



Clinical Trial Research News

From the Office of Clinical Research

Volume 9, Issue 4

July / August 2007

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This newsletter is published on a bi-monthly basis and is designed to provide an information source for anyone interested in Clinical Research. Please contact Trish Berry if you would like to be added to / deleted from our mailing list.

Announcement

It is our great pleasure to be able to announce that Lorie Forbes has been appointed as the Administrative Manager, Research Enterprise in recognition of her integral role with Human Resources, Health and Safety and support management for basic and clinical research activities. Congratulations Lorie!

Statistics and Medical Research

Selecting and Reporting a Patient Sample

Samples and Populations

Medical research typically involves studying a sample drawn from a population in order to compute a sample statistic (e.g. sample mean, sample survival rate) which can be used to estimate or make inferences about the corresponding population parameter (e.g. population mean, population survival rate). Sample statistics can also be used to test hypotheses about population parameters.

There is no method of sampling, short of selecting the entire population, that ensures the sample statistics will equal the corresponding population parameters. However, by selecting a random sample of a given sample size the researcher is able to state with a certain level of confidence how close a sample statistic is to its corresponding population parameter. If a sample is not representative of a population it is biased and conclusions drawn from the analysis of the sample data may not be valid or generalizable to the larger population.

Samples and Study Design

The nature of the sample drawn in a research study depends on the experimental design of the study. There are a number of common study designs in medical research:

(1) *Prospective or cohort studies*

The first design approach is an observational study in which a researcher "observes" a study sample over time by measuring certain variables. For instance, a researcher may study two groups (one a cohort of smokers and the other a cohort of non-smokers) to determine prospectively the incidence of lung cancer.

(2) *Retrospective or case-control studies*

A second type of observational study involves comparing a sample of patients with, for instance, a disease of interest (cases) to a second sample who do not have the disease (controls). Often the controls are matched to the cases on the basis of certain important variables (e.g. age, gender, previous medical history) which may potentially influence the outcome of the study.

(3) *Experimental studies*

In these types of studies the researcher intervenes or "experiments" in one or more samples to see how the sample subjects respond to an intervention or treatment regime. The nature of the sample is critical in determining the validity of experimental studies. Three types of samples are usually employed in these studies:

(a) *Accidental or convenience samples*

These samples are often self-selected or chosen on the basis of availability and convenience. They are almost never representative of the population of interest and can produce very misleading results. A common example in the popular media is phone-in polls involving some question of social concern, where the respondents are usually non-representative of the whole population. In medical research, samples which are drawn from a medical clinic or specific treatment program strictly on the basis of convenience or opportunity fall into this category.

(b) *Simple random samples*

A simple random sample is the best way of ensuring the sample is representative of the population. In general, the larger the sample size the more likely the sample will be representative and lead to accurate estimates of population parameters. Simple random samples have two defining characteristics: (1) every member of the population has an equal chance of being included in the sample; (2) each member is selected independently, i.e. the selection of one member has no effect on the selection of another member. With simple random samples it is possible to determine the degree of sampling error so confidence intervals can be calculated to specify the limits within which the population parameter will fall based on the sample statistic (e.g. 95% confidence intervals).

(c) *Stratified random samples*

A random sample may also be obtained by dividing a population into groups called strata, based on certain characteristics of the population (e.g. age, gender, socio-economic status) and then drawing simple random samples from each strata. Samples derived from this method ensure that certain salient characteristics of the population are represented in the sample in proportion to their distribution in the population.

Random samples are obtained through a variety of methods, including a coin toss, drawing numbers from a container and random number tables. The latter technique often utilizes computer-generated sequences of random numbers and is the most widely used method of obtaining a random sample.

Reporting Information about Samples

o Researchers should always report the reasons for selecting a particular sample and the methods of doing so. The full range of potentially available subjects should be precisely stated so that the informed reader can determine the population sampled by the investigator.

