



Hôpital St-Boniface Hospital

Clinical Trial Research News

From the Office of Clinical Research

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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.

Announcement

Welcome!

The Office of Clinical Research is pleased to introduce the following new staff member;

Joanne Riddell – OCR Administrative Secretary and Recording Secretary for the RRC (phone: 235-3623)

Statistics and Medical Research

Regression Analysis

Regression analysis is one of the most widely used statistical techniques in scientific research and has many useful applications in the field of medical research and study. Regression techniques were first developed in the early 1800s from the mathematical theory of least squares and gained prominence from the work of biologist Francis Galton. He studied the phenomenon later known as "regression toward the mean" by empirically demonstrating that the descendants of tall ancestors tend to regress downward over time to more average values. Galton's work was extended by statisticians Karl Pearson and R.A. Fisher who developed the statistical underpinnings of regression by describing the properties of the joint distribution between dependant and independent variables.

Statistical Basis of Regression

Regression analysis is used for prediction and forecasting, determining which independent variables are related to a dependent, outcome or criterion variable, and exploring the nature of the dependant-independent relationship. In a more technical sense, regression analysis enables the researcher to understand how the dependant variable (Y) changes when one of the independent variables (X) is varied, while the other independent variables are fixed. The purpose of linear regression is to specify a functional relationship between X and Y so that Y can be predicted from X. Regression analysis fits a straight line or *regression line* to the points in a joint distribution, using the criteria of least squares.

Regression is based on the correlation between dependent and independent variables. In the simplest case, with one dependent and one independent variable (simple linear regression), the pair of scores of each subject in the sample data can be plotted as a scatter diagram. A regression line is then mathematically fitted to the data points to produce the best predictive fit. For a perfect correlation, $r = +1.0$ or $r = -1.0$, all the data points are precisely aligned in a linear slope and the corresponding regression line is a perfect fit, enabling the researcher to exactly predict the values of one variable from the values of the other variable. When there is no correlation between variables, $r = 0$, it is not possible to make a prediction. The higher the correlation between variables, then the greater the degree of the prediction.

The regression equation is written as $Y = a + bX$ where:

- Y = dependent variable
- X = independent variable

- a = the intercept constant and is equivalent to the value of Y when $X = 0$
- b = the regression coefficient or slope of the regression line, showing the rate of change in Y with a unit change in X

Evaluation of the Regression Model

The goodness of fit of the regression equation is usually evaluated by calculating the R-squared index (amount of variance accounted for), while statistical significance is usually measured by an F-test of the overall fit and t-tests of individual parameters such as the b value or regression coefficient. There is always a degree of error in prediction. The *standard error of estimate* is the measure of the error in predicting the dependent variable from the independent variable(s) and can be used to construct confidence intervals (CIs) around predictive scores (typically 95% or 99% CIs).

Assumptions

Regression analysis is based on a number of fundamental assumptions;

- The study sample must be representative of the population in order to make valid inference predictions.
- Observations or scores of the dependent variable are independent and normally distributed. However the independent variables are not required to be normally distributed.
- There must be a linear relationship between the dependent and independent variables rather than a non-linear relationship.
- The variance of scores from the regression line (called residuals) is uniform for all values of the dependent variable, a property termed *homoscedasticity* (the roots of this word mean "equal spread").

Types of Regression Analysis

There are a number of forms of regression analysis other than simple linear regression:

- Multiple regression is an extension of simple linear regression. Adding new independent variables to the regression equation increases the amount of variance accounted for in the dependent variable, thereby increasing the accuracy of the prediction. The interpretation of multiple regression coefficients is more complicated than simple linear regression.
- Logistic regression is used when the dependent variable is bi-variate or dichotomous, i.e. has only two outcomes (male/female; patient/control). The independent variables may be categorical, ordinal or interval scaled.
- Advanced methods of regression analysis include nonparametric regression, time series and curve fitting analysis, Bayesian regression methods and trend estimation.

