutions) for meeting development milestones with payments and royalties. Typically, institutional owners share these rewards with the inventors, though the latter may receive additional research funding, often referred to as “sponsored research.” The commercial partner will eventually realize rewards in profits from protected markets, competitive advantage, and technological superiority. Technology transfer also contributes to the economic development and global competitiveness of the country.

Licensing

Licensing occurs when an owner of an intellectual property right gives a third party the permission, in the form of a license to use that intellectual property. A license is a type of contract between the party granting the permission (“licensor”) and the party to whom the permission is granted (“licensee”). In a license the consideration is the permission which is given in exchange for payment. A license does not transfer the ownership in the IP; it simply allows the licensee to use the property. Ownership remains with the licensor.

There are three main types of license: exclusive; sole; and non-exclusive. With an exclusive license only the licensee can use the licensed rights during the term of the license. The licensor retains the ownership of the rights, but nothing else. A sole license prevents the licensor from granting right to anyone else, but the licensor retains rights to use the licensed property. A non-exclusive license is one that can be granted by the licensor to as many licensees as the licensor wants.

Business Terms of a License Agreement

In addition to the normal legal terms found in many contracts, (such as terminations, indemnification, confidentiality, etc.) licenses have a number of specific business terms:

Table 2: Glossary of a Business Terms

Field of Use	intellectual property rights that cover more than one business area, e.g. diagnostics and/or therapeutics
Jurisdiction	specifies where the licensee has rights
License Fee	an upfront payment used to recover prior investment costs
Annual Maintenance Fee	annual payment to keep the license in effect and ensure that a licensee develops and markets the technology
Milestones	timelines that various development hurdles must meet
Development Financial Milestones	payments made to the licensee as development and regulatory hurdles are crossed
Royalties	a percentage of the net sales of products and services that fall within the scope of the licensed rights

Since each licensing agreement has its own unique set of circumstances, each also has its own unique set of terms and conditions. The negotiation of a license requires both parties to look to the future to arrive at a workable agreement that satisfies the anticipated needs of both parties.

Key Points

- A contract is an agreement enforceable by law with obligations on all signatories.
- The academic institution determines who is authorized to sign a contract.
- Types of contracts:
 - Confidentiality agreement: one party divulges information that the receiver agrees not to reveal
 - Industry sponsored research agreement: provides a budget from a for-profit company in exchange for “considerations”
- Contracts define signatories’ obligations, and may involve:
 - intellectual property (IP) rights,
 - confidentiality,
 - public disclosure,
 - indemnification/insurance,
 - budget, and
 - completion and termination.
- License agreements with commercial entities help new technologies development into commercial products or services.

References

The Hospital for Sick Children’s Toronto: Research and Policy Review Task Force Report

<http://www.sickkids.ca/ABDO/>

[For CCHCSP Web Users LINK TO HSC_Policy.pdf + ISCR.pdf]

The content of this article is provided for general information purposes only and does not constitute legal or other professional advice or an opinion of any kind. Users of this article are advised to seek specific legal advice from legal counsel regarding any specific legal issues. The writers of this article do not warrant or guarantee the quality, accuracy or completeness of any information in this article. This article should not be relied upon as accurate, timely or fit for any particular purpose.

Setting Up a Research Program: Short- and long-term needs

Neil Sweezey, MD, FRCPC

Department of Pediatrics
University of Toronto
Toronto, Ontario, Canada

Compared to the management of people or time, managing your resources (money) should be relatively straightforward. Your resources are held in accounts, and you spend them on the salaries of your people or to purchase supplies you need to do your work. Of course, you will need to acquire the resources to start your enterprise (often through intramural start-up funds negotiated as a part your hiring), and then replenish resources (operating funds) as you spend. Overseeing the ebb and flow of these resources requires planning and management skills, not scientific brilliance.

The objective of this chapter is to identify some of the managerial responsibilities that will fall on your shoulders as your research career develops. Detailed descriptions are not provided in this chapter since local processes will vary widely. Before you launch your research career, you should become knowledgeable about all of the regulations pertinent to your research and your institution.

Preliminaries

Balancing Research and Clinical Activity

As a clinician scientist, your department may expect you to generate a portion of your income through clinical activity. The dilemma is how much time is appropriate. For those who have not secured adequate protected time to engage in research, it can be tempting to undertake more clinical activity. However, if you are committed to a career as a clinician scientist, the benefit of the extra income is, in almost all cases, simply not worth it. Especially during the critical years when you are trying to establish yourself both as a consultant clinician and as an independent investigator, the value of time spent on research cannot be paid back later. Although personal debts may seem daunting at first, these can be paid off as income rises over time, commensurate with rising stature.

Start-up Funding

Academic institutions may sometimes provide a new clinician-scientist with start-up funding to run his or her research projects for the first two or three years. This is done with the expectation that he or she will be

more self-sufficient by that time. The amount of money provided will vary depending on the need to do the research and the amount of protected time. Considerations such as the availability of major equipment and material will be factors to determine the amount of funds provided. For highly competitive clinician scientists who will spend 70% to 80% of their time on research, today's highly competitive market often supplies a two-year commitment including one research assistant's salary and the consumables needed to show preliminary results. Whatever the amount offered initially, it will never cover your ongoing needs, so you should expect to write grant applications to a variety of funding agencies: government (federal or local), foundations, or industry (pharmaceutical companies and the like). Although industry may offer relatively easier funding, it will usually provide distinctly less freedom. Governments and foundations will deliver the best balance of freedom and responsibility.

Even the most successful researchers may encounter disappointment. Although funding agencies do not usually give a terminal grant to well-rated but unsuccessful renewal applications, some local institutions award bridge funding for the highest ranked unsuccessful renewal grant applicants. Find out what bridge funding opportunities are available at your site before challenges arise.

Financial Management

Personal Finances

Some highly successful academics do not manage their personal finances well at all. Often, taxes and other issues are neglected, due to a lack of time or personal interest. Early consultation with a financial advisor or accountant may prove helpful, especially if, like many of us, you are not particularly interested in this area.

Grant Operating Funds

Large national agencies will commonly provide operating funds for two to four years for successful young investigators or for programs that are not viewed as stable or well-established. Highly rated grants from stable programs can be awarded funds for five years. Requesting the maximum number of years of funding on your first application would be presumptuous, but failing to ask for it when submitting a strong renewal application would be foolish.

Budgets

Planning

Planning a research operating budget is complex and difficult. Often a mentor or former supervisor can be asked to provide a copy of one of his or her recent successful applications for funding, and the actual award letter with the final budget provided in comparison to the amount requested. Consultation with other colleagues can usually provide you with “rules-of-thumb” in your field.

Finding funding for trainees (graduate students, post-doctoral fellows, and others) is important and can be very time consuming. Obviously, the better qualified the trainee, the more likely you will be able to find an extramural award for his or her stipend. It is especially challenging finding funding for a trainee from overseas, especially if the rating system in the home country is different from your own country, because evaluators have difficulty assessing the credentials. Any additional objective details you can provide the committee to assist them in this regard can only enhance your foreign trainee’s application, to your mutual benefit.

You have to be realistic and fair in your planning. You cannot make commitments to spend funds that you merely hope to receive, but have not yet received. Institutions will no longer permit investigators to run deficits on their research expense accounts. If, as you approach the end of a funding cycle, you realize that you could be vulnerable if any specific grant fails to be renewed in competition, it is probably to your advantage to discuss the potential outcomes well in advance with your institutional administrators. Given sufficient warning, and a modicum of reason to think that a resubmitted revised application might have a fighting chance of getting funded in the next competition, they may be in a position to provide some bridge funding support for a limited period of time. It is far less helpful to approach the administrators for this type of support after finding out that your research enterprise has gone broke.

Records

Ask your institutional grants administrator(s) about your record-keeping responsibilities. Even though they will usually know much more about these issues than you do, and can help you with your reporting requirements, you still need to read the fine print of the terms and conditions applicable to

each individual award. You are ultimately responsible. In particular, check the agency’s regulations concerning whether you must spend the awarded funds exactly as proposed in your application, or if you may spend awarded funds as you deem best for the original project. Also determine if you are allowed to carry-over unspent funds to subsequent years of a multi-year grant, and if so for how long. Most agencies will eventually claw back funds that remain unspent for too long. Currently most agencies, if they do permit carry-over of unspent funds at all, will only do so for 12 months.

Audit

You will need to audit your expenses, to give a reality check to your planning, and to avoid or reduce waste in your laboratory. Even with the best will in the world, errors occur, and will go undetected if you do not check on a regular basis.

Regulatory Issues

It is appropriate to teach what you have learned of the art of resource management to your senior trainees, especially to those with ambitions to eventually run their own research enterprises. This would apply to PhD candidates finishing their laboratory work or post-doctoral fellows who could even take on some resource management responsibilities. As laboratory technicians gain experience, you can progressively delegate some of the routine aspects of management to them. Major equipment or salary expenses are things over which you will have to retain micro-managing control, but the time-consuming day-to-day matters should not take up your time.

Licensing (Radioactivity, Biohazards, etc.)

It is vital that you comply with all legal and institutional requirements. Before you undertake any laboratory activity that is regulated, become familiar with your institutional responsibilities and check to ensure everyone is appropriately trained. Provide the required information, getting help from those who have successfully done it before. Even if one individual has the responsibility for your entire group, insist on learning how to deal with this yourself; sooner or later you will need this skill.

Research Ethics and Animal Care Committees

If you propose to conduct patient-based or animal-based research, one of the main points on managing the research ethics process for the committees (Institutional Review Board [IRB] or Research Ethics Board [REB] or Animal Care Committee [ACC]) is to understand that they all require a great deal of preparation. The required lead time is often measured in months, sometimes in years. Trying to push the committee to move faster does not work. Nor will trying to convince it that its concerns are not important.

Research ethics committee members come from a variety of disciplines, including lay and professional members. They will not all understand your professional background and may not understand the jargon of your field of study. One of the most successful approaches you can take to expedite a research ethics review is to ensure that all submissions (oral and written) are provided in straight-forward, everyday language. It is often helpful to have your submission critically pre-reviewed for language by an intelligent but scientifically unsophisticated person.

When the research ethics committee has raised an issue, you must address it to their satisfaction. Often there will be a helpful committee officer or chairperson willing to provide you with feedback as to what exactly they want from you before you will be permitted to do the work. Seek out this advice early and often, to save untold grief, delays, disappointment, and frustration.

Materials Transfer Agreements

If the type of research that you do will involve the use of any unusual materials, animals, or tools generated by another investigator, you will increasingly find that the investigator himself or his institution may require you and your institution to sign some detailed legal commitments before you can receive or use the materials. You will need to find out what your own institution's rules are in this regard before sending along to any extramural collaborator anything novel, proprietary, or patentable that you may have generated (see Chapter 9).

Data

Whether it is for bench laboratories or for human subject studies, the data you generate are the foundation upon which your work is based. You have a responsibility to safeguard the integrity of the data and its confidentiality. The rights of ownership of, and access to, these data are often easily dealt with within a small, close group of people, but there are always opportunities for misunderstanding and conflict if the rules are not agreed upon in advance. These problems seem to be more prevalent when there is a significant potential for commercialization, especially if a significant proportion of the funding of the research is coming from business sources. These issues are dealt with in Chapters 3 and 8.

Key Points

- Negotiate terms of employment with protected time to undertake research appropriate for your research potential.
- Negotiate a start-up funding package appropriate for your research training and needs.
- Learn how to manage and monitor research funds and who to approach in the research financial office for assistance.
- Become knowledgeable on the all of the regulatory requirements of your institution for the research procedures you will be using.
- Ask your mentor to help you understand and follow the research regulations of your institution before you establish your research program.

Links and References

Bonetta L. Burroughs Welcome Fund/Howard Hughes Medical Institute.
<http://www.hhmi.org/resources/labmanagement/>

- Making the Right Moves: A Practical Guide to Scientific Management for Postdocs and New Faculty.
- Training Scientists to Make the Right Moves: A Practical Guide to Developing Programs.