- o Eligibility criteria should also be clearly specified and the reasons for possible exclusion of patients reported (e.g. outside a specified age range, unable to answer questions due to illness or language barriers, etc.)
- o The number of potential subjects excluded should be documented under the eligibility criteria. The rationale of excluding patients for more than one reason should also be specified (e.g. priority sequencing).
- o If the eligibility criteria were altered during the course of the investigation, this information should be reported (e.g. unforeseen problems, recruitment difficulties).
- o The details of randomization should be reported, including (1) the method of randomization (e.g. table of random numbers); (2) whether stratification or matching was used in the randomization process; (3) details of the exact nature of the process of randomization (e.g. were subjects randomly assigned to treatment groups or were treated patients randomly given one or another clinical tests).
- o Blinding or "masking" in which certain information is concealed from the study participants or members of the research team should always be reported in detail. For instance, patients may be blinded to their treatment group or the time that certain observations are made. The clinician who classifies treatment outcome or the pathologist who interprets specimens may be blinded to the treatment condition.
- o The effectiveness of blinding should also be discussed in situations where the person who is blinded may inadvertently learn or guess concealed information (e.g. side effects which accompany one treatment but not another).
- o Loss of observations (e.g. dropouts from a clinical trial or incomplete clinical tests) should always be reported.
- o When the sample size in a Table or Figure is different from the original sample size the difference should be accounted for (e.g. patients lost, specimens contaminated, test not completed).
- o It is very important that loss of patients to follow-up (e.g. due to non-compliance or death) should be reported. It is likely that such patients are atypical in critical ways and this information affects the interpretation of study results.
- o Treatment complications and side effects are a frequent occurrence in medical studies. These unintended adverse (or beneficial) effects should be reported objectively and in detail as they often provide useful information from a study and may lead to new research initiatives.

This article is authored by OCR statistical consultant Doug Staley. Doug teaches statistics at the School of Medical Rehabilitation, University of Manitoba and has conducted medical research at SBGH for more than 25 years. Readers are welcome to submit questions or suggest topics of interest. Doug can be contacted through the OCR or by email: dstaley@mts.net or extension 2690.

Upcoming Workshops

Fall 2007 Clinical Research Lecture Series - U of M Bannatyne Campus

Presented by: St. Boniface General Hospital Office of Clinical Research & the University of Manitoba
Bannatyne Campus Office of Research Services

Interested in getting involved in clinical research? Clinical research refers to all research conducted with human subjects. These comprehensive lectures are specially designed for individuals with little or no previous research experience. The lectures will present an overview of the language of clinical research, project design and management, roles and responsibilities of the Investigator and the research staff, and the regulatory and ethical environment for the conduct of clinical research.

Introduction to Clinical Research September date to be confirmed

Clinical Research Ethics September date to be confirmed

**Clinical Research Guidelines,
Policies and Regulations** October date to be confirmed

**Clinical Research Project and
Documentation Management** October date to be confirmed

For more information or to register for one or all of the lectures contact:
Terry Sawicz-Hanesiak, SBGH – Office of Clinical Research
(204) 237-2226 or e-mail tsawicz@sbgh.mb.ca

Good Clinical Practice Workshop

Date: Tuesday, October 30, 2007
Time: 8:30 – 4:00 pm

In response to several requests, the Office of Clinical Research is considering presenting another full day Good Clinical Practice workshop.

The cost to attend the one day workshop would be \$150 (breakfast, lunch and break refreshments are included). Registration will be limited to 20 participants. For more information or to have your name placed on the waiting list please contact Terry Sawicz-Hanesiak, SBGH – Office of Clinical Research (204) 237-2226 or e-mail tsawicz@sbgh.mb.ca

Monitoring Clinical Research Workshop:

Date: Wednesday, November 14, 2007
Time: 8:30 to 4:00 pm

Date: Thursday, November 15, 2007
Time: 8:30 to 12:00 Noon

In response to several requests, the Office of Clinical Research is considering developing a 1-½ day workshop on monitoring Clinical Research Studies. This course will focus on use of forms for hands-on monitoring, and the rationale for monitoring practices. The workshop would be open to anyone who has experience working in Clinical Research and has taken some form of GCP training.

