



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.

Statistics and Medical Research

Factor Analysis

Factor analysis is a powerful statistical technique that has broad applications in medical and scientific research. Basically, factor analysis is a method of data reduction whereby a large number of variables are grouped into a smaller number of "factors" without losing essential information. Factor analysis examines the variability and inter-correlations among observed variables to uncover an underlying structure reflected in a smaller number of unobserved or latent factors, thereby reducing the total number of variables in a data set.

Three pioneering researchers in the field of psychometrics are generally credited with the development and widespread application of factor analysis. English psychologist and statistician Charles Spearman studied the pattern of children's test scores on a wide range of seemingly unrelated school subjects and found that they were positively correlated, suggesting the presence of an underlying general mental ability which he called *g*. Raymond Cattell expanded Spearman's work based on his own psychometric testing and use of factor analysis to develop a multi-factor theory of intelligence and personality. His central belief was that theory should be derived from research and empirical observation and not vice versa. Finally, American psychologist Louis Thurstone formulated a model of intelligence based on independent "primary mental abilities" which were derived from factor analysis. His seminal 1947 publication *Multiple-Factor Analysis* is credited with introducing factor analysis to a wider academic and research community. The early factor analysis investigators labored in their work without the use of high-speed computers. The complicated calculations involved in the complex factor analytic mathematical procedure were done by hand and teams of graduate students often worked days and even weeks to produce results which today's computers can generate in less than a second.

Type and Applications of Factor Analysis

The most common form of the procedure is "exploratory factor analysis" which seeks to reveal the underlying structure or pattern of the relationship between a large set of variables. "Confirmatory factor analysis" attempts to determine if the factor structure of a set of variables is consistent with what would be expected on the basis of a pre-determined theory or published factor analytic research on the same variables. The major practical applications of factor analysis are data reduction, instrument development and theory development:

- One goal of scientific inquiry is *parsimony* or simplicity of explanation. Factor analysis, by reducing the amount of data, provides a means of creating one or more composite variables (factors) out of a large set of variables. These factors may then be used in subsequent data analysis (e.g. regression or analysis of variance).
- Factor analysis can play a significant role in the creation of new measurement tools and instruments. For instance, items on a psychometric test may be evaluated by factor analysis to determine which items are central to the construct being measured and which are redundant or irrelevant.

- Scientific research is based on the building of theories to explain phenomena. Factor analysis can play a crucial role in exploratory levels of research which lead to theory development by identifying constructs which unite a set of elements, explore relationships between variables, build systems of classification and test hypotheses.

Assumptions

Factor analysis is based on the correlation matrix of a set of variables and the same basic assumptions which pertain to bivariate correlations also hold:

- A representative sample for the study should be randomly selected from the population.
- The relationship between variables must be linear rather than non-linear (e.g. curvilinear or skewed).
- Variables should be normally distributed.

Variables which do not meet these criteria are best removed from the factor analysis. As well, the number of variables in the factor analysis should be related to the sample size of the study. As a general rule of thumb, a ratio of at least five subjects for each variable is desirable in order to generalize from the study sample to a wider population.

Computational Procedure

Factor analysis proceeds through a specific, well-defined computational procedure which leads to a final solution:

- The initial stage is the calculation of a correlation matrix between the variables in the study.
- The second step is the creation from the correlation matrix of an unrotated factor matrix (where rows = variables, columns = factors) in which the amount of variance accounted for by each successive factor is maximized. For instance, factor I may account for 27% of the variance between variables, factor II 16% and so on.
- The elements or values in the factor matrix are unrotated *factor loadings* — numbers ranging from -1.00 to +1.00 — which may be thought of as “correlations” between each variable and each factor. The squared factor loading is the percentage of variance in a variable explained by a given factor. The sum of the squared factor loadings for all factors for a specific variable is called the *communality*. Likewise, the sum of squared loadings for each factor is called the *eigenvalue* for the factor and represents the total amount of variance in the total sample explained by a factor. The higher the eigenvalue the greater the amount of variance explained.
- To determine the number of potentially interpretable factors contained in the data either factor eigenvalues or percentage of variance explained are used. Typically, researchers interpret factors which have eigenvalues > 1 (sometimes using a *Scree plot* to refine the decision process) or account for at least 5% of the variance.
- The final stage is to create a rotated factor matrix from the unrotated factor matrix. This process aligns variables which are highly correlated with each factor and allows the factors to be meaningfully interpreted. The most common method of rotation is *Varimax* rotation based on an orthogonal rotation of the factor axes but other methods are also available (*Equimax*, *Quatrimax*, *Oblique*).