Cech T. Advice on obtaining a faculty position and achieving tenure, leading a research team, mentoring students, balancing research and teaching, and more.
<http://www.hhmi.org/resources/labmanagement/moves.html>

Your First Academic Home:

A: How to find your first appointment

Robert Bortolussi, MD, FRCPC

Professor of Pediatrics
Dalhousie University
Halifax, Nova Scotia, Canada

Neil Sweezey, MD, FRCPC

Associate Professor of Pediatrics
University of Toronto
Toronto, Ontario, Canada

To be competitive, you must be able to show that you can master research techniques, develop a research hypothesis, perform the experiments to test the hypothesis, and write manuscripts that are publishable in highly regarded journals. There is no advantage in trying to rush this process. Only when you have reached this point should your mind turn to finding an academic appointment.

The objective of this chapter is to outline the process institutions in the developed world may follow when recruiting, and to explain how to engage in this process.

Preliminaries: When, Where, Why, and How

When

The search for an academic appointment can start anytime, but appointments usually begin at the start of the academic year (September). Announcements are usually posted eight or nine prior. Unofficial announcements, however, will often circulate by word-of-mouth a few months before the official one is posted. In addition, some departments are able to create new positions for highly desirable candidates. Others may have an ongoing recruitment policy in any of a number of fields, though they may not advertise them all of the time. So keep your ears open for opportunities, and be sure your supervisor, mentors, and colleagues know you are looking.

Official postings of academic positions can be found in newspapers, journals, and at research conventions where “job fairs” have become popular. Ask your supervisors and mentors what journals or meetings you should attend to for such opportunities.

Target your responses to those positions for which you are well qualified. Avoid sending impersonal letters to blanket the potential market. Your letter to the chair of the search committee should be personal, short, and direct. It should indicate how you learned of the position, why you are interested and qualified, and when you would be able to visit them if they are interested. Enclose your CV but do not provide reference names at this stage.

Where

Where should you plan to work? This is a highly personal question unique to your needs and desires, but we can address a few general points. First of all, you must be flexible. You have become highly specialized during your long training career. This may limit the number of universities and cities that have positions suitable for your background. So seek a balance between the ideal place and the reality. A decision of this magnitude must be made in partnership with your loved ones; your spouse or partner will have career needs and if you have children their needs are important too (relatives, friends, and schools should all be considered). Balancing all of these considerations will be difficult. You should strive to find the academic work place that will provide the best intellectual environment – a place where your colleagues will share excitement for your research, and who will offer insights and advice when you will need it. This should be the major goal. One of the best predictors of a successful career is the quality of the university where your work is done.

Why

Why do you want to become a clinician scientist? What is your motivation? If your answer is financial gain, you have chosen the wrong path. Surveys of scientists on what motivates them show that they rank a stimulating job, intellectual challenge, and professional friendship above an expensive home or car. Though they should be comfortable, clinician scientists rarely become rich. Before you entertain thoughts on what you want in your new position, think carefully on what it is that gives you the most joy in your life and set your goals for the new academic position accordingly.

How

Departments vary in their approach to the recruitment process, but some common elements exist. The search committee should respond to your letter. If they ask for details on your background and for referees, they are

showing interest. You have passed the initial hurdle. If you make it to their short list, they'll ask you to visit at their expense. The first visit is usually exploratory. From their perspective, you have qualities that they want, on paper at least, and from your perspective, they may have an environment to excite you. On this visit they will try to "wow" you with what they have to offer. Expect them to show you the research environment in its best light and to introduce you to people who may become your colleagues. At the same time you should try to "wow" them. Plan to present the most exciting aspects of your research. Come prepared to give a presentation to show your clinical knowledge as well.

A few pointers on how to behave:

Dos and Don'ts for the First Visit

Do:

- Arrive well rested (no jet-lag).
- Show interest in the city.
- Show enthusiasm for what you hear.
- Know CVs of the people you will meet.
- Show appreciation.
- Send a personal follow up letter.

Do Not:

- Refuse anything because of "tiredness."
- Compare the city to other places.
- Talk about other offers you have.
- Ask "why are we meeting?"
- Complain about anything.
- Wait for them to call.

A second invitation clearly indicates they are serious. On this visit you should explore the technicalities of your move in detail. Prior to traveling, let the institution know what your spouse or partner will be looking for in the city and ask if you can both come on the second visit (once again, at the institution's expense). Send them a list of people you want to meet or revisit. Explore in greater detail what is needed for you to work there.

You should show them you are serious as well. Now is the time to do your detailed homework: read about the history of the city, the university, and the people with whom you would work. Read their published papers and visit their websites (personal, laboratory), as well as the websites of the department, hospital, and university. Assess stated priorities and how well they fit with your own. Before you return, talk to everyone you know who

has connections to the institution, as well as anyone you trust who has worked with the key players or at least heard them speak. Ask pointedly about both weaknesses and strengths. Assess the clinical reputations of your potential future colleagues – will you be comfortable leaving your patients in their care when you are conducting your research? Ask about the number and quality of the clinical trainees that they routinely attract – how will these factors impact your ability to succeed? Try also to find people who have left the place in the recent past – their comments, and reasons for leaving, can be quite informative. If your first visit has permitted you to identify anyone there who is unhappy, try to find out why.

You and/or your partner may ask for help looking at houses and finding out about living expenses. Plan your visit so you can formulate a list of the things you will absolutely need, would like to have, or will need access to for your work. At the end of this visit, it should be clear to you and to the institution what obstacles to your recruitment may exist. Only when you are convinced that you would like to move and have expectations that your needs can be met should you begin detailed negotiations with the department head.

Negotiations

Explain what you expect.

In some universities the selection process is done by a group at arm's length from the actual head of the department. Thus your negotiations for salary etc. may be done with a person who is not completely aware of your needs and expectations. To be absolutely fair to all those involved, it is a good idea to make a detailed list of what you understand will be available when you arrive and what you may need in addition. Specify, at a minimum, your detailed expectations for:

- start-up funds for your research enterprise, including the amount and duration of institutional funding for technician salary and operating funds for supplies, animals, computers, etc.;
- office space, secretarial support, provision of office supplies;
- laboratory space and equipment, whether shared or personal to you, and whether already in place or to be acquired;
- exactly when each component of your list will be available to you; and
- any understood conditions or limitations on any of the above.

Make the list exhaustive and complete – this will be your best, and possibly only, opportunity to secure what you will require for success. The list should be copied to the chair of the search committee to check for accuracy and to allow him, if necessary, to explain the background for the request to the department head. Once the department head has acknowledged that the list is reasonable and “doable,” you can begin detailed negotiation. At the same time as you negotiate other issues, the head can keep you informed on how each item on your list will be addressed.

Balance research and clinical activity.

As a clinician-scientist, you will need to spend a portion of your time engaged in clinical activity. The dilemma is how much time is appropriate. Too little, and clinical expertise is lost; too much, and research output is jeopardized. The time available for research will undoubtedly impact on your potential for a successful research career. So it is critical to determine this before accepting a position. In general, well trained clinician scientists with a good potential will need to spend 60–80% of their time on research to be competitive in national or international grant competitions. Department heads who can offer such protection make a wise investment in the academic competitiveness of their department, but not all will have the flexibility to do so.

Salary

In clinical disciplines, some academic departments have developed a pooled income arrangement, sometimes called a “group” or “alternate payment” plan, to provide salary support for scientists. Such plans offer important advantages. In addition to providing a secure income, they disassociate income from clinical load. Like everything else, the acceptability of the program depends upon the details. How much security is provided? Is there sufficient staff to handle the clinical load? How are weekend and overnight call schedules arranged? These are all issues that will need to be clarified in writing before accepting a job offer.

The department may ask you to apply to an external salary award competition as a condition of providing you with protected time for the

first two or three years. If you win such an award, your department will benefit from a savings on your salary. One danger, however, is that the department may come to depend on the renewal of your award rather than plan for the future, leaving it unable to pay you when your award draws to a close. It is thus essential for you to clarify such issues in writing before agreeing to accept any extramural salary award. A similar issue can arise from a feature of operating grants in some countries (such as the USA) where grants may contribute to the salary of the principal investigator (PI) in proportion to his or her time commitment to the project. If the PI is unable to renew such an operating grant, he or she may find their salary, or even their employment, threatened.

Other Items

For information on start-up funds, hiring personnel, regulatory requirements, and other employment issues, see Chapters 3 and 12.

Key Points

- Be patient; look for an appointment only when you are truly ready.
- Understand when and where to look for an appointment.
- Be open and honest with the people you meet.
- Be clear and consistent on what you will need.
- Determine the amount of protected time you will have to do research and ensure that the resources are present to accomplish this.

Reference

Cech TR. Advice on obtaining a faculty position and achieving tenure, leading a research team, mentoring students, balancing research and teaching, and more:
<http://www.hhmi.org/resources/labmanagement/moves.html>

Your Academic Home:

B: Mentoring and navigating your career path

Robert Bortolussi, MD, FRCPC

Department of Pediatrics, Dalhousie University
Halifax, Nova Scotia, Canada

Once you have found an academic home, one of your first tasks should be to find a mentor(s) to help you navigate your early career path. A mentoring program is one of the best ways to help new faculty members reach their full potential. Not only does mentoring improve new faculty members' success, it is also seen as a competitive edge the institution has over other recruiting centres.

Success in a career as a clinician scientist can depend on three factors:

- early experience in various dimensions of the scientific process,
- training in a top academic centre, and
- involvement with a good mentor,

Of the three, mentorship is probably most important for clinician scientists who relocate to a new university for their first academic appointment. Here they may find themselves isolated in an unfamiliar city and academic culture. The clinician scientist may also encounter challenges starting in a new laboratory with limited financial support and without the assistance of technicians familiar with the methodologies important to that endeavour. The ability to problem-solve and to generate new ideas is not easy without help from senior colleagues to brainstorm the issues. All of these challenges can lead to academic frustration and possible failure. And all these issues can be overcome with the help of a good mentor.

The goal of this chapter is to present the rationale for a mentorship program and provide a model to achieve such programs.

Preliminaries

The word *mentor* is derived from Greek mythology. Odysseus asked Mentor to take charge of supervising his son, Telemachus, while he was fighting in the Trojan War. The implication from this myth is a single directional relationship between Mentor and Telemachus (from the top down).

Today, the role of a mentor has evolved. In this chapter, the term mentorship is used to describe a personal, one-on-one, relationship

between an experienced person (the mentor) and a scientist-in-the-making (the mentee). Mentors are exposed to the energy, enthusiasm, and ideas of the mentee, while the mentee receives the guidance and encouragement of the mentor.

Please note that the role of a mentor differs from that of a supervisor or an advisor, both of whom have a one-way relationship with trainees. The mentor/mentee relationship is bidirectional, collegial, and sustained with the goal of imparting sound judgment to the mentee and supporting his or her development.

Steps to Attaining Academic Success

To gain success in a new environment the clinician scientist must navigate through a great deal of unfamiliar territory.

Learning the Processes

The new clinician scientist must learn what his or her faculty evaluation committee uses as criteria for promotion and tenure. Simply doing a good clinical job will not help someone develop the national or international profile needed for academic promotion. In fact, the firm commitment of the division director regarding time and resources is essential to achieve academic success.

Since, as a new investigator, your job description is the main criterion on which academic performance will be judged, you must learn to say no if the activity does not conform to your job description. This response should be acceptable to colleagues and senior department members – whose support is essential. If, after a time, your job description no longer coincides with your career goal, it is important to discuss changes with your department head to develop a revised job description that better reflects the reality of the situation.

Documenting Performance

Academic success is usually based on excellence in one or two specific areas, rather than “good” performance in many. As a new clinician scientist, you will need to develop special expertise in one aspect of academic life and link this to your clinical interest. In addition to documenting research activity, you must develop a teaching and clinical dossier with objective evidence of performance. It is essential to develop

and maintain a system to track and record these data. This is not the time to be self-effacing, but rather to record accurately your successes.

Planning

One of the hardest tasks for a clinician scientist is to manage time efficiently. Setting aside time to work on academic projects and to deal with daily distractions (phone calls, correspondence, etc.) is challenging. One useful method to overcome this challenge is to develop and then carefully follow a timetable to meet one's objectives (for preparing grants, writing manuscripts, developing courses, etc.). These scheduled activities should be outlined with goals for the short term (one to two years) and longer term (five years); once a schedule has been established it is important to try to maintain it and resist the temptation to accommodate extra (especially extraneous) demands.

Coping with Setbacks

However careful the plan and scheduling, progress is not always steady or easy. Not every grant, manuscript, or course will be successful. The most successful scientists learn to develop a thick skin from such disappointments and use the feedback from these experiences to make success more likely in the future. Understanding that one's work may need to be retuned from time to time is a means to cope with such setbacks.