The cost to attend the 1-1/2 day workshop would be \$200 (breakfast, lunch and break refreshments are included). Registration will be limited to 20 participants. For more information or to have your name placed on the waiting list please contact Terry Sawicz-Hanesiak, SBGH – Office of Clinical Research (204) 237-2226 or e-mail tsawicz@sbgh.mb.ca

HCPAM Lab Stats Workshop by Lynn Torbeck

HCPAM is pleased to offer this three-day workshop LabStats by Mr. Lynn Torbeck. To register for this workshop please complete a training application form (see back of Newsletter) and fax back to HCPAM at (204) 942-3833.

Date: Tuesday, July 17th, Wednesday, July 18th and Thursday 19, 2007
Place: Canad Inns, Polo Park, 1405 St. Matthews Avenue; Winnipeg, Manitoba R3G 0K5
Time: 8:30 am - 4:30 pm
Course Fee: HCPAM Members \$750.00; Non-members \$950.00

Introduction:

This is a pragmatic introductory course for those that have not had a course in statistics or for those that wish to have an introductory refresher of basic concepts.

Business Objective:

The goal of this course is to enable the attendees to begin immediate use of statistical techniques. This is not a theory course.

Description:

This is done by presenting a set of statistical concepts written in a modular format. Case studies and exercises are used to teach the material. The course will have minimum lecture and maximum hands-on activity. Video tapes will augment the lectures.

Prerequisites:

There are no prerequisites for this course. This is an introduction for those who have not had a course in statistics. No prior statistics background is needed, but a background in basic algebra is assumed. Attendees should be working in a pharmaceutical, biopharmaceutical or medical device environment. Extensive use of graphics and modular worksheets facilitates analysis and intuitive understanding.

Handouts:

Each attendee will receive course notes and a booklet of statistical modules that can be immediately used on the job to solve statistical problems. Unlike typical books on statistics, these modules present the information for each topic in a standard format. Step by step procedures are paralleled with a worked example. A list of the statistics topics that will be include follows.

Course Format:

The course format is intended to mimic the working research & development and production environments. Problems are presented and small teams of attendees will work together to conduct the exercises, collect the data, calculate the summary statistics and write conclusions for the projects. The majority of the material will be learned by doing the activities using the modules, not by lectures. The video tape series "Against All Odds" will be used to present concepts.

Bring to Class:

Attendees are requested to bring a calculator that can calculate two variable statistics, a 12 inch ruler, a mechanical pencil and an eraser. Color highlighters are suggested. Graph paper, course notes and the booklet of modules will be provided.

Who should attend:

This introductory seminar is intended for pharmaceutical and biopharmaceutical analytical chemists, chemical engineers, product formulators, process development engineers, quality assurance specialists, and production technologists. It is highly recommended for directors, managers and supervisors of analytical technical staff.

Found Resources

New WHO Web Portal for Clinical Trials

(www.who.int/mediacentre/news/notes/2007/np22/en/index.html)

Doctors, patients and journalists can now go online to search easily and quickly for information on clinical trials from around the world. The World Health Organization has launched the first global online search portal for clinical trials, including unpublished ones. CIHR contributed to the development and through its continued leadership, accelerated the move toward greater transparency of information about clinical trials. In addition, CIHR took the decision back in 2004 that all randomized controlled trials it funds be publicly registered.

