



Hôpital St-Boniface Hospital

Clinical Trial Research News

From the Office of Clinical Research

Volume 13, Issue 1

January 2011

To Contact Us:

Dr. Bram Ramjiawan, Ph. D.

Director, Research Innovation
And Regulatory Affairs
Ph: 235-3206

Karen Swanson

Admin Secretary SBRC
Ph. 235-3206

Lorie Forbes

Admin. Manager
Ph. 258-1044

Terry Sawicz-Hanesiak

Regulatory Affairs / QA Associate
Ph: 237-2226

Krista Vandewaeter

Admin. Secretary Research Review Committee
Ph: 235 -3623

Douglas Staley

Statistical Consultant
Phone: 237-2690 or dstaley@mts.net

This newsletter is published on a quarterly basis and is an information source for anyone interested in Clinical Research. Please contact Terry (237-2226) if you would like to be added to / deleted from our mailing list.

Statistics and Medical Research

Chi-square and Fisher's exact test

The Chi-square test and Fisher's exact test are extensively used in medical research when the dependent variables are categorical in nature. The Chi-square test was first developed by Karl Pearson more than a century ago (the Pearson correlation coefficient is named after him), while Fisher's exact test is named after British statistician R.A. Fisher.

Fisher played a crucial early role in the design and analysis of statistical experiments and created a famous randomized experiment (later recounted in a book *The Lady Tasting Tea*) which was the basis of Fisher's exact test. An Englishwoman, Muriel Bristol, claimed that she could tell whether tea or milk was added first to a fresh cup of tea. Fisher devised an experiment to test the validity of her claim. He gave her 8 cups of tea, in which half had milk added first and half had tea added first. The order was randomized. Ms. Bristol was able to correctly identify all 8 cups, and Fisher, using the methodology that resulted in Fisher's exact test, calculated that the probability of this happening was 1 in 70 or $p = .014$.

Applications

Both the Chi-square test and Fisher's exact test are used with categorical data and test the null hypothesis that the frequency distribution of outcome measures in a sample (observed values) is consistent with a theoretical distribution (expected values). In particular, the Chi-square test is applied to test two types of comparisons, the goodness of fit test and the test of independence. The goodness of fit test measures the degree to which an observed frequency distribution differs from a theoretical distribution, and is often displayed graphically. The test of independence assess whether variables in a contingency table (e.g. a 2 x 2 table) are associated or independent of each other.

Fisher's exact test is used with categorical data with binary outcomes (e.g. yes-no) and is typically applied to 2 x 2 contingency tables. When sample sizes are small Fisher's test is more appropriate than the Chi-square test for analyzing 2 x 2 contingency tables. For small samples Fisher's exact test is able to calculate precise probability values while the Chi-square test can only compute approximate p-values. When sample sizes are larger, the Chi-square test is recommended as more appropriate.

Assumptions

The two tests have a number of important assumptions:

- The sample data is randomly sampled from a population.
- The outcomes of the classification variables must be mutually exclusive.
- The outcome observations are independent of each other. If the data is related or matched then McNemar's test should be used.

- The cells in the contingency table must have sufficient cell counts. As a general rule, no expected frequencies should be less than 1 and no more than 20% of expected frequencies should be < 5. When these assumptions are not met Yate's correction is applied to the calculation of the Chi-square statistic.

Cautions

Researchers should be aware of a number of statistical considerations when working with the Chi-square test and Fisher's exact test:

- The most common statistical error in using the two tests is violating the assumption of independent observations by treating correlated or paired data as independent. An example would be a research design in which a sample of subjects are evaluated for the presence of a clinical marker (yes-no) before and following a treatment intervention. This creates a 2 x 2 contingency table with four cells. However, the observations in the cells are not independent as the same subjects are measured twice (before and after treatment). The proper test for this design is McNemar's test.
- One of the assumptions of the Chi-square test is the requirement that there be sufficient observations in each cell of the contingency table. This is especially problematic with large contingency tables (e.g. 4 x 6). A pragmatic workable solution is to collapse the categories by combining similar categories to create a smaller contingency table, thus ensuring sufficient number of observations in each cell.
- Although Fisher's test gives exact p-values, some statisticians argue that the test is conservative and that it leads to rejecting the null hypothesis at a rate that is lower than might be expected. However, computer modeling techniques suggest that the effect is small and that the Fisher's test is generally accurate with regard to p-values.

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, by email: dstaley@mts.net or directly at 237-2690.

Updated Lab Services Form – Version October 5, 2010

Please be advised that the Lab Services form was recently updated. Please discard versions you may have that are dated prior to October 5, 2010. An updated electronic version is available on the internet as follows under the heading Templates;

<http://www.sbrc.ca/content/blogcategory/86/131/>

Updated Pharmacy Contact Information

Please note the following Pharmacy Investigational Drug Services (IDS) changes Effective December 1, 2010;

- 1) Don Mestdagh has retired and Rhonda Fusee is the new approval signature for Pharmacy
- 2) IDS office has moved to main the pharmacy area DG011
- 3) Hours are Monday to Friday 0830h -1500h
- 4) Contact Names, Phone and Fax Numbers:

Debbie Hrabí (235-3501), Marnie Boyle (235-3908), Fax (235-3780)

Denise Sawatzky who has fulfilled the role of investigational Drug Pharmacist for many years is now working with in patient services. The Office of Clinical Research would like to congratulate Don on his retirement and to Denise we wish her much success in her new role and would like to take this opportunity to thank Denise for her dedication and outstanding work during her many years as Investigational Drug Pharmacist.