Developing an Academic Network

No woman or man is an island. To achieve success, scientists need to collaborate with colleagues in their field. In addition to providing helpful ideas and incentives, colleagues can become spokespeople for your achievements. But remember that relationships work in two directions; it is important to be receptive to colleagues who ask for your help reviewing their manuscript, teaching a course, or seeing a patient. Young investigators should be prepared to assist colleagues whenever it is within their area of expertise. Finally, but by no means least important: no matter how busy, we all need to make time for ourselves, our family, and our friends. Your own health and well-being are important to all the people in your life.

What can the mentor provide?

There are several possible roles a mentor can play:

- adviser, sharing knowledge of career experience and development;
- supporter, giving emotional and moral encouragement;
- tutor, providing honest and supportive feedback on your performance;
- sponsor, providing information about opportunities and the support to obtain them; and
- role model, demonstrating the kind of person (and eventually the kind of mentor) you should strive to become.

In reality, it is unlikely that one individual can excel at all possible roles. For this reason, new recruits should consider finding more than one mentor.

Mentors and mentees often have different ideas about what the mentor should provide. The question has been asked at several workshops on mentoring with groups divided into mentors and mentees. Table 1 is a list drawn from several such meetings.

Table 1: What will the mentor provide

Mentors' perceptions:

- provide impartial advice,
- act as a role model,
- be an advocate for the mentee,
- help the mentee to focus,
- provide conflict resolution,
- provide life skills advice,
- guide people through institutional politics,
- provide advice on career path, and
- provide critical review of cv, grants, papers, etc.

Mentees' perceptions:

- be available for timely feedback,
- offer realistic views of what may lie ahead on the career path,
- inform on politics,
- be a listening post,
- provide nonjudgmental guidance,
- share their own personal experiences, and
- provide constructive criticism

How to Select a Mentor

Not everyone is destined to be a good mentor. At several workshops on academic mentoring, the author of this article has asked the audience what attributes are needed in a mentor for success to occur. Table 2 is a list we've compiled.

Table 2: Characteristics of a Good Mentor

- patience
- availability
- efficiency
- vision
- supportive disposition
- nurturing attitude (supportive of others' success)
- openness to reciprocal learning
- encouragement of mentee to surpass the mentor
- good listening skills
- respect/sensitivity
- inspiration
- integrity
- willingness and ability to be a role model
- advocacy for success of mentee
- advice on career strategy and thinking

For anyone who may wish to become a mentor, there are both incentives and disincentives. The major block for a potential mentor is time. It is very important that the mentor agrees to the time expected of them for this task. Fortunately, this issue is usually balanced by the personal satisfaction and intellectual stimulation that the mentor receives. Many will see it as a means of achieving posterity through the success of the mentee. Departments can also encourage participation by recognizing and reinforcing the effort of mentors through annual evaluation and promotion incentives that demonstrate that the mentoring role has institutional value.

Model of a Mentoring Program

Every new academic recruit should be supported through a mentoring program of some kind. The intensity of mentoring support will depend on the needs of the recruit and resources of the institution. What is outlined below is an enhanced mentoring program that has proven to be highly successful in one institution for individuals expected to undertake a great deal of research (50% or more of their time).

Selection of Mentee

The department and institution determine which new faculty members will benefit most through an enhanced mentoring program and then commit resources to ensure the program's goals can be met. The process of selection should be as open and transparent as possible, and should involve the potential mentee in the decision.

Selection of Mentors

The recruit is asked to select two people that he or she thinks will be appropriate. Some institutions encourage selection of one internal mentor who is familiar with the local situation and one external mentor who is an acknowledged expert in the recruit's field.

The research director and the recruit discuss potential mentors to determine who they feel will be the best choices. Once they have come to a mutual agreement, the research director will contact the mentors to explain the expectation of the program. A letter is sent to the mentor with copies to the mentor's dean and department head. This is done to ensure that proper credit will be given to the mentor for their effort.

Mentoring Meetings

The external and internal mentors meet with the faculty recruit as soon as possible after the selection process. Since one of the mentors is often from an outside institution, arrangements for travel will need to be made. During the visit, the external mentor will often be asked to present grand rounds or conduct a seminar. The new faculty member should also be asked to make a research presentation to the mentors and other members of the department.

Several private meetings with the mentors and the new faculty member should be scheduled during the visit. Through prior correspondence, the mentors should be familiar with the mentee's job description, duties, and CV. They should also have an opportunity to meet with the new faculty member's department head and collaborators. At meetings, it works well for the new recruit to present his or her last three to six months' clinical, teaching, and research activities and accomplishments. This will lead to a more meaningful discussion of appropriate short- and long-term goals. A discussion of issues or problems can ensue in this or subsequent meetings.

At the end of the visit the mentee will be asked to summarize these discussions. After review by the mentors, the written summary can be submitted to the sponsors of the mentoring program, usually the department head and the director of research.

The local mentor and mentee are encouraged to meet regularly (about monthly) on an informal basis over lunch or dinner to discuss any issues the mentee may have. Both mentors are expected to take an active role in reviewing grant applications and helping the mentee prepare for academic advancement. The external mentor is expected to meet in person annually.

Assessment

An annual review is done by the director of research on the progress of the mentee. At this time he reviews the level of satisfaction of all involved in the process. The contribution of the mentors is highlighted in his annual report. At appropriate opportunities the mentors' contribution is acknowledged to the department head and dean. One of the goals in formalizing the process is to create a means for such contributions to be credited to the mentor for promotion and tenure assessment.

Pearls of Wisdom

- Good judgment comes from experience, and a lot of that comes from bad judgment. (Walt Whitman)
- If you find yourself in a hole, the first thing to do is stop diggin'. (anonymous)

Key Points

- Know what your job is, and do it.
- Know the system.
- Focus your career.
- Document your achievements.
- Plan ahead.
- Develop a thick skin.
- Plan your daily activities.
- Say no (politely) to administrative tasks, but yes to personal ones.
- Make friends.
- Be nice to yourself.

References

Handelsman, Jo, et al. Howard Hughes Medical Institute. "Entering Mentoring: A Seminar to Train a New Generation of Scientists." <http://www.hhmi.org/resources/scientists.html> (Free access)

Success Strategies for Women in Science. Elsevier Academic Press, Edited by Peggy A Pritchard, 2006.

Academic Scientists at Work. Plenum Publishers Kluwer Academic, by Jeremy M Boss and Susan H Eckert, 2003.

"Nature's guide for mentors," A. Lee, C. Dennis and P. Campbell *Nature* 447:791–797. 2007.

Acknowledgement

Appreciation to Peter Rosenbaum MD, FRCPC McMaster University, Research Chair in Childhood Disability, Hamilton, Canada for his input and review of this module.

Person to Person Management: Tips on hiring and collaborating

Neil Sweezey, MD, FRCPC

Department of Pediatrics
University of Toronto
Toronto, Ontario, Canada

Hiring the people who will do the hands-on work of your research enterprise is one of the most important things you will do in your career. With an academic career come responsibilities that will keep you away from your lab. Much of the hands on work in the lab will eventually be entrusted to your technicians, post-doctoral fellows, and students. The quality of their work will ultimately determine the success or failure of your career. It follows, therefore, that you should invest a great deal of time and effort in the hiring process.

Even if you hire the best person possible to do the work, you will need to monitor performance. Evaluation can be continuous and informal, but should periodically be formalized. An annual written evaluation should be performed, even when everything is going well. Not only will this protect you if things do not work out well, but it is also useful for acknowledging your team's accomplishments, enhancing their development, establishing working standards, and setting immediate and long-term goals.

Hiring

There are a variety of ways to deal with the hiring process, so do your homework. If this is your first time, ask your mentor for advice and tips on what to look for and what to avoid. Make a ranked list of the talents, knowledge, and personal qualities that are important to you. Consider the minimum attributes that are truly essential, and then do not compromise on them. Review others' ads, and note the approaches you find attractive. Post notices in common areas frequented by your target audience and advertise in the type of publications they are likely to read (lay press and/or academic). State the major points that you are looking for in the most concise manner possible and emphasize the desirable aspects of your enterprise. Before interviewing anyone, collect resumés, transcripts, and letters of reference, and ruthlessly weed out all but the top two or three. Ask your mentor to critically review those who survive this process.

Now you are ready to interview. The interview process should be polite, formal, and business-like – not casual. You need to inform the applicant about your goals, expectations, and activities every bit as much as you need to find out about him or her. If the position is grant-funded, be sure the applicant understands the implications for ongoing employment.

In the interview, you will naturally probe the applicant's abilities and attitudes, but be conscious of legal and ethical restrictions on what may or may not properly be asked. Stay away from topics related to applicants' personal life. These are usually irrelevant to the job and could get you into trouble. I suggest that you do ask some questions that put applicants on the spot, just to see how they cope with the unexpected. Questions of this type ask for examples of something they are most or least proud of in their career. What was their greatest accomplishment and greatest failure to date? How have they responded to each of these situations? If you find something about an applicant that bothers you, whether you can specifically identify it or not, listen to your instincts. In general, initial feelings of unease are often valid, though initial positive feelings may be less reliable.

Before hiring anyone, verify the main points picked up in the interview. Do not make any commitment in the absence of such confirmation. Ask for permission to speak to individuals who are knowledgeable about the applicant, and talk to them on the phone directly. The most recent former supervisor will be an important contact. An applicant can rarely have legitimate reasons for hesitating to identify or give you permission to talk to the previous or current supervisor, and you will have to judge the validity of any reasons offered on a case-by-case basis. You need to speak in person to the authors of any letters of recommendation, verifying the authenticity of what you read. You should also ask the referee to speak about any concerns he or she may have been uneasy about putting down on paper. Ask if the referee would hire the applicant, given the opportunity. If it is not obvious, ask why it has not happened. Ask challenging questions, such as the greatest identified strengths and weaknesses of the applicant. If there are particular attributes that are essential to you, make sure the applicant has them in good measure. Key attributes include honesty, integrity, intelligence, resourcefulness, stability, loyalty, and capacity for verbal and written communication.

When actually hiring the applicant, make use of the talents of your human resources department. They can help to construct the job description, assign the appropriate levels of pay and benefits (if any) that go with the particular position, and advise about the detailed wording of contracts (for technicians) or memos of understanding and mutual undertakings (for PDFs and students). Be sure the person in HR is familiar with grant restrictions that apply to possible benefits and job security. Thoroughly familiarize yourself with your institutional and academic department's regulations. Ask about probation periods, during which either you or the newly hired person can walk away without notice or penalty. If the position is funded by research grants, have the new person acknowledge in writing the duration of the current grant and that continued employment is contingent upon ongoing grant support.

Identify at the very beginning the important potential causes for dismissal, and the process by which it could happen, as well as any established conflict resolution, complaints, and formal grievance procedures. Document in writing that you have informed the new person about critical regulatory requirements with which they must comply, safety regulations for example. Inform new people of any orientation activities that may be organized for their benefit. Many of these introductory activities can be delegated, but the ultimate responsibility for ensuring that they actually happen rests with you.

Performance Evaluation and Firing

Where deficiencies are identified, corrective plans should be developed, including evaluation criteria and the schedule by which they are to be applied. Especially if there are any serious problems, the evaluation document needs to be signed and dated by both you (the principal investigator) and by the trainee/employee, with a copy to be retained by each of you.

It is convenient to use standardized forms to structure the evaluation process. A common approach is to ask the trainee or technician to complete a draft of the document as a self-assessment exercise, to be submitted to you a few days in advance of a confidential personal interview. At this time you present your evaluation, contrasting and comparing it on a point-by-point basis with the self-assessment draft. After a full discussion, you prepare a final version of your comments.

Ask your mentor or colleagues if they have an evaluation form for research assistants. If none is available the HR department will usually have a standard one.

Should serious problems arise, the evaluation criteria will be accompanied by an outline in writing of specific, concrete consequences that will ensue if predefined changes have not taken place by a predefined deadline. If a member of your team has to be fired, you will need to be able to demonstrate how the person fell short of the minimum acceptable standards and also to produce documentation that the person:

- has been warned of identified deficiencies and their consequences,
- has been notified of the associated timelines, and
- has been given the opportunity and assistance to correct the problem.