Background documents:

* CIHR Policy about the International Registration of Randomised Controlled Trials (www.cihr-irsc.gc.ca/e/24107.html)

* International Randomized Controlled Trial Register (ISRCTN)
(www.controlled-trials.com/isrctn/search.html)

* Ottawa Statement on Trial Registration and publications
(<http://ottawagroup.ohri.ca/>)

Journal of Clinical Research Best Practices

The Journal of Clinical Research Best Practices is a free on-line journal that often contains interesting articles on both basic and clinical research practices. The Journal has attracted over 60,000 subscribers with its practical, insightful and sometimes controversial articles. Subscribe free today at www.firstclinical.com/signup.html

Volume 3, Number 5, May 2007

READ THE JOURNAL

www.firstclinical.com/journal

Articles:

Reinventing the Site Questionnaire
That's a good question

Ethical Pitfalls for Sponsors in Developing Countries
There will be a day of reckoning

Institutional Conflict of Interest in Research
Stop trying to push me around

Missing Data Means Lost Opportunities
Whoops

Reviews:

"Strategic Research: A Practical Handbook for Phase IIIB and Phase IV Clinical Studies" It's not just a playground for marketing

"The Impact of Genomics on Clinical Trials and Medical Practice" Do you have the reading gene?

"FDA: A Century of Consumer Protection"
It was quite a ride

Columns:

MAGI News
Update on MAGI, the Model Agreement Group Initiative

Good Clinical Practice Q&A: Focus on Recruitment Advertising You too can be a GCP expert

First Clinical Research Stock Index (FCRI)
Steady as she goes, but look what happened to biotech stocks

What am I Missing Here? Thought-Provoking Questions for the Clinical Research Industry Hidden errors; IND safety reports

New Report on De-Identification and an Anonymization Tool Case Study

*Our final report for the project funded last year by the Office of the Privacy Commissioner of Canada entitled "Pan-Canadian De-Identification Guidelines for Personal Health Information" is available on-line at: <http://www.ehealthinformation.ca/documents/OPCReportv11.pdf> . This report covers all of the re-identification studies that we did over the last year and provides an anonymization decision process that can serve as a starting point for the release of personal data.

*We also have just released the first (small) case study using our PrivacyAnalytics tool, which automates some of the anonymization functions: <http://www.ehealthinformation.ca/documents/PACaseStudy-1.pdf> . We are developing more case studies and so you should see more (and more detailed) examples in the next few months.

Products and Food Branch (HPFB) Strategic Plan 2007-2012

Via HCPAM, Information from Health Canada & Food Branch
Dear Stakeholder:

I am pleased to present the Health Products and Food Branch (HPFB) Strategic Plan 2007-2012. This plan sets out six inter-related strategies that will guide us in the next five years in our on-going commitment and desire to continue to make significant contributions to promote and protect the health and safety of Canadians.

HPFB's last strategic plan was a major milestone in the Branch's evolution, providing a clear roadmap that identified five key strategies to ensure that Canadians have timely access to safe and effective

health products, safe and nutritious food, and the information they need to make healthy choices. A Progress Report on the HPFB 2004-2007 Strategic Plan, being released with this new plan, highlights the significant progress we made towards those strategies.

Recognizing the pressing need to modernize our approach to regulating health products and food, HPFB launched a comprehensive review in the fall of 2006, the Blueprint for Renewal. Blueprint II completes our Strategic Plan by providing a longer term roadmap for transforming Canada's regulatory system so that it can meet the challenges and complexities of the future.

We are grateful to our stakeholders, partners and the Canadian public for their continued engagement, contribution and confidence in the Branch. Together with HPFB's dedicated staff, I look forward to working with you on these key strategies to achieve our vision of protecting and promoting the health and safety of all Canadians.

Neil Yeates
Assistant Deputy Minister
Health Products and Food Branch

The above documents can be located on the Health Canada Web site at:
www.hc-sc.gc.ca/ahc-asc/pubs/hpfb-dgpsa/strat-plan-2007-2012_e.html ,
http://www.hc-sc.gc.ca/ahc-asc/pubs/hpfb-dgpsa/prog-2004-2007_e.html and
http://www.hc-sc.gc.ca/ahc-asc/branch-dirgen/hpfb-dgpsa/blueprint-plan/blueprint-plan_II_e.html

Research Canada

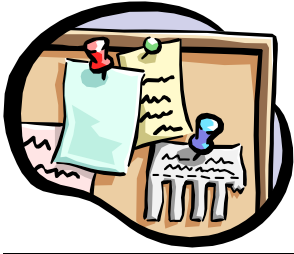
Research Canada is a not-for-profit, voluntary organization that is a strong national voice for health research advocacy in Canada. It's mission is to help Canadians maintain and improve their health by ensuring Canada is a world leader in health research. Working for all Canadians, its membership is drawn from all sectors dedicated to increasing investments in health research, including the leading health research institutes, national health charities, hospitals, regional health authorities, universities, private industry and others.

