



Hôpital St-Boniface Hospital

# Clinical Trial Research News

From the Office of Clinical Research

Volume 13, Issue 2

April 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](mailto: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

### Analysis of Variance or ANOVA

One of the most powerful and commonly used inferential statistical methods in medical research is the analysis of variance (ANOVA). Although the antecedents of the analysis of variance have been traced to the early work of researchers in the 19<sup>th</sup> century, the first formal articulation of the procedure was presented by British statistician Sir Ronald A. Fisher in 1918. The ANOVA became widely known to researchers with the publication of his seminal work *Statistical Methods for Research Workers* in 1925.

Essentially the ANOVA is an extension of the t-test, which compares the means of two groups, to a comparison of three or more groups. The ANOVA can also be used to compare the means of two groups and the results are identical to the t-test ( $F = t^2$ ). A common statistical error by novice researchers is to compare pairs of means in a study with three or more groups (A,B,C) by t-tests, e.g. A vs B, A vs C and B vs C. The problem with this approach is the lack of independence with multiple t-tests, leading to an inflated Type I error rate. Assuming an  $\alpha = .05$ , for three independent t-tests the probability of a Type I error =  $1 - (1 - \alpha)^2 = 1 - (.95)^2 = 0.14$ . For this reason the ANOVA should be used to compare the means of 3 or more independent groups.

### ANOVA Models and Mathematical Properties

The mathematical basis of the ANOVA is the partitioning of the variability of a dependent or outcome measure in a study into various components reflecting different sources of variation, e.g. between groups variability, within subjects variability. The ANOVA is usually expressed as an F-value statistic (named after Fisher):  $F = \frac{\text{between variability}}{\text{within variability}}$

The F statistic is then evaluated for statistical significance based on the magnitude of the F-value and the degrees of freedom (reflecting the number of groups and total number of subjects).

ANOVA models generally fall into three classes:

- Fixed-effects ANOVA where the primary interest is in making statistical inferences about the set of main effects.
- Random-effects ANOVA where treatment conditions are randomly sampled to infer population effects.
- Mixed-effects ANOVA where both fixed and random effects are present in the experimental situation.

### Assumptions of the ANOVA

There are a number of assumptions underlying the ANOVA paralleling those of the t-test:

- Observations are independent, i.e. observations within groups are not influenced by each other.

- Scores on the outcome measure(s) are normally distributed. The ANOVA is robust to violations of the assumption of normality for an independent variable with a fixed number of levels.
- Homogeneity of variance whereby the variability of scores in each treatment group are equal. The ANOVA is generally robust to violations of the assumption of homogeneity of variance, especially when cell sizes are equal.

### Types of ANOVA Designs

There are many different types of ANOVA designs, ranging from the relatively simple to the very complex:

- At the simplest level the F-statistic can be used to test the hypotheses that the variability in the scores of two groups are homogeneous (an assumption of both the ANOVA and t-test). An index is computed,  $F = \text{ratio of the larger group variance to the smaller group variance}$ , and then evaluated for statistical significance.
- One-way ANOVA which tests for mean differences among three or more independent groups in order to determine whether the observed differences are likely to have arisen by chance.
- Two-way or factorial ANOVA examines two independent variables and their interaction, and can test several hypotheses about differences between group means simultaneously. Two of these hypotheses pertain to the effect of each variable or factor viewed separately and a third to the interaction between factors.
- Repeated measures ANOVA is appropriate for a within subjects model in which the same subjects are measured a number of times, e.g. a longitudinal study. The simplest case is a pre-post design but the number of repeated factors can be extended to any number of measurements.
- Multiple analysis of variance (MANOVA) where there are more than one dependent or outcome measures. It is an extension of the one-way ANOVA and examines the relationship between multiple dependent measures simultaneously.
- The analysis of covariance (ANCOVA) is a statistical method for examining data from one-way and factorial designs using information from an independent variable called a *covariate*, which removes systematic individual differences among subjects from the estimate of experimental error in the calculations. The covariate contains information about differences between subjects before the experimental study is conducted (e.g. age, severity of illness, comorbid diagnoses).

### Non-parametric Equivalents of the ANOVA

The Kruskal-Wallis test is the non-parametric analog of the one-way ANOVA and an alternative to the ANOVA when its assumptions are not met. It substitutes ranks for actual scores in its computational procedure and is not as powerful a statistical test as the ANOVA. The Friedman test is the equivalent of the repeated measures ANOVA and can be used to compare non-normal distributions of repeated measurements. Like the Kruskal-Wallis test, the Friedman test is based on ranks, although the Friedman ranks are calculated differently.

### Follow-up Tests

The ANOVA is an omnibus test and a statistically significant F-value must be further explored with follow-up tests. These tests may be *a priori* (planned before analyzing the data) or *post-hoc* (performed after the data has been analyzed). They assess which particular groups in a study are different from each other or test other particular experimental hypotheses. Some of the best known post-hoc comparisons are Scheffé's test, Tukey's HSD test and the Newman-Keuls method.

### Power and Effect Size

Statistical power analysis is frequently used in ANOVA designs to determine the sample size required to reject the null hypotheses at a certain level of certainty. The power analysis takes into account the ANOVA design, effect size in the population, sample size and  $\alpha$  level.