Thus, meticulous record-keeping becomes particularly important if things are not going well. Again, HR can be invaluable in dealing with these issues. You may well wish to have an HR person join you when you break the news, especially if you think there may be a need to have the person escorted out immediately for security reasons.

Collaboration

The benefits to collaboration and the dangers associated with isolation are too great for a scientist not to collaborate. But important caveats exist; collaboration is not always appropriate. Generally it is productive to collaborate liberally and often, but only when it is safe to do so. Your mentors should be called on for advice on these issues.

When to Collaborate

If there is a project in which both you and an academic colleague have an interest with clearly defined roles, and each of you contribute something that could not be done as well or as quickly without the other, then the timing is excellent to collaborate. Fundamentally, a collaboration, like any other partnership, will only be sustainable if the work is in some way important to all partners, if all partners benefit, and if each benefits roughly in proportion to the effort and resources invested in the enterprise. Otherwise, the collaboration should either be reconfigured to the benefit of all, or else terminated.

There are basically two kinds of collaboration. First, there are the small, concrete arrangements to complete the components of a circumscribed, specific project, after which the relationship may end. In this case, neither party to the deal will be excessively vulnerable should the project not flourish. The problem with this kind of collaboration is that the project is often not of equal priority to all partners so that, with the best will in the world, the project may not move along at a pace that would satisfy the person to whom it is the most important. However, if the initial working together actually does work, new opportunities can grow, to the benefit of all.

Second, there are the longstanding major collaborations whereby the career plans of two or more people become interwoven. This, of course, requires an entirely different intensity and level of interaction. It can work out to the enormous advantage of both parties, but there are serious concerns that have to be considered.

Choosing Collaborators

A major collaboration can lead to enhanced productivity and efficiency, in which synergy between researchers produces more than the sum of the individual parts. Unless there is a rough balance in these areas there will be a real problem for the more junior partner to establish independence and the respect of colleagues. The arrangement will probably work out the best if the partners have complementary experience, knowledge, and areas of expertise. Collaborators are usually in the same city, if not within the same institution. In this day and age of the Internet and e-mail, however, close collaborations can occur between cities.

Personalities and styles of work can complement or conflict, and need to be considered in the context of the personalities of the individuals involved. An overly cautious investigator may benefit from collaborating with someone who is a little more willing to take risks. Collaborators must also agree on prioritizing projects and authorship for all grant applications and manuscripts. As much as possible these should be agreed upon in

advance. In general, if the personalities are compatible, the individuals are tolerant and adaptable, and the abilities are complementary, the collaboration is feasible. One of the most important qualities of a good collaborator, just as in a good manuscript or grant application reviewer, is the capacity to be truthfully and thoughtfully critical, even if it hurts. This quality should be balanced between the collaborators in order for a truly helpful give and take. The good collaborator thus provides what we so often need and cannot give ourselves: perspective.

If a collaboration does not work out, it can be a painful experience, but should be terminated in a civil manner. If it does work out, it is one of the most enjoyable benefits of research.

Key Points

- Invest the time to hire the best person for the job you have to offer.
- Speak frankly to referees and “Do your homework.”
- Get advice from your mentor and HR on the hiring process.
- Provide regular feedback and a formal evaluation of all employees.
- Seek out collaborators who you can offer skills you need.
- Nurture positive collaborations; give as much as you receive.
- If collaboration doesn't work, end it in a civil manner.

Other Sources of Information

Bonetta L, ed. *Making the Right Moves* (particularly chapters 4 and 12). Burroughs Wellcome Fund/Howard Hughes Medical Institute. 2004.

Barker K. *At the Helm – A laboratory navigator* (particularly chapter 3). Cold Spring Harbor Laboratory Press. Cold Spring Harbor, NY: 2002.

<http://www.hhmi.org/resources/labmanagement/>

Managing Time: A friend, not an enemy

Neil Sweezey, MD, FRCPC

Department of Pediatrics
University of Toronto
Toronto, Ontario, Canada

You may be starting your fellowship, post doctoral training, or your first academic appointment. Time management may seem easy – after all, your daily appointment book is blank. You are actually looking forward to appointments; collaboration will be your path to success. You want to succeed in both the clinical and scientific arenas and as a teacher and mentor. All of these goals can be achieved. But at what price?

This chapter provides some tips to help you achieve your goals without sacrificing your personal life. It can be done with planning, focus, and efficient use of time. Focus is the most important element. There is nothing like keeping your sights on the main target to avoid time-consuming and potentially career-disrupting distractions that tempt us all. Your short-, medium-, and long-term goals need to be feasible and address the big pictures in your life.

Short-, Medium-, and Long-term Planning

Long-term Planning (5–10 years)

Formally plan your long-term goals, in writing. The mere act of formulating your plans will help you to critically evaluate which aspects of your activities motivate you the most. Ask yourself where you want to be in five years. Then, reason backwards – in order to be there, what are the identifiable hurdles on the way and when will you need to have surmounted them? Early on in your career, ask those who have been successful within your institution for guidance in understanding how the system works. The medium- and short-term goals will logically flow from the long-term ones.

It is difficult to see much farther ahead than a few years, no matter how hard you plan. There are too many intangibles; things change too quickly. Periodical revision of your long-term goals is required in response to these pressures in order to keep yourself on a course that, in the long run, you can be happy with.

Medium-term Planning (6 to 12 months)

Goals in the medium-term include things such as writing papers or research operating grants, or setting up a clinic for a defined group of patients. These goals are the nuts and bolts of a clinician scientist's successes and failures. Each is made up of a series of short-term goals (such as writing the methods section of a paper). The trouble is that there will be other, lower priority (but still necessary) activities continuously competing for your time. The devil, as they say, is in the details, especially in the details of how you prioritize and deal with the multitude of short-term tasks.

Short-term Planning (next few weeks)

Beware of the common pitfall of saying yes to too much. Your natural reaction is to want to help others. This inclination, coupled with ambition, and the fear of antagonizing somebody important, will often convince you to agree, even if you really shouldn't. Once started, your perfectionist tendency will make you perform as well as possible, to establish a reputation for excellence. In reality, only some of the things you will do are actually crucial to your main professional enterprise. For these, it makes eminent sense to strive to do the best job possible. For most other things, trying to do an outstanding job won't help and may actually hurt, by taking you away from the main focus.

Commitments

Some clinical and administrative assignments must be expected – they are needed for the running of all academic institutions. There is no way to completely avoid such tasks try to be selective. Learn to say no (politely) to tasks that don't interest you or relate to your main goals. Say yes to those that are of interest to you, will complement your work, or will be advantageous professionally. Volunteering (quickly) for the tasks that are most to your liking will show your collegiality and put you in a better position to refuse other requests of less value.

Clinical

Your clinical goals and activities should ideally be closely related to those of your research enterprise. For clinical investigators, interests related to patients, clients, and research subjects may even coincide; issues discussed in your research and clinical realms may be relevant to care-givers and researchers alike. There is the added difficulty that the literature of your scientific and clinical interests may be written in two

different languages. This problem provides an opportunity. Because of your research training, you may be uniquely positioned to bridge communication gaps which otherwise can impede progress. So, be receptive to busy clinics that treat complex conditions in your research field. On the other hand, minimize as far as possible, busy clinics that do not relate to your interest or expertise.

Committees

For the first few years in your career your focus must be in developing your academic goals. Committee involvement can be a bottomless pit into which you pour your time. For the gregarious personality (common in clinician scientists), there is the added danger that work on committees can feed the basic need for social interaction, especially if overwork has led you to neglect that aspect of your personal health. Committee work, however, can be inefficient, and there are usually healthier and more entertaining ways to pass your time.

Selecting Committees to Serve On

Avoid:

- Hospital committees that have nothing to do with research
- Committees requiring reviews of multiple lengthy proposals, such as research ethics boards or committees overseeing laboratory animals

Consider:

- University committees related to your investigative interests
- Education or intramural grant review committees

Seek out:

- Formal internal grant review panels. (Participation in these exercises is highly useful. The skills learned in these exercises are directly applicable to your research enterprise, and often cannot be picked up elsewhere.)
- National grant review panels, especially ones to which you may eventually apply. (First become an external reviewer and later, perhaps a member.)
- The editorial boards of recognized journals in your field (first for reviews of manuscripts and later as an associate editor).

Although involvement on committees can be a major time commitment, it can provide an opportunity to learn and gain recognition by your peers for your expertise. So learn to be highly selective and become familiar with polite ways of saying no. Find out all you can about the level of commitment and ask your mentor before you agree.

Protected Time and Interactions with Colleagues

A highly prized commodity, protected time is something for which you must always fight. Honing your skill at these battles will be crucial to your long-term success. Without adequate and sustained protected time, the compelling clinical, teaching, and administrative interruptions will prevent you from successfully conducting research. You need to jealously guard your protected time as if your professional life depends upon it – it does. The trick is to do so in an enlightened way that perpetually keeps the big picture in view. Having trusted colleagues with whom you share a group clinical practice is essential to securing protected time. It is impractical for a caring clinician scientist to try to work on his research while worrying about the adequacy of the care his or her patients and clients are receiving. Equally, it is impractical, at least in most clinical fields, to be continuously on call. You need help in providing for your patients' and clients' urgent care 24 hours a day, 7 days a week.

An extension of this logic is that your clinician-specialist colleague requires your support, appreciation, and encouragement – never your contempt. In an academic health sciences centre, scholarly clinicians or clinician-teachers are worth their weight in gold. They may lead no research themselves and serve as a collaborator on only a study or two, but they make essential, enabling contributions to the research productivity of the entire group. In a modern academic health sciences centre, clinician-teachers lead the concept of protected time.

In a healthy professional association, the relationship between clinician scientists and their clinician-specialist(s) is synergistic and mutually supportive. The clinician scientist provides the opportunity for his clinician-specialist and clinician-teacher colleagues to collaborate in research endeavours they could not dream of running on their own. We also help them stay abreast of aspects of the research literature which they would not necessarily have the time or expertise to critically digest. In return,

our clinical skills and appreciation of the clinical literature are kept sharp and current through the example and teaching received from colleagues who are leaders in these areas.

A variety of sometimes-conflicting opinions circulate regarding how to deal with these issues. In my opinion, when considering your future in a given workplace, it is important to determine if the institutional and group leadership truly understand this approach. If they do not, or if they are unable to apply such an approach in practice, I suggest you seriously consider working somewhere else.

Day-to-day Practicalities

Delegate tasks

The delegation of your work can both help and hinder your career. It is an essential method of maximizing your efficiency. It is essential that you know what your delegates are capable of, and that you remain on top of what is being done in your name. Trainees and assistants can fail to recognize ambiguity, can make naïve assumptions, or can overlook important details. If you fail to pick up on them, it can obviously be dangerous. If there is a delay in your appreciation of the situation, it can take more time to straighten things out than it would have taken to do all the work yourself. Nevertheless, the room to try things out and to make mistakes seems to be a requirement for certain types of learning to occur. It will be essential, at times (especially when trying something new), to accept some level of inefficiency, but in the long run the whole process is rewarding. You just need to maintain a balance between your trainees' educational requirements and your need for efficiency and productivity.

Being Unavailable

Formal allotments of even substantial amounts of “protected time,” even up to 80% of total professional activity, mean little if you don't aggressively manage demands placed upon your time by powerful competing interests. Careful scheduling is important. It is not necessary for you to be available to everybody at all times. Indeed, it is very much necessary that there be regular, announced times when you are, in fact as well as in name, not available. Put these times in your schedule, and expect yourself as well as others to honour these appointments with reading, writing, and thinking.

Electronic Tools

Although electronic scheduling and messaging tools are available, it is important to control them and not let them control you. If you have administrative support, use it to help sort out those messages that really need to be responded to urgently from those that can be “batched.” When you are occupied, a delegate can answer at least some of your pages on your behalf, assess the urgency of the call, and arrange an appropriate time for you to respond. A good administrator runs interference in this way, and will track you down in urgent situations.

Give your administrative assistant access to your electronic schedule to independently book appointments for you according to explicit criteria upon which you have previously agreed. If you carry Blackberry® or Palm® Pilot you can book things on the fly while avoiding conflicts or forgotten meetings.

Teach people to use your pager or mobile phone for urgent matters, and your office voicemail for things that can wait.