2nd Edition of Tri-Council Policy Statement (aka TCPS 2) Released in December 2010

The *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (TCPS) is the joint research ethics policy statement of the federal research agencies –Canadian Institutes of Health Research (CIHR), Natural Sciences and Engineering Research Council of Canada (NSERC) and Social Sciences and Humanities Research Council of Canada (SSHRC). TCPS 2 is the first comprehensive revision of this Policy since its adoption in 1998. This document highlights some of the key elements of TCPS 2 in relation to the 1st edition.

TCPS 2 is available on line at:

<http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/Default/>

What is the same?

- underlying value of respect for human dignity as basis for the core principles scope of research ethics review
- proportionate approach to research ethics review

- respect for academic freedom and acknowledgement of associated responsibilities
- respect for the law and the need to balance it with ethics principles
- requirement for free, informed and ongoing consent
- responsibilities associated with participant privacy and information confidentiality
- fundamentals of research ethics board (REB) governance conflict of interest requirements

What has changed?

- core principles consolidated
- guidelines updated in the areas of:
 - clinical trials
 - human biological materials
 - human genetics
- terminology (e.g., “participant” instead of “subject,” or “delegated review” instead of “expedited and departmental reviews”)

What is new?

- three chapters
 - Multi-Jurisdictional Research (Chapter 8)
 - Research Involving First Nations, Inuit and Métis Peoples of Canada (Chapter 9)
 - Qualitative Research (Chapter 10)
- clinical trial registration
- research ethics review during publicly declared emergencies
- institutional responsibilities associated with security of information
- reporting incidental findings
- research directives
- document structure
- index and glossary

What has been clarified?

- scope of REB review, including exemptions
- increased emphasis on principles and proportionate approach to research ethics review
- REB independence
- consent requirements
- continuing research ethics review
- critical inquiry
- roles and responsibilities of those involved in the research process

Message from U of M Research Ethics Boards

Course in Human Research Protection Program (CHRPP)

Please review the attached memo from the Office of the Vice President of Research regarding important information on mandatory ethics education training requirements for all research team members to be phased in by September 2011. Most major institutions have in place mandatory educational training requirements which require research personnel to attend mandatory training sessions or complete on-line tutorials similar to the CHRPP tutorial.

For information on accessing the website for those that do not have a University of Manitoba e-mail address please contact:

Monica Woods
 Research Quality Assurance Manager
 University of Manitoba
 053H Apotex Centre
 750 McDermot Avenue
 Winnipeg MB Canada R3E 0T5
 Ph: 204-272-3121
 Fax: 204-272-3122
 Cell (204) 803-1193
Monica.Woods@umanitoba.ca
www.umanitoba.ca/research

Research Review Committee at St. Boniface Hospital

Deadlines for RRC Submission

January 5, 2011
January 26, 2011
February 23, 2011
March 30, 2011
April 27, 2011
May 25, 2011

Meeting Date

January 12, 2011
February 2, 2011
March 2, 2011
April 6, 2011
May 4, 2011
June 1, 2011

Please note there is no meeting in July 2011

Submissions to the RRC must be received in N1004 by 11:00 AM on the deadline date.

Contact **Krista Vandewaeter** at **235-3623** with any questions you may have regarding your RRC submission. Please always refer to the Office of Clinical Research and RRC web site for the most recent submission forms and updates.

<http://www.sbrc.ca/content/blogcategory/87/132/>

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

Deadline for REB Submissions

January 10, 2011
February 14, 2011
March 14, 2011
April 4, 2011
May 16, 2011
June 13, 2011

Meeting date

January 24, 2011
February 28, 2011
March 28, 2011
April 18, 2011
May 30, 2011
June 27, 2011

Please note there is no meeting in July 2011

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

<http://www.umanitoba.ca/faculties/medicine/research/ethics/index.html>

Education and Training Events

Good Clinical Practice (GCP) Workshop

Date: Wednesday, March 23, 2011
Location: St. Boniface General Hospital – Room N1026
Time: 8:30 am – 3:00 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 (lunch and break refreshments are included in the registration fee).

Registration will be limited to 20 participants. For more information or to receive a registration form please contact Terry Sawicz-Hanesiak, SBGH – Office of Clinical Research (204) 237-2226 or e-mail tsawicz@sbgh.mb.ca

Life Science Association of Manitoba (LSAM) – Training Events

Through an industry led steering committee, LSAM offers a variety of courses and training resources so that companies can effectively train their employees to meet their current needs. LSAM has offered 1141 courses and trained more than 11,700 individuals since 1994.

Upcoming Training – “Biotechnology and Beyond: An Introduction into the Life Sciences Industry” - February 1 & 2, 2011

To view more details about this session and a list of other scheduled training events please visit their training website:

www.lsam.ca/calendar.cfm