Effect sizes can be calculated from an ANOVA to measure the strength of association between independent or predictor variables on the dependent variable. One common measure of effect size in ANOVA designs is eta-squared ( $\eta^2$ ) which describes the ratio of variance explained in the dependent variable by an independent variable or predictor while controlling for other predictors. Omega-squared ( $\omega^2$ ) is a measure of the strength of the treatment effect for fixed effects ANOVA and the intra-class correlation is an effect size measure for random effects ANOVA.

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](mailto:dstaley@mts.net) or directly at 237-2690.

**\*REVISED\* Standard Operating Procedures – March 15, 2011 Edition now available!**

The Office of Clinical Research is please to announce that the 2011 edition of the St. Boniface Hospital “Manual of Standard Operating Procedures for Clinical Research” is now available for distribution. All Investigators and Research Nurses / Coordinators directly involved with Clinical Research are required to sign off on the SOPs as a condition for Institutional (RRC) approval.

If you are an Investigator or Research Nurse/Coordinator actively involved in Clinical Research who would like to receive a hard copy of our SOP manual, or if you have any questions please contact Terry Sawicz-Hanesiak at 237-2226 . SOPs are also available on the INTRANET at:

<http://intranet.sbggh.mb.ca/DeptOCR/SOPManual.html>

REMEMBER - Going forward, all new submissions and amendments will require the new 2011 SOP agreement be signed and returned to the OCR before approval will take place.

**\*REVISED\* Clinical Research Information Pamphlet – now available for ordering**

The Office of Clinical Research has recently revised the bilingual information pamphlet entitled “Taking Part in Clinical Research Studies at St. Boniface Hospital”. Hard copies of the bilingual pamphlet can be ordered using a “Stock Requisition – Catalogue Items” form. The hospital catalogue number of the clinical research pamphlet is 7102 6090 1. You can also view the questions and answers that are on the pamphlet on our INTERNET site:

<http://www.sbrca.ca/content/blogcategory/91/136/#faq62>

**The Clinical and Research Nursing Network of Manitoba (CRNN)**

The Clinical and Research Nursing Network of Manitoba (CRNN) was established in 1994. It is a group of nurses and allied health professionals who share an interest in clinical practice and research practice related to health. CRNN is committed to the promotion of a communications network and the establishment of a forum for ongoing education. There are three dinner meetings per year. Membership Fee is \$50.00 per calendar year

For further information or to become a member, please contact the CRNN Treasurer

Norma Reinhardt RN  
c/o Diagnostic Imaging JK1  
Health Science Centre  
**820 Sherbrook St.**  
Winnipeg, MB R3A 1R9

**U of M Research Ethics Boards –Question about Case Reports – Do they need REB approval?**

The following information is copied directly from the BREB/HREB website:

<http://umanitoba.ca/faculties/medicine/ethics/2086.html>

**“Case Report Studies**

Our general approach to case reports is to request that authors obtain the patient’s consent whenever possible, write up the case study, and then submit it to the Health Research Ethics Board (HREB) before sending it off for publication. We review the case report largely to assess the risk that patient identity may be inadvertently revealed by the author(s) in the write-up. This is our primary concern in this situation. If the probability of inadvertent identification of an individual is unacceptably high (e.g. very rare condition, a lot of demographic data is provided in the write-up, etc.) we will request changes (that hopefully don’t result in the loss of critical information) designed to lower the risk of inadvertent individual identification from the publication of the case report. In cases in which patient/family consent is either impossible or extremely difficult (and thus quite impractical to obtain) as well as cases in which attempting to obtain consent from a living or from the family of deceased patient would be too traumatic for those involved we may waive the requirement for consent on a case-by-case basis.

Case Report Submission Requirements;  
Cover letter (include a brief description of consent process)  
Consent form (unsigned template presented to patient/individual)  
Case Report article

Please contact Shelly Rempel-Rossum at 789-3389 if you have any question regarding ethics review and approval of case report studies.”

## Research Review Committee at St. Boniface Hospital

### Deadlines for RRC Submission

March 30, 2011  
April 27, 2011  
May 25, 2011

### Meeting Date

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.sbr.ca/content/blogcategory/87/132/>

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

### Deadline for REB Submissions

March 14, 2011  
April 4, 2011  
May 16, 2011  
June 13, 2011

### Meeting Date

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

### **Critical Care Research in Progress (April to June – Time: 12:15 – 1:15 PM)**

Date	Location	Presenter
April 13	HSC GC434	<u>H</u> eparin <u>A</u> nticoagulation to reduce <u>D</u> eath in <u>S</u> eptic Shock:
	SBGH BG002	The HADES Pilot - Ryan Zarychanski
May 11	HSC GC434	Delirium in the ICU - Rakesh Arora
	SBGH C5004	
June 8	HSC GC434	TBA - Kendiss Olafson
	SBGH C5004	

### **Tri-Council Policy Statement – 2 aka “TCPS 2” - Regional Workshops – May 19 and 20, 2011**

On May 19<sup>th</sup> and 20<sup>th</sup>, the University of Manitoba will welcome the Interagency Advisory Panel on Research Ethics (PRE) here at both the Bannatyne and Fort Garry campuses. More information is provided in the attached March 2011 U of M “Research Quality Management Newsletter”.

### **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. 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](http://www.lsam.ca/calendar.cfm)