Voicemail, well managed, is a powerful tool. Your recorded greeting needs to explicitly direct callers with urgent clinical issues to an appropriate anytime source. Your caller needs to expect that you will reply, but that your response will not necessarily be instantaneous. If you are seriously concentrating on something important, voicemail allows you to ignore the ringing of your phone with the knowledge that nothing of consequence will be missed.

Efficient Use of Time

Make use of “downtime” (unanticipated free time) resulting from cancellations etc. Respond to some of your waiting messages, sign correspondence, read an article, or delegate appropriate tasks.

Keep an eye out for opportunities for one project to serve multiple functions. If you have reviewed a topic in writing, watch for opportunities to present a seminar on the same subject. If you have taken the time to prepare a presentation for a research conference, it may not take much additional effort to publish a review article or to give a lecture to a student group on the same topic. The classic opportunity for any academic clinician is to profit from opportunities to do clinical care and education at the same time, all the while scouting new possibilities for research.

Key Points

- Develop short-, medium-, and long-term goals – and the strategies to achieve them.
- Learn how to meet commitments to your department without sacrificing your academic goals.
- Select committees carefully, learn how to say no and when to say yes.
- Develop efficient working strategies by learning:
 - how and when to delegate,
 - how to use downtime, and
 - how and when to use electronic tools.
- Guard your protected time.

Links and References

Bonetta L, ed. Making the Right Moves. Burroughs Welcome Fund/Howard Hughes Medical Institute, 2004

http://www.hhmi.org/resources/labmanagement/downloads/moves2_ch6.pdf
(When accessing this and other sites listed here set computer settings to allow popups)

Barker K. At the Helm – A Laboratory Navigator. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press, 2002.

Reis R. Tomorrow's Professor – Preparing for Academic Careers in Science and Engineering. Piscataway, NJ: IEEE Press, 1997.

Presentations:

How to successfully communicate your research story

Norman D. Rosenblum, MD, FRCPC

Department of Paediatrics
Canada Research Chair in Developmental Nephrology
University of Toronto
Toronto, Ontario, Canada

You may ask why it is important to spend time communicating research results to both scientists and non-scientists in seminar format. The answer is simple: to improve the quality of health care, you must be able to convince people from your own and other disciplines of the importance of your research discoveries. In order to transform your research conclusions into product development, you must become skilled at persuading stakeholders that your work is important, unique, and therefore worth supporting.

The objectives of this chapter are to provide ideas on how to prepare for your seminar and design your slides presentation.

Preliminaries

Who is your audience?

A strong presentation must be geared to the level of knowledge and understanding of the audience. Your delivery will be radically different for scientists in your discipline, scientists in other disciplines, and non-scientists. Immersed in our own fields of interest, we may not realize that the language we use with our colleagues can be nonsense to others. On the other hand, you must strive to be clear for your audience members without insulting their intelligence.

What is your story?

Refine the story you are going to tell so the key elements are clear. I've heard this point made in different ways. For example: the elevator test. If you were on an elevator with the president or prime minister, how could you deliver your key message between the 1st and 7th floors (or before security takes you away)? Another example: the cocktail test. Can you deliver a compelling one-liner on your project at a cocktail party? In either test the desired outcome should be curiosity and enthusiasm. If, on the other hand, you hear snoring, it's time to rethink your message.

Creating an Effective Story

What are the learning objectives for the audience?

Objectives should be relevant to the audience and achievable in the time available for the seminar. To begin with, limit yourself to two or three of the most important objectives. State each objective as a short sentence or phrase and ask yourself:

- What is the key message within the objective?
- Does this message relate directly to the storyline?

Prepare material for each objective.

Assemble material that may be useful to support each objective. Support material may include conceptual background, details on the experimental approach, data in the form of tables, pictures, schematics, or interim summaries. Remember that an image can often make your point more compellingly than text alone.

Slides

Your slides are there to serve the objectives of your presentation, not to demonstrate PowerPoint gimmicks, so keep it simple.

Animation

While animation can be effective, it can also be misused. Too much of a good thing can distract and irritate the audience, so be sparing. For example: let text simply appear, rather than having it fly in from the side or jiggle wildly as it enters. Your primary goal is to impart knowledge, not to entertain.

Text

Use six or fewer lines per slide, in a font greater than 16 point. Use data that can be quickly explained.

Well chosen bullet points allow you to speak directly to the audience, which is more engaging than reading at them. Use clear and concise words or phrases; don't exhaust your audience with an essay.

Graphics

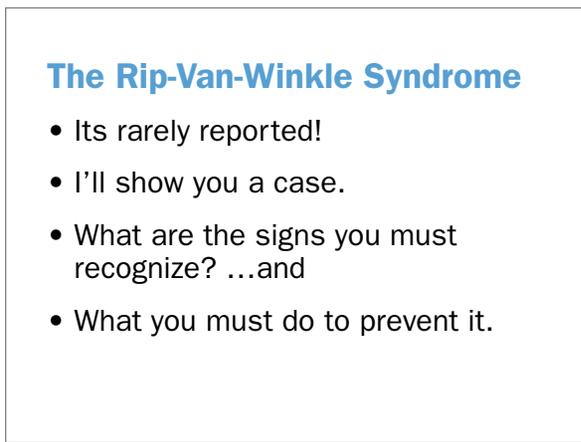
You do not need a bulleted list on each slide. In fact, it is often easier and more effective to talk around a graph or photo than it is to labour through a dry list of statistics. Use schematics to illustrate unfamiliar experimental

protocols. The average attention span of an intelligent listener is less than 10 minutes – now is the time to engage.

Colours

Choose primary colors that are pleasant and plain to see. Black text works well on most backgrounds, and white or yellow on a blue background is fine. Red on green does not work; 10% of the males in the audience are probably red/green color blind, and others may be near-sighted, so pick colors easily visible to everyone.

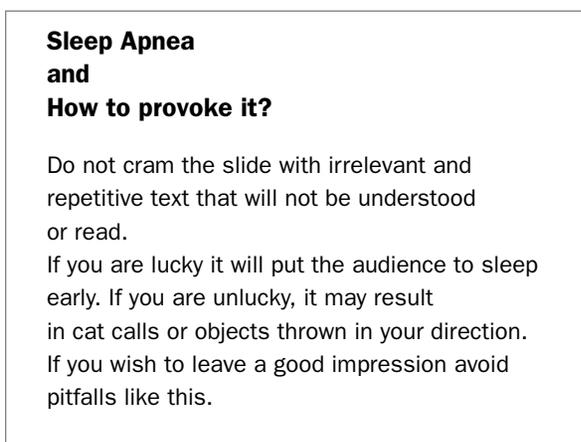
This is an example of a useful slide:



The Rip-Van-Winkle Syndrome

- Its rarely reported!
- I'll show you a case.
- What are the signs you must recognize? ...and
- What you must do to prevent it.

This is a not-so-useful slide:



**Sleep Apnea
and
How to provoke it?**

Do not cram the slide with irrelevant and repetitive text that will not be understood or read.

If you are lucky it will put the audience to sleep early. If you are unlucky, it may result in cat calls or objects thrown in your direction.

If you wish to leave a good impression avoid pitfalls like this.

Preparation and Planning

As a general rule, use one slide for each minute you will speak. Depending on the usual pace of your speech, this should give you enough time to pause and fiddle with the pointer.

The usual order of slides is as follows:

- title slide
- background
- objectives
- data slides
- interim summary
- big picture
- acknowledgements
- questions

Once you have selected your slides, practice the presentation out loud, noting how long you take. Be sure you can tell your story comfortably in the time permitted. You may need to limit the objectives or cut the number of slides by summarizing several in one. Rehearse your speech and body position relative to the slide projection and the audience. Once you are comfortable with your talk, practice in front of colleagues, soliciting and considering their feedback. Try to anticipate questions you may encounter, and allow enough time to speak to them and any comments you receive. (If you respond to the points raised from the floor and acknowledge the limits of your work, you will leave a good impression.)

If possible, rehearse your presentation in the room where it will be given. You may discover AV compatibility problems, and if so it's best to discover this in advance.

Title

Choose a title to interest a wide audience – not just us science nerds! A bit of humor or hyperbole is acceptable as long as it isn't demeaning or offensive. The title slide should also name all presenters and their affiliations.

Background

This is your chance to capture the audience's attention by presenting the big problems and big ideas your presentation will deal with.

Objectives

The objectives should follow logically from the background information that you have just presented. If you have presented the problem strongly, the audience will already be asking themselves questions that coincide with your planned objectives. Now state the objectives in clear, universally understood language, making sure that the audience appreciates why the objective is important.

Data Slides

Relate each data slide to the story you outlined:

- the question
- the approach
- the model
- the results
- the implications

Interim Summary

At this point, repeat the objectives in the same words as you used originally. If you had more than one objective, summarize the relevant facts for each objective:

- "We found A, B, C..."
- "This means..."

Be sure to state what the result means in relation to the objective. And honestly acknowledge limitations and opportunities to improve.

Big Picture

Undoubtedly, new questions may arise from the findings you have presented. Point some of these out and try to put them in perspective of the big picture you introduced at the start of your talk. Suggest what the next step may be to complete the overreaching objective of this research.

Acknowledgements

Gracious acknowledgements show:

- gratitude for those who played a key role,
- that you have a group working with you,
- your role in training, and
- that you have support for your research.

While showing the slide, be sure to elaborate on:

- people who actually did the work (and what they did),
- other collaborators, and
- sources of financial or material support.

Key Points

- Create an interesting storyline.
- Tell the story in a manner appropriate for your audience.
- Appear to be fascinated with your topic.
- Don't wander off topic.
- Be clear and succinct.
- Illustrate your story clearly and simply.
- Don't read from notes.
- Use one slide per minute you talk.
- If you open a door, be prepared to enter (don't show anything you don't want to talk about).
- The 8:1 rule (preparation vs. length of talk).

Other Sources of Information

<http://www2.noctrl.edu/academics/departments/biology/seminar/tips.php>

<http://pages.cpsc.ucalgary.ca/~blob/503/2004/presentation-notes.pdf>

Writing a Manuscript: Planning, drafting and publishing

Noni MacDonald, MD, MSc, FRCPC and Robert Bortolussi, MD, FRCPC

Department of Pediatrics
Dalhousie University
Halifax, Nova Scotia, Canada

Science is an altruistic endeavor: the more others use (cite) our freely given work, the “richer” we are. (Robert K. Merton, Science, Technology and Society)

Why it is important for a researcher to publish?

There are many responses to this question, but the central role of publication in science is to communicate new knowledge. If a study is undocumented, it cannot become generalizable knowledge. In fact, if human subjects have been involved or public money was used to do the research, it is our ethical duty to publish. Some would even say that failure to publish is failed science.

There are other motivations to publish your research: as an academician, you should appreciate that publications (mentions in the press etc.) can be viewed as the “currency” of science. Publishing can lead to all kinds of interesting opportunities.

The objectives of this chapter are to allow you to understand:

- relevant concepts central to the philosophy of science,
- the role of publication in the scientific process,
- pertinent concepts in the sociology of science,
- why the current publication model can sometimes be frustrating, and
- some practical issues related to manuscript preparation and publication.

Getting Started

Some key points to remember at the beginning and throughout the process:

- In preparing a manuscript, try to tell a single story with your publication. The focus should be clear and easily understood.
- Prepare the figures and tables first. If well done, the figures and their legends will present the story and the text will follow in an easy manner.
- Never submit a sloppy manuscript to an editor.

Steps to Preparing a Successful Publication

Authorship

An “author” is generally considered to be someone who has made substantive intellectual contributions to a published study. The selection of authors and the order of their presentation have enormous potential to create future discord. Therefore, it is always best to settle such questions upfront, taking the journals’ guidelines for authorship offered by the journals into consideration. Many journals now follow the International Committee of Medical Journal Editors criteria for persons named as having participated in submitting original research. Although it is helpful to work in a collegial manner (Watson and Crick tossed a coin to decide authorship order), friends can become enemies over these issues (Watson and Crick failed to acknowledge use of Roselyn Franklin’s lab data).

Choice of Journal

The major criteria to use in selecting a journal to submit your manuscript are the following:

- content of the manuscript you have prepared,
- journal prestige and quality,
- speed of editorial process and publication, and
- probability of acceptance.