Selecting Variables for Regression

One of the aims of regression analysis is to find the smallest group of independent variables that will account for the greatest proportion of variance in the dependent variable. A number of procedures have been developed to maximize the predictive power of the regression equation:

- Forward solution: The independent variable with highest correlation with the dependent variable is entered first, followed by the next variable which will yield the greatest increase in R-squared, and subsequently followed by variables with the highest partial correlation with the dependent variable.
- Backward solution: All of the independent variables are entered into the equation to create the maximum R-squared value. Then variables are deleted, one at a time, to determine their effect on R-squared. The most robust variables are retained in the final regression equation.
- Stepwise solution: This method combines the forward and backward procedures and overcomes many of the statistical difficulties associated with the other two solutions by controlling the entry of independent variables into the regression equation based on maximum predictive power.

Common Errors in Regression Analysis

- Correlation and regression methods are used to measure the degree of linear relationship between variables. If the calculated correlation and regression coefficients indicate no relationship or predictive power it does not mean that there is no association between dependent and independent variables. There may be, for instance, a significant curvilinear, exponential or other non-linear association.
- Researchers must be careful when using regression analysis in attempting to make predictions based on values outside the range of the observed data. Serious errors often result through such a process of extrapolation since the regression relationship that holds for a particular range of data may not be valid outside this range.
- Predictions made on the basis of correlation or regression analysis do not imply causality. A statistically significant correlation or regression relationship does not mean that there is a cause and effect relationship, only that there is an association.
- A statistically significant correlation or regression coefficient does not necessarily imply a meaningful clinical finding. If the sample size is sufficiently large, for example, highly statistically significant p-values may be obtained for correlation coefficients or regression equations, but the findings may have no practical value whatsoever.

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.

Research Review Committee at St. Boniface Hospital

Deadlines for RRC Submission

Meeting Date

SEE PAGE 4 OF THE NEWSLETTER FOR A COMPLETE LIST OF DEADLINES & MEETING DATES FOR 2012

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

Contact the RRC 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.sbrca.ca/content/blogcategory/87/132/>

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

Deadline for REB Submissions

Meeting Date

SEE PAGE 4 OF THE NEWSLETTER FOR A COMPLETE LIST OF DEADLINES & MEETING DATES FOR 2012

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

Study Coordinator Training Program - January 27 & 28, 2012 – EDMONTON, AB

Weiser Research, Inc. is conducting a two day intensive training program created for Canadian study coordinators to enhance their skill set and knowledge base of clinical trial research. This course is filled with practical, hands-on presentations and workshops and has been designed for coordinators at all levels including veteran coordinators and those working in a hospital, private clinic, emergency room or critical care setting. Both sessions must be attended to receive a course certificate. Note: Space will be limited to 24 people and is open to coordinators on a first-come first-serve basis. More information is available at www.clinicaltrials.ualberta.ca/resources_education.php

Manitoba First Nations Research Conference – February 7-8, 2012

The Assembly of Manitoba Chiefs (AMC), Chiefs Task Force on Health (CTFoH) and Health Research Information Governance Committee (HIRGC) are hosting the first Manitoba First Nations Research Conference on February 7 & 8th, 2012 to be held in Convocation Hall at the University of Winnipeg. This conference will bring together First Nations community and academic researchers, students, Elders, and leadership in the Manitoba region to showcase the Self Determination of First Nations thru Health Research, Ethics and Ethics Review.

More information can be found at www.manitobachiefs.com/mfnrc2011.html or please contact Leona Star at: The Assembly of Manitoba Chiefs, Toll Free: 1-888-324-5483, Direct Line: 204-957-8457 or E-mail: lstar@manitobachiefs.com

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

Study Submission Deadlines 2012

ST. BONIFACE HOSPITAL

2012 RRC Submission Deadlines 2012 RRC Committee Meeting Dates
 Submission must be received in N1004 by 11:00 a.m. of deadline date

January 4	January 11
January 25	February 1
February 29	March 7
March 28	April 4
April 25	May 2
May 30	June 6
NO MEETING IN JULY	
July 25	August 1
August 29	September 5
September 26	October 3
October 31	November 7
November 28	December 5

Submissions due no later than 1 week prior to meeting dates

UNIVERSITY OF MANITOBA - BANNATYNE

2012 REB Submission Deadlines 2012 REB Committee Meeting Dates

January 9	January 23
February 13	February 27
March 12	March 26
April 10	April 23
May 14	May 28
June 11	June 25
NO MEETING IN JULY	
August 13	August 27
September 10	September 24
October 5	October 22
November 9	November 26
November 26	December 10

Submissions due no later than 2 weeks prior to meeting dates