Interpretation of Factors

The interpretation of the factor structure of a set of variables is both a science and an art. There is no one final definitive interpretation and researchers often try multiple interpretations before settling on the most meaningful solution based on the empirical results of the factor analysis, knowledge of the area of research under investigation, previous research, and intuitive insight. More than any other statistical technique, factor analysis requires the full exercise of one’s creative potential.

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.

REMINDER - 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.

Panel on Research Ethics Launches the TCPS 2 Tutorial

The Interagency Advisory Panel on Research Ethics (Panel) is pleased to announce the launch of a new, online tutorial, [TCPS 2: Course on Research Ethics \(CORE\)](#). CORE supersedes the introductory tutorial that supported the 1st edition of the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (TCPS), developed in 1998 by Canada's federal research agencies – the Canadian Institutes of Health Research (CIHR), Natural Sciences and Engineering Research Council of Canada (NSERC), and the Social Sciences and Humanities Research Council of Canada (SSHRC). CORE was designed to support the 2nd edition of the TCPS (TCPS 2) that was released by the Agencies in December 2010.

CORE is an educational resource primarily for researchers and research ethics board members who wish to increase their familiarity with TCPS 2. It is designed to be done independently, and can be completed at the user's own pace, in a single session or a series of sessions – depending on the extent to which each user chooses to explore the associated case studies, multi-disciplinary examples and media excerpts.

CORE consists of eight modules that cover the general guidance in TCPS 2. The modules target subjects such as consent, privacy, conflict of interest, and fairness and equity in research participation. CORE presents multi-disciplinary scenarios that depict a broad spectrum of realistic research situations and the ethical dilemmas they present. Interactive exercises put users in the role of participants, researchers and REB members and require them to make decisions regarding these ethical questions. Media-rich materials focus on Canadian content. Links to relevant articles in TCPS 2 appear throughout the course.

The Panel intends to update CORE on an ongoing basis with the addition of new scenarios, exercises and quiz questions. Tutorial users are encouraged to provide feedback by participating in an online survey that is available upon completion. They are also welcome to submit case studies relevant to their individual disciplines for possible inclusion. In a second phase, the Panel is planning to add modules on more specialized TCPS 2 chapters, such as Clinical Trials and Qualitative Research. The first such module, on research with First Nations, Inuit and Métis Peoples, is currently under development.

You may access CORE at: www.pre.ethics.gc.ca/eng/education/tutorial-didacticiel/.

Please note: for all researchers submitting an ethics protocol for U of M REB review, the REB deadline to complete the CHRPP or CORE tutorial remains September 1, 2011. Those who have already completed the CHRPP tutorial will NOT be asked to complete the CORE tutorial. For further information, please feel free to contact the Research Quality Management Office at 272-3121.

Reminder from the REB Regarding Continuing Approval/Annual Approval

This notice is being sent to remind all sites of their responsibility to ensure continuing approval is obtained by the expiry date noted on either the initial or annual certificate of ethical approval.

Over the past couple of months the University of Manitoba Research Ethics Boards (REB) have noted that funding agencies and regulatory bodies are enforcing annual approval dates by suspending study activities and suggesting that data collected during lapse in approval will not be used in data analysis.

Unfortunately, the REBs are unable to grant retrospective approval for lapses in approval. Therefore, it is imperative that the research sites submit a hard copy of the annual study status report along with the consent forms presently in use for review within **3-4 weeks of the expiry date** noted on the initial certificate of approval or last annual approval certificate. For studies funded by **US Federal Funds (e.g. NIH, CDC, Veteran Affairs, etc.)** there may be a requirement under the Federal Wide Assurance for the study to have annual review by the full board. In these instances we ask that you review the requirements for full board submissions on the website or contact our office to ensure the annual reports and required documentation are received **4-6 weeks prior to the expiry date** noted on the last initial approval or annual approval certificate.

The responsibility lies with the research site to ensure all approvals are in place and up to date. At this time the REB does not have the resources or capability to send regular reminder notices regarding upcoming expiry dates and thus request research sites are diligent in ensuring these reports are submitted on time by marking their calendars with these important dates. As the REBs adopt a new database for tracking REB submissions we hope to be able to send automated reminder notices to researcher in a systematic fashion 8 weeks – 10 weeks prior to the expiration of the study.