Create a shortlist of three or four journals. Give first place to a journal that is somewhat more prestigious than you think your article merits, and move down the list to conclude with one that is slightly less prestigious. In this manner, if you receive a rejection, you will be prepared to resubmit within two weeks (unless a serious flaw has been identified).

Content

When selecting potential journals, it is helpful to consider their preferences. For instance, the Lancet and the British Medical Journal publish more international material, JAMA has some leaning towards pediatric papers, and the Canadian Medical Association Journal prefers clinical research.

Impact Factor

The impact factor is an index of journal quality; it represents, more or less, the average number of citations a journal article receives in the first one or two years. Journal impact factors cannot be compared across

disciplines. For example, general medical journals are most frequently cited and thus have a higher impact factor than specialty journals.

Table 1: Impact Factor of Some Popular Journals

General Journals:	Nursing Journals:	Pediatric Journals:
• N Engl J Med 44.0	• Birth 1.8	• Pediatrics 4.3
• Lancet 23.4	• Nurse Res 1.5	• J Am Acad Child Psy 4.1
• BMJ 9.1	• Res Nurse Health 1.1	• J Pediatrics 3.8
• CMAJ 7.4	• J Clin Nurse 1.0	• Pediatric Res 2.9

Speed

Many journals indicate the date the manuscript was first received, when it was accepted, and when it was published. Though it can take a while, journals are as interested in speeding the process as are authors. Some journals proceed in a step wise fashion to accomplish this goal, with the editor intercepting a manuscript and evaluating it without peer review. The time between acceptance and publication also varies (for example, two months at NEJM, four months at Obstetric. Gynecology, and instantaneous publication at BioMed Central).

Acceptance

Be realistic regarding your chances. The most prestigious journals are in greatest demand and will therefore produce the highest rejection rate – more than 90% rejection rate at NEJM and 70% at CMAJ).

First Draft

Preparing a paper for publication is a challenge; there may seem to be many reasons to wait, but they are often excuses. Don't worry about style and "wordsmithing" in the first draft. Just do it.

We recommend proceeding in the general order described below. There is no need to worry about the title or the abstract in this early stage. They will come later when the text is nearing completion.

Introduction

The introduction should clarify what your research was and why you did it. In two to four paragraphs with pertinent references, indicate what the problem is and what we know (and don't know) about it. The introduction usually should not include any description of results or conclusions.

Methods

Science must be reproducible. The methods section in your paper is the key to ensuring readers understand how the study was done. It is important to keep detail balanced: established methods can be mentioned briefly and supported with a reference, and new methods should be adequately described for other researchers to reproduce them.

Be sure to follow the journal's submission guidelines. Some journals have a very limited amount of space for methods, so be concise and avoid mixing results into this section.

Results

Make the order of results presentation logical. Be concise – only important observations should be elaborated in the text, while the tables, figures, and graphs show your detailed findings. Do not repeat in text what should be clear in the figures. Past tense is preferred.

Discussion

The discussion is the hardest section to write. It can usually be broken into four sections:

- brief summary of major findings,
- explanation of findings, including comparison and contrast with existing literature,
- discussion of limitations of study, and
- conclusions and future directions.

In the discussion, be careful to avoid redundancy or repetition of points raised in the introduction, methods, or results.

Congratulations – if you have completed these four sections with reasonable skill, you are approaching the mid-point of the process. To paraphrase Winston Churchill, you've reached the end of the beginning. After feedback from coauthors and colleagues, plenty of revisions will likely follow.

Revisions

In the initial review of the first draft, ask your co-authors and mentors to provide you with content editing of the manuscript. Is the message clear? Is the hypothesis clear? Is there flow? Is there repetition? Are all statements correct? Clarify and correct these issues before moving to detailed (copyedit) issues.

When you get to the detailed editing, check spelling and grammar and double-check facts and figures for clarity and accuracy. Check references to be sure they are appropriate in context and are written in the style required from the journal. Also ensure that you have followed “author instructions” for all sections.

Finishing Touches

Once the text and conclusions are complete, you may write the abstract for the paper. Depending on the journal, the abstract is usually about 250 words. Treat it as a miniature paper, with brief purpose, methods, and results sections. The conclusion of the abstract should be confined to the principle conclusions only.

Choose your title with great care, remembering that it will be read by many more people than those who read the whole paper. It should be a concise and specific “label” for its contents. Usually six to twelve words will suffice. For ideas, read titles of other papers in the journal you are submitting to.

Most journals will ask you to select key words to help categorize the subject matter. If necessary, ask your librarian to help you select appropriate words from MeSH. Finally, write the acknowledgements section following the journal’s instructions. If allowed by the journal, list key people who assisted you or provided reagents and materials. Be sure to list the grants and awards that have been used to accomplish the work you describe.

A Note on Citation Scores

Citations (i.e., documented use of published work) are taken by many as a measure of the quality and impact of one’s research. But if you understand the scientific process, you will know when you have made a contribution. In fact, some Nobel Prize winners have gained recognition for their breakthrough work with papers that had relatively modest citation scores.

Key Points

- Don’t worry about style in the first draft. Just do it.
- Be sure all authors agree on their inclusion and order.
- Write in IMRaD order, introduction, method, results, and discussion.
- Information belonging in one section should never be repeated.
- During revisions, focus on high-level content before the micro issues.
- Never submit a poorly written paper; revise, revise, revise until it is perfect.
- Select a journal appropriate for the research that is presented.
- If the journal does not accept your paper, read the comments carefully. If there are no “fatal flaws” identified, prepare to revise and resubmit to the next journal within two to four weeks of receiving the rejection.

Acknowledgements

The authors gratefully acknowledge the contribution of KS Joseph MD, PhD, to this chapter, the text of which was inspired from his presentation to the CCHCSP at its annual meeting in Vancouver BC, October, 2006.

Links

Guidebook for New Principal Investigators CIHR Institute of Genetics by Roderick McInnes, Brenda Andrews, Richard Rachubinski
<http://www.cih.ca/e/27491.html>

International Committee of Medical Journal Editors – “Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication” – Available online at: <http://www.icmje.org/>

Writing a Research Grant: Strategies for a successful outcome

William W. Hay, Jr., MD

Department of Pediatrics
Neonatal Clinical Research Center and Perinatal Research Center
University of Colorado Health Sciences Center
Aurora, Colorado, USA

There are many roads to a successful academic career for a clinician scientist. One fast track to achieving this goal is to be awarded a national peer-reviewed grant. Such an award provides undisputed validation that a clinician scientist has reached a level of recognition and achievement of national significance.

Although grant-writing skills can be honed and perfected, an important and novel idea must be at the core of any success story. The objective of this chapter is to guide new (and old) clinician scientists in processes to ensure that the value of their research will be understood and rewarded.

Preliminaries

In preparing for your first (or 2nd, 3rd, or 4th) grant proposal, you must remember that there is no substitute for one essential ingredient: a great idea. Don't even attempt to write a proposal to a national peer-reviewed funding agency unless you are convinced that you have a novel idea and hypothesis to propose. The hypothesis must be:

- clear and testable (consult with a statistician first),
- of finite scope (i.e., can be completed in less than a lifetime),
- important as well as interesting,
- unique, and
- provide knowledge to solve a problem.

How will you know whether the time is right? There are no absolute answers, but you should sit down with your mentor to discuss your plans (see the chapter on mentoring). Your mentor should know the opportunities available and can give you a realistic opinion on the likelihood that you will be successful. He or she can also help you to develop a network of other researchers who may become internal reviewers or collaborators. It is important for you to begin this process early in order for them to share some enthusiasm and contribute to your plans.

Letter of Intent

Most large granting agencies now require that applicants submit a letter of intent (LOI) before the actual application process begins. For some, this is only a formality, the equivalent of registering for your application. However, many are using this as a means to weed out the applicants who have little likelihood of success. Read the instructions for the LOI carefully. They usually will indicate their purpose.

Approach the LOI as if it were a mini grant application. Your main goal will be to convince the granting agency that you are a credible researcher and that your research will meet the objectives of the agency. Pay careful attention to the goals of the agency. Use these as a template for the LOI if possible. At this early stage your methods probably will not be well formulated, but if the agency requests it, articulate your hypothesis clearly. Also, be sure to list all of the strengths that you will have, especially research mentors and collaborators who are well established scientists (and likely to be known by the agency).

Steps to Success

Writing Style

The person evaluating your application is a human being who will have several applications to evaluate. Help the reviewer by writing clearly. Ask colleagues for copies of highly ranked grants to get a sense of their style and rhythm. To get the rhythm and tools to express clearly, read a few good articles in Nature's "News and Views" or other outstanding journals. Read the journals that your mentors publish in or highly recommend.

Keep these guidelines in mind:

- Be organized: make an outline first, write the text second.
- Write clearly and lucidly.
- Use short sentences.
- Use first and third person in the active voice (i.e., "I will analyze the samples," not, "the samples will be analyzed.")
- Use font size 12 or higher.
- Use figures to illustrate important points.
- Be concise (don't even think about exceeding page limitations).
- Start each paragraph with a great lead line.

Specific Aims

The objectives of the “specific aims” page are to:

- Generate interest: get the reviewer interested in the research question.
- Demonstrate importance: convince the reviewer of your project’s relevance.
- Display good writing: good writing reflects clear and precise thinking. In fact, it often forces clear and precise thinking.

The “specific aims” section begins with a brief (no more than one page) statement of the goal(s) of the research. Focus your aims to one or two main ideas. More than two specific aims are usually too many. For each aim, include a brief statement of the purpose, rationale (including significance, impact, and innovation), and methodological approach. Begin each aim by stating it in just one simple sentence, saying as directly as possible what will be done, and fill in the details from there. Each aim either should be, or include, a hypothesis to be tested.

Background and Significance

This section should be about half of the application for a first-time grant applicant, a little less for a veteran. The introductory paragraph should give a bird’s eye view of the field and why this area of research is important. What are the big questions? A common error is to conclude with a strong sentence that could be slightly reworked into a superb lead sentence. So don’t be afraid to make such changes in later drafts.

The background section also must summarize pertinent literature on the subject; this demonstrates that you have a command of the field, provides the rationale for what you propose to do, and puts your research in perspective by showing the importance of the results.

Always indicate and show your own preliminary data. This will demonstrate that it can be done and that you have mastered the state-of-the-art methods you are proposing. Preliminary findings also can illustrate and strengthen the hypothesis you have proposed. There is, however, a fine balance to be struck in presenting preliminary data. Too much prior proof may suggest there is no reason to fund the proposal, while not enough prior proof might lead the reviewers to feel that the work is too risky, too unlikely to succeed.

Methods

Your experimental design and methods are a critical part of the grant. In this section, repeat each specific aim (and hypothesis), then outline the research plan or general approach. Next, describe the specific experiments you will use – this is the main part of the experimental approach. Also include the essential statistical designs and analyses to show how you will interpret the data.

It is also wise for a new researcher (or veteran, for that matter) to outline potential pitfalls (and how they will be handled) and alternative courses should the primary approach fail.

One of the commonest errors for a new investigator is to propose more work than can be done within the time and budget available. Discipline yourself to be realistic. Estimate the time required for each specific aim and consult a senior researcher on your accuracy.

Table 1: Words and Phrases to Use and Avoid

Avoid These	Use These
describe	prove/disprove
evaluate	test
characterize	determine/define
look at/compare	measure
estimate	quantify
correlate	to identify the...
study	our approach will...
alter or change	increase by... (be specific)

Grant Summary Page

Begin with a few sentences that set the general (biological/health/social) stage. The level here should be highly polished, comparable to a “News and Views” in Nature. Remember that while only the assigned reviewers will likely read the body of the grant, everyone on the panel is likely to read the summary.

Next, present the general objective and the two or three specific aims of your research proposal.

- “The general objective of our research is to...”
- “To attain this objective, we have three specific aims...”

Now, using direct and active phrases, state why you are undertaking the proposed research and provide the rationale.

- “To determine x, I/we will...” or
- “To measure attitudes about genetic testing, I/we will...”

Conclude this paragraph by stating why you are using a specific strategy (e.g., “since this method has been shown to...”)

Finally, indicate the significance of the work in a short but sharp paragraph. You must state your case well. For example: “This work will enhance our basic understanding of xyz and create a foundation for determining [disease category].” If possible make a disease link to illustrate the relevance of the research without overstating the linkage to treatment or cure.