More information is available on their website <http://www.rc-rc.ca/en/>

FDA Warning Letters

FDA recently published a warning letter which was issued to a Principal Investigator working at the University of Washington Medical Center in Seattle, WA. The 6 page warning letter lists several deficiencies including improper informed consent procedures, protocol deviations, along with incomplete and inaccurate records. The warning letter is an excellent example of things Regulatory Inspectors look for when inspecting a clinical trial site. The complete letter can be found at;

http://www.fda.gov/foi/warning_letters/s6360c.pdf



Notice Board

Research Informed Consent Forms in the Main Hospital Charts

This is just a reminder of your obligation to include copies of Research Informed Consent Forms in the main hospital charts of patients involved in research studies (the original ICF would be kept in your research files).

These are the links to the relevant hospital policies which state this requirement.

Section 3.18

http://intranet.sbggh.mb.ca/PolicyProcedureManuals/files/Admin_VI-350.pdf

Section 5.5.10

http://intranet.sbggh.mb.ca/PolicyProcedureManuals/files/Admin_VI-360.pdf

The only exception would be for example if the Research Ethics Board requested that there be no mention of the study in the subject's medical charts. This exception would be made to comply with TriCouncil Policy Statement, Article 8.2. "The researcher must ensure that the results of genetic testing and genetic counseling records are protected from access by third parties (e.g. insurers, employers), unless free and informed consent to do so is given by the subject)."

If you have any questions or concerns do not hesitate to contact either April Hughes or Terry Sawicz-Hanesiak in the Office of Clinical Research.

"Why Don't We do it in our Sleeves?"

Further to the Clinical Programs Council meeting held on May 24, 2007, the video "Why Don't We do it in our Sleeves?" is on the SBGH intranet under News & Events/Newsletters/Preparing for Pandemic Influenza or click on http://intranet.sbggh.mb.ca/Newsletters/News_PandemicInfluenza.html

Research Review Committee at St. Boniface Hospital

Deadlines for RRC Submission

July 25, 2007
August 29, 2007
September 26, 2007
October 31, 2007
November 28, 2007

Meeting Date

August 1, 2007
September 5, 2007
October 3, 2007
November 7, 2007
December 5, 2007

PLEASE NOTE THERE IS NO MEETING IN JULY

The Biomedical (BREB) / Health Research Ethics Board (HREB) Submissions

Deadline for REB Submissions

August 13, 2007
September 10, 2007
October 15, 2007
November 9, 2007 (Friday)
November 26, 2007

Meeting date

August 27, 2007
September 24, 2007
October 29, 2007
November 26, 2007
December 10, 2007

PLEASE NOTE THERE IS NO MEETING IN JULY

Contact **Ethics** at **789-3255** with any questions you may have regarding your REB submission. Noreen is available to assist you with consent form development and the submission process. Please always refer to the Research Ethics Board web site for the most recent submission forms and updates.

HISP Update

Congratulations everyone for the HISP success. All research staff who need it should have their HISP access up and running. The HISP group sends periodic updates which will continue to be circulated to research staff via email. In addition, we will print out hard copies of bulletins and post them onto the research notice boards out side of our offices in the Education Building. Please let us know if we can be of further assistance with updates.

Electronic Source Data Integrity Questionnaires

If anyone is receiving "Electronic Source Data Integrity Questionnaires" from drug trial sponsor's or any other such document that asks questions regarding electronic data storage compliance with FDA regulations please contact either April Hughes or Terry Sawicz-Hanesiak in the Office of Clinical Research for further assistance.