Thank-you for your attention to this matter. If you have any questions regarding this notice please contact Lynne Wichenko at 789-3255 or Shelly Rempel-Rossum at 789-3389.

Message from the REB regarding ClinicalTrials.gov

Please consider the following information as required by FDA.

"The FDA has issued a final rule requiring drug developers to include in informed consent paperwork the disclosure that clinical information from the trial will be entered onto ClinicalTrials.gov.

The rule—21 C.F.R. § 50.25 in Section 801 of the FDA Amendments Act of 2007 (FDAAA)—was effective March 7, but the compliance date is exactly one year later for trials initiated on or after the compliance date. That means the FDA intends to enforce the rule only for informed consent documents and processes for clinical investigations begun on or after March 7, 2012. Trials begun prior to that date will not be required to modify their consent process or to re-consent subjects.

The new rule requires sponsors to include this exact wording in their consent paperwork: "**A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.**"

It amends 21 C.F.R. § 50.25 and the requirements for informed consent documentation and process in FDA-regulated clinical trials of drugs, biological products and medical devices, in an effort to increase transparency.

The regulation states, "Alerting potential clinical trial participants to the existence of a publicly accessible databank, whether in the informed consent or during the process, can reassure them that a transparent system exists to help ensure greater accountability and responsibility of investigators."

For complete announcement on this notice please refer to the following website:

<http://www.centerwatch.com/news-online/headline-details.aspx?HeadlineID=1284>

<http://edocket.access.gpo.gov/2011/pdf/2010-33193.pdf>

The Bannatyne Campus Research Ethics Boards will remind researchers of this requirement and will likely apply the rule to all studies that require registration on the Clinical Trial.gov website. Please review your consents prior to submissions to ensure applicable studies have this wording included in the consent form.

BREB Announcement: New Biomedical Research Ethics Board Chair

Dr. Brian Postl, Dean of Medicine, would like to sincerely thank Dr. Nick Anthonisen for his important contributions to the Faculty as Chair of the Biomedical Research Board for the past 11 years. Dr. Anthonisen will step down as Chair on July 1, 2011 after serving as a dedicated member of the committee for more than 12 years and providing leadership and research expertise to the board. Dr. Anthonisen, former Dean of the Faculty of Medicine, is also a distinguished academic researcher.

Dr. Lindsay Nicole, a prominent ID specialist and former Department Head of Internal Medicine, will assume the position of BREB Chair effective July 1, 2011. Dr. Lindsay has research experience as a Principal Investigator and has held administrative roles within the HSC and U of M.

Research Review Committee at St. Boniface Hospital

Deadlines for RRC Submission

July 27, 2011
August 31, 2011
September 28, 2011
October 26, 2011
November 30, 2011

Meeting Date

August 3, 2011
September 7, 2011
October 5, 2011
November 2, 2011
December 7, 2011

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

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

Deadline for REB Submissions

August 15, 2011
September 12, 2011
October 11, 2011
November 14, 2011
November 28, 2011

Meeting Date

August 29, 2011
September 26, 2011
October 24, 2011
November 28, 2011
December 12, 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

Fall 2011 – Clinical Research 3 Part Lecture Series at St. Boniface Hospital

Interested in getting involved in Clinical Research? Clinical research refers to all research conducted with human subjects. These comprehensive introductory courses are specially designed for individuals with little to no previous research experience or those wanting a “refresher” on the latest information. The courses will present an overview of the language of clinical research, project design, roles and responsibilities of the Investigator and the research staff, and the regulatory and ethical environment for the conduct of clinical research.

Lecture Title	Date and Time	Location
Introduction to Clinical Research And Research Ethics	Tuesday, November 1, 2011 1:00 PM to 3:00 PM	St. Boniface Hospital Room N1012
Good Clinical Practice (GCP) and Clinical Research Regulations	Tuesday, November 15, 2011 1:00 PM to 3:00 PM	St. Boniface Hospital Room N1012
Clinical Research Project and Document Management	Tuesday, November 29, 2010 1:00 PM to 3:00 PM	St. Boniface Hospital Room N1012

There is no charge to attend the lecture series but registration is required. For more information or to register contact Terry Sawicz-Hanesiak at (204) 237-2226 or 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. 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

Save the Date!

“Ethical Considerations in Research”

Wednesday, October 12, 2011 – Afternoon
Samuel Cohen Auditorium
St. Boniface Hospital Research Centre

More details to come later this summer from the U of M Research Quality Management Office!