If You Don't Get Funded

If your first attempt is unsuccessful, don't be discouraged. The competition you have entered is one set to extremely high standards with many other excellent grants in competition. The committee may have decided on the side of caution, going with a less risky proposal of equal merit. Even great researchers can have a grant application rejected. Before abandoning your research plan, take some time to think. Put the review and the application aside for a week or so, then re-read it thoughtfully and with the intent to improve it. Only then will you be ready to appreciate the reviewers' comments.

Read the reviews carefully. There might be several reviewers who comment in contradictory ways. Find the comments of the scientific officer of the committee. These usually are the most important since they summarize the consensus of the committee in trying to balance different views and also reflect the discussion held by the committee. Call on your mentor to help decipher the meaning of the comments; he or she has been on review panels before and should be able to form a more objective interpretation and also help you read between the lines, if necessary.

If at the end of this process, you and your mentor feel you should reapply, consider the following for your rebuttal.

- Address exactly each and every concern raised by the reviewers.
- Keep detailed responses directed at the principal problems.
- Acknowledge points of the review that you agree with.
- If you disagree with any point, support your position with strong arguments and evidence.
- Above all, be polite.

Key Points*

- Organize an internal review panel (and listen to them).
- Start early (12 weeks before deadline).
- Write daily, at least a little.
- Finish the “junk” in a month (CV module, cost quotes, etc.).
- Follow the tips outlined here for writing style.
- Using the structure recommended above.
- Choose external reviewers carefully.
- Develop a realistic budget and time frame for your work.

Links and References

CIHR Grant Writing Advice Links: <http://www.cihr-irsc.gc.ca/e/1465.html>

Howard Hughes Medical Institute: <http://www.hhmi.org/grants/office/international/> (free access)

*McInnes R, B Andrews and R Rachubinski. Guidebook for New Principal Investigators, Advice on Applying for a Grant, Writing Papers, Setting up a Research Team and Managing Your Time. <http://www.cihr-irsc.gc.ca/e/27491.html> (Free access)

*The editor and author of this module are grateful to the Institute of Genetics for allowing us to make use of text from its “Guidebook for New Principal Investigators” (see link listed above) Their guidebook is intended for all researchers (new and experienced) who write grant applications in any area of health research, including basic biomedical research, clinical research, the social sciences and the humanities.

Policy Research:

How to communicate your research story to influence health policy

Jeffrey Wright, MSW, PGDBA

Director, Research and Outcome Measurement
Ontario Ministry of Children and Youth Services
Toronto, Ontario, Canada

If your research is to bring about change in the quality of health care, you will need to successfully share and communicate your research discoveries with the right decision-makers in government. For most clinician scientists, the process of engaging government and influencing policy is relatively unknown. The objective of this chapter is therefore to:

- help you navigate government in a way that will allow you more seamless access to the levers of policy development,
- make you aware of the various types of human service government ministries you can approach with your discoveries,
- increase your awareness of how government conducts and accesses research to support policy and planning, and
- provide you with a summary list of strategies to better have your research applied.

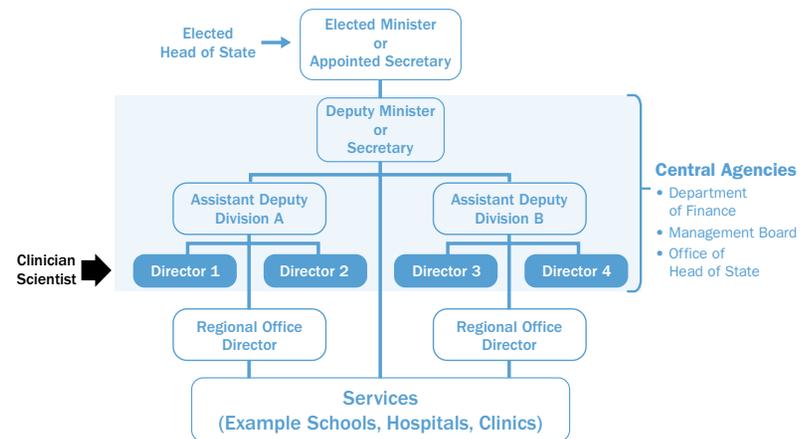
Preliminaries

Government departments or ministries are typically organized in a hierarchical manner composed of functional divisions which are subdivided into branches and then sections or units (figure 1). Most departments or ministries function primarily to deliver goods and services within their area of jurisdiction while central agencies manage the allocation of human resources and funding. In the United States the head of a department is a presidential appointee called a “Secretary”, while in other countries the head is referred to as a “Minister” and is an elected member of parliament. Both are appointed by the head of state (president or prime minister). The political department head is assisted by a career bureaucrat called the deputy minister or deputy secretary. Divisions are led by an assistant deputy minister (ADM), or secretary (ADS), while branches are led by directors, and sections and units are led by managers.

Historically, policymaking¹ decisions have been made at the “political,” minister’s level. But a shift in the way policy is developed appears

to have emerged in many jurisdictions over the past 10 or 15 years. Increasingly, political parties have focused on their electability and crafting and delivering on the associated platform², with the task of policymaking left squarely in the realm of the bureaucracy. This shift has implications for anyone interested in effectively influencing government. Ultimately, the greatest window of opportunity for influencing the platform of elected government is in the “run-up” to an election. This window is clearly opening in jurisdictions that are legislating fixed elections. In this case, the target of influence would meaningfully be the relevant minister, secretary or local member of government. More often, however, and over the course of a government’s mandate, the target of influence would naturally be the bureaucracy, given their heightened policy leadership role.

Figure 1. Typical Organizational Structure of a Service Ministry



¹A *policy* is a course of action or inaction taken by the sitting government to address a new or emerging issue impacting a significant portion of the electorate.

²A *platform* is the declared political “high-level” strategic direction of a government party, typically comprising a handful of priorities (e.g., economic growth, reduction of poverty, safer communities, etc.).

Steps to Effective Interaction

Persons and groups seeking to influence the bureaucracy are often stymied because they attempt to enter, so to speak, through the wrong door. The politics accompanying hierarchies will often impinge free exchange of information within them. It is therefore important for a clinician scientist to enter through the right door.

Persons seeking to influence system-level decision-making by entering through the service agency or regional office door are likely to be unsuccessful. These levels are too far removed from the policymaking process. Conversely, some influence-seekers attempt to enter at the DM or ADM level. Though more likely to achieve success, these routes are not without their limitations. DMs are consumed with how their ministry will interpret and manage the myriad political influences and direction received by the minister and premier or prime minister on a daily basis. ADMs are strategic leaders and, as such, naturally have a lesser command of the details of the policy development process. In both cases, their span of control is typically so expansive that they are unable to meet with or receive information from influence-seekers in a timely fashion, unless that information is critical to the political or strategic dilemma they face at the moment. A key benefit of entering through this door, however, is that a clinician scientist will likely be referred to a policy and/or research director who oversees a branch related to the research interest. It is here, at the director-headed, branch level, that the clinician scientist should focus his or her efforts to share discoveries.

Corporate branches act as conduits of planning, information, and knowledge between field-level operations and the highest echelons of government decision-making. The job of branches is to regularly engage service provider, academic, and public stakeholders in the planning process, and to synthesize and communicate their views, needs, and wishes to decision-makers. In this process of engagement, branches also communicate to the stakeholders the direction and focus of government.

How to Make the Right Contact

Very often, clinician scientists narrowly focus their efforts to engage decision-makers by making contacts within the ministry that focuses on health care provision. This is by no means a bad place to start –

as the scope and breadth of its operations typically account for 50–60% of a government's total annualized budget. This being said, several other ministries typically have some portion of their policy and operational practices associated with the topic of health. Examples include ministries whose focus is:

- health promotion (e.g., community marketing to influence smoking and obesity),
- public safety and correctional services (e.g., contagious disease management),
- community and social services (e.g., quality of life for persons with developmental disabilities), and possibly even
- education (e.g., standardized inoculation).

Furthermore, many provincial and federal governments have or are beginning to create stand-alone ministries focused on research and innovation. Such ministries provide excellent opportunities for clinician scientists to access resources, through various granting processes, to further their discovery, and, in some cases, applied research interests.

Clinician scientists, like any other users of government services, are likely to begin their efforts to contact government decision-makers by consulting a phone book. This approach is likely to be minimally helpful since the corporate level policy and research branches of government are not typically referenced here. To access these targets, the clinician scientist could “Google™” various ministry websites where he or she will be able to access a full organizational chart and general phone and e-mail address directory for relevant divisions. Alternatively, and in an effort to better refine the contact search, governments annually update a series of directories that are available to the public, which identify the various corporate ministry divisions, branches, sections, and regional operations, as well as provide the names, titles, and key contact information for all associated personnel. Examples for Ontario, Canada, would include:

- The Government Telephone Directory
- <http://www.serviceontario.ca>
- <http://www.infogo.on.ca>

How Governments Access and Conduct Research

Very often, policy and research branches within governments access research from clinician scientists with whom they have forged a relationship. In this case, “relationship” usually means the following:

- the two parties have met and/or conversed several times,
- the nature of the scientist’s research interests are understood, and
- the bureaucrat has developed an understanding of the past and current quality of the scientist’s work.

Very often, the most influential scientist researchers are those who have taken the initiative to contact the relevant government branch and associated personnel themselves, and then, have managed them like customers – checking in by phone or e-mail from time to time to:

- assess emerging research questions for government,
- identify the forthcoming release of their study results that may be relevant to policy makers,
- communicate specific results, and
- tease out opportunities for potential funding and collaboration.

Who to Engage

When making initial contacts with government policy and research branches, it is important to know who to specifically engage and how. Directors of branches are good places to start. Many successful clinician scientists send a letter of introduction to the relevant director. It indicates:

- their research interests,
- current projects and their status,
- relevance of past and current projects to policy making,
- their willingness and enthusiasm to work with government, and
- their publications.

Successful clinician scientists also communicate the above in live meetings with managers, research and policy analysts, and advisors within branches. This is critically important since the analysts and advisors manage very specific health topic files. *They need you and your information*

as much as you need them. But ensure that you engage the right ones by cross-referencing the person’s sectional responsibility (contained in the earlier mentioned government directories) against your area of expertise.

When to Engage

Timing, as they say, is everything. It is critically important that the clinician scientist be aware of the basic elements of the government business planning cycle. For many governments, the start of a funded year (known as the fiscal year) commences April 1st and finishes March 31st. Policy and research branches typically begin their planning for the upcoming fiscal year in June of the previous year. It is at this time that they begin to consolidate their thinking around the specific amounts of money and nature of resources that they will require to answer policy questions and design and implement policy. Eventually, their overall request will be submitted to the central agencies (treasury and management boards) and final notice regarding their fiscal year allotments will be forthcoming no later than one month prior to the commencement of the new fiscal year. So, when attempting to influence policy and research branches within government, it is important for clinician scientists to make contact with the relevant personnel no later than six months prior to the start of the fiscal year. Occasionally, contact at the end of the fiscal year may be useful if there are unspent funds available in the closing year’s allocation.

It is also immensely useful for the clinician scientist to contact the relevant government research branch at the beginning of the fiscal year (i.e., April 1st). This is because research branches are typically provided significant monies to grant to researchers to answer targeted questions of relevance to government. Not unlike traditional granting bodies (e.g. NIH [USA], MRC [UK], CIHR [Canada]), the government puts out calls to the research community in the form of:

- grants-in-aid (to assist researchers and community partners to craft a successful application for project funding),
- letters of intent, and
- full research proposals.

Applications are adjudicated based on criteria including: relevance (in terms of alignment to government transformation), scientific merit,

and outcome focus. By contacting relevant research branches within government in early April of each year, clinician scientists will be advised of specific amounts and types of grant funds available to them and of the processes and timelines for accessing these funds.

Once you have forged a strong relationship with policy and research branches within government, don't be surprised if you begin to receive calls from analysts and advisors throughout the year, asking for your advice or to participate in policy working groups. To be sure, these will provide real-time opportunities to offer your expertise and effect public policy.

Key Points

- To influence a political party's platform, contact political party leaders early in the year "run-up" to an election with your completed research.
- To impact government policy with your research, cultivate a friendly and strong working relationship with analysts and directors within relevant ministry policy and research branches.
- Identify appropriate contacts within policy and research branches. Use the web to do so. Do not limit your search to contacts in the ministry responsible for health.
- Once a relationship is forged with analysts and directors, keep in touch periodically (e.g. April and September). Volunteer to be available to respond to their ad hoc queries or to sit on policy work groups, time allowing.
- Become familiar, through your new associates, with non-traditional research grant opportunities of governments.
- Be flexible. Try to empathize with the needs of government staff and adapt your practices accordingly. Then and only then will your discoveries be embedded in policy that impacts the greatest number of citizens.

Recommended Readings and Courses

Readings

Lomas J. Finding audiences, changing beliefs: the structure of research use in Canadian health policy. *J Health Polit Policy Law*. 1990 15:525-42.

Leggat SG. Turning evidence into wisdom. *Health Pap*. 2003 3:44-8.

Courses

A range of offerings are available to decision makers, policy analysts, and researchers. In Canada, clinician scientists should check with the many training programs offered by the Canadian Health Services Research Foundation (CHSRF): <http://www.chsrf.ca>.

Knowledge Translation and Exchange:

How to ensure your research has impact in practice, policy, and health care

Melanie Barwick, PhD, CPsych

Director, Knowledge Translation Child Health & Evaluative Sciences
Departments of Psychiatry and Public Health Sciences
University of Toronto
Toronto, Ontario, Canada

Donna Lockett, PhD

The Hospital for Sick Children
Toronto, Ontario, Canada

The last decade has seen greater emphasis on research that has relevance for addressing real world problems. Moreover, there is recognition that more can be done to bridge the gaps between research, practice, and policy. Knowledge translation activities and strategies can facilitate interaction between scientists and decision-makers and ensures more evidence-based decision-making.

Various terms for translation of research knowledge are used, including *knowledge transfer*, *knowledge transfer and exchange*, and *knowledge translation*. In this chapter, *knowledge translation* is defined as follows:

“...the exchange, synthesis and ethically-sound application of knowledge – within a complex system of interactions among researchers and users – to accelerate the capture of the benefits of research for... improved health, more effective services and products, and a strengthened health care system” (Canadian Institute of Health Research, online).

Granting agencies are now asking for a knowledge translation plan and associated budget as a part of the grant submission. This helps the agency to show accountability to the public and to determine the potential impact of the research. This may also move science into practice more quickly. Granting organizations may also ask that decision-makers be actively involved in the research process as a strategy to link the research to an implementation process.

The objective of this chapter is to improve knowledge translation competencies for clinician scientists.

Developing a Knowledge Translation and Exchange (KTE) Plan

The transfer of research information to health care providers requires attention to four critical elements: the source, the content, the method, and the audience.

Health care providers need access to the research knowledge (library resources) as well as venues for sharing their knowledge with others, including scientists and decision-makers. Successful implementation of new knowledge into practice requires strategizing at multiple levels – the practitioners, the organization, the system, the nature of the evidence, and the methods of transfer and implementation. An understanding of practitioners’ attitudes toward evidence-based practice is needed to address skepticism, distrust, and resistance. Thus, effective elements in knowledge translation and exchange should be employed:

- The transfer of new knowledge is more successful when there is active collaboration and partnership with all stakeholders from the beginning. Passive dissemination is generally ineffective in changing practice.
- Knowledge is transferred best when done face-to-face, allowing for the communication of tacit knowledge.

A well developed KTE plan addresses several questions.

Your target audience(s)	Families, MOH policy-makers, general public, advocacy groups, consumers, clinicians	Who could or should act upon results, and who will be impacted by the results? Will the recommendations mostly be geared toward government policy makers, hospital managers and executives, or health practitioners?
How to engage audience(s)	Invite them to sit on advisory committees, personal meetings, etc.	Having an advisory team of stakeholders gives early buy-in and ensures the research is relevant. Allow the target audience to review preliminary results, test initial assumptions, and identify issues and emerging trends.
When to engage audience(s)	Some partnerships have been formed or will be formed ASAP to help guide the project. Others will be recruited once findings are synthesized.	The earlier the better. The target audience should be involved at the earliest feasible stage of the project as well as throughout its lifecycle. Even before research begins, researchers can work with audiences to determine key issues and the most relevant questions to the current environment.

How to package message	CHSRF report 1-3-25 format*, pamphlets, media, presentations, journals, newsletters, conferences, etc.	Consider who will be the messenger, how the material will be packaged, how main messages will be identified (e.g. through advisory team etc.), and what kind of language will be used.
How to deliver message	Roundtable discussions, workshops, face-to-face meetings, websites, etc.	Partners or advisory group may provide an excellent start to key opinion leaders and user networks to help disseminate the results. The researcher should take the results to the people who can use them, and must have credibility with the group receiving the research.
What you hope to achieve	Change in policy or practice, increased awareness, changed attitudes, etc.	You may want to consider including an evaluation component to determine whether your message has achieved the desired impact.

The 1-3-25 format: 1 page of main messages, 3 pages of executive summary, 25 pages or report.

Communicating and Disseminating to Non-academic Stakeholders

Communication is a key aspect of KTE. To be effective for a diverse audience, the main messages must be compelling, relate to a decision or set of decisions, and be backed by rigorous research. Thus, it's important to know if research findings are ready for transfer:

- Research findings are ready for transfer if they a) can confirm or refute other studies, and/or b) can inform practice – through practitioners, decision-makers, and/or policy makers
- Research findings are not ready for transfer a) if they are inconclusive or provide no “take-home” message of use to decision-makers, and/or b) when accountability mechanisms are not in place to ensure “take-home” messages are appropriate to the decision-making environments to which they are directed.

What to Consider When Communicating

Source

The person delivering the message is the source for the audience and must be credible and highly regarded.

- Researchers and advocacy groups work well.

- The more distant the source of a communication from the world of the decision-maker, the less influential it is. (local opinion leaders work well.)
- Multiple sources are very effective.

Channel(s)

Channels of communication include journals, newsletters, web pages, television, newspapers, conferences, seminars, etc.

- Multiple channels are effective for alerting decision-makers to the availability of the research, clarifying its implications, and ensuring “hard copy” availability when the opportunity comes for the use of research results in decision making.
- One-on-one and face-to-face interaction is the most persuasive communication.

Audience(s)

The audience is everything. One size-fits-all communication strategies are rarely successful.

- Segment your audience and tailor your messages to those segments; for example: consumers, decision-makers, policy developers, general public.
- Give people the information they need, not what you think they ought to know.
- Listen to the audience and involve it in developing, discussing, and delivering the message.
- Be specific and know your audience, including consumers, clinicians, managers, local policy developers, the general public, and national and international decision-makers.

Main Message

“Main messages” are the lessons others can take from your research. Effective key messages explain what the research means, why it is important, or what actions should be taken. They are not simply a summary of results. Keep it brief and simple.

- Main messages are a clear, concise, audience-focused set of statements.
- The tone, content, and language of a key message need to be appropriate for the intended audience.

- Because the results of a single study can differ from the body of research on a particular issue, it can be helpful to include the context as part of the message (how these results fit with the body of related evidence).
- Messages in the form of “ideas,” not “data,” influence decision-making the most – over time, ideas enlighten decision-makers about an issue and how to handle it.

Partnerships

Tips for Developing and Sustaining Partnerships

- Cultural sensitivity: researchers and decision-makers need to understand the characteristics and differences of each other’s communities.
- Trust: both groups need to recognize the contributions that each makes, whether it is time, information, or the other necessary ingredients of a partnership.
- Commitment: research partnerships are not always easy; partners need to be able to make long-term commitments.
- Clear roles and expectations: partnerships work when all parties are clear about their intentions, assumptions, and limitations at the start.
- Partner with an organization, not an individual: if an organization as a whole takes an interest in a project, it is not likely to be forgotten after changes in staff.
- Organizational support: it is a lot easier to participate when employers support the endeavour.
- Continue to support, and liaise with your partner even when there isn’t a research agenda: “I’ll scratch your back if you scratch mine.”

Partners in the Initial Stages of Research

Choosing your team is the first and most important task. Be sure to include the key stakeholders and decision-makers who will use the research when it is completed. Consider the skills, disciplines, and expertise that you will require in choosing the team members. Be clear from the onset what the roles and responsibilities will be of each partner and be prepared to

negotiate these if needed. Stakeholders can be involved as full partners or as advisory members. Once the team is formed the next steps will be to:

Develop a research question:

- Allow plenty of time.
- Break down the problem or issue into its key elements.
- Separate needs for information from needs to make value choices.
- Consult and communicate clearly, concisely, and often.
- Target a single information gap.

Chart a course:

- What is the appropriate research approach?
- How and when will team members meet to discuss progress and make decisions?
- How will results be disseminated?
- How much funding will be allocated to the research itself, the meetings and interactions, and the dissemination of results?

Nurturing Relationships

There will inevitably be ups and downs in the research process. It is thus important to maintain the team’s motivation by ensuring that the program reflects its goals and that team members feel their contribution is worthwhile and valued. Periodically assess research milestones and the status of the partnership.

- Anticipate and plan for stress and burnout. Recognize that everyone has a demanding “day job” in addition to the research collaboration.
- Address conflicts when they are small; don’t let them grow.
- Update partners on progress regularly. While being careful to avoid prejudging the results, presentations and discussions about the progress of a program can:
 - build a roster of decision-making audiences interested in the final results,
 - provide useful feedback to refine or deepen the program, and
 - help ensure that the research program remains relevant to both the researchers and the decision-makers.

Key Points

- Evaluate research options as a group – researchers and decision-makers often value different kinds of research.
- Plan to meet regularly and often throughout the program, not just the beginning and end.
- Don't underestimate the value of informal and less-structured gatherings – an excellent way to deepen relationships.
- A dissemination plan will evolve throughout the program. Start with the basics of who will be interested in the results and how best to reach them.

References

Davis D, M Evans, A Jadad, and L Perrier. The case for knowledge translation: shortening the journey from evidence to effect. *BMJ* 2003 327:33–35.

Community-Campus Partnerships for Health's Community-Engaged Scholarship Toolkit. <http://depts.washington.edu/ccph/toolkit-intro.html>

Canadian Health Services Research Foundation. The CHSRF has a section on KTE with several articles, resources, and tools to help you. <http://www.chsrf.ca>

Knowledge Transfer Program, University of Toronto. This program develops and tests interventions that improve the process by which evidence is adopted by potential users of health information. <http://www.ktp.utoronto.ca>

Canadian Institute of Health Research. How CIHR views knowledge translation, including an overview of its five-year plan to require KTE as an essential component. <http://www.cihr-irsc.gc.ca/e/29529.html>

WHO. Knowledge Translation in Global Health. <http://www.who.int/entity/bulletin/volumes/83/10/editorial21005html/en/>

Additional Learning Material

The CCHCSP website (www.cchcsp.ca) contains additional educational material, including updates to the handbook, new references, and information not available in the book including case scenarios. These materials are intended to stimulate discussion among peers and experts in the field. Access to the CCHCSP website requires a username and password. For information on how to obtain access, contact <training@cchcsp.ca>

CCHCSP Website participants are also able to access case scenarios exploring ethical, interpersonal, and career-planning problems. These cases are used at 11 Canadian universities involved in training health care professionals. References to chapters in the Handbook are included with each case to guide trainees and facilitators. Some examples:

- A protagonist must develop a research proposal and deal with ethical issues in order to work with a minority group.
- A trainee discovers that a colleague may have fabricated research data and must also deal with a dispute over authorship on a paper.
- Other cases deal with negotiating one's first academic appointment, starting a research program, developing a network of collaborators, and finding ways to protect research time.

Senior researchers who wish to act as a facilitator for group discussion of the cases may purchase "Coach's Corner," a booklet that provides insights into the cases, ideas on how to facilitate discussion, and suggestions for experts to invite.

Additional Purchases

Copies of the "Handbook for Clinician Scientists" and "Coach's Corner: a facilitator's guide to group discussion of cases" may be purchased from the CCHCSP at 555 University Ave, Toronto, M5G 1X8, Ontario, Canada, 1-416-813-7654 x4304, or by emailing a request to: <training@cchcsp.ca>

Corrections

Every attempt has been made to ensure that journal and website references used in the Handbook are correct. However, web citations may change and journal or book citations may be incorrect. Readers are encouraged to write to the editor (robert.bortolussi@dal.ca) if they have corrections or suggestions for additional chapters or case scenarios. Corrections to the citations will be listed on the CCHCSP web page www.cchcsp.ca.