

## Letter from the Director

Welcome! As I transition to the position of CHRP Director this is my first issue writing this letter. I would like to thank Dr. Kimberly Galt for her tireless efforts as CHRP Director over the past 10 years. Our growth from a health services research program to a university-wide center would not have been accomplished without her vision and hard work. I would also like to thank the faculty and staff of CHRP for their continued support. You have made this a smooth transition for me and I look forward to many years of working together to advance the health services research agenda at a local, regional, and national level.

This issue features a methods article on meta-analysis, presents a wrap-up of the Grants Boot Camp workshop series, and shares with you a student reflection on the value and importance of interprofessional patient safety education.

This will also be the last CHRP newsletter until the fall, as we will be undergoing a small transformation to enhance our content. The new and improved CHRP newsletter will be published on a quarterly basis. Expect regular columns highlighting health policy issues, student research, a continuation of the methods series, and spotlights on nationally-relevant studies impacting the field of health services research.

I look forward to continue advancing the important work of CHRP and hope you will all join me on this journey!

Kevin Fuji, Pharm.D., M.A.  
Director

## Volume 5, Issue 3

Summer 2014

## Synthesis through Meta-analysis

By William Raynovich, N.R.E.M.T.P., Ed.D., M.P.H.

Bringing about an evidence-based change to clinical practice standards requires strong positive scientific evidence, for which the gold standard is the existence of several statistically significant double-blind randomized controlled trials. Often, as the knowledge base about new therapies is building, the early evidence consists of several published reports of observational studies and just a few small clinical trials, none of which is individually powerful enough to provide a compelling recommendation for or against the accepting the proposed new therapy as a standard of care. One approach to formulating a compelling case for adopting a new therapy is to synthesize a compelling recommendation based on a combination of the published studies. There are two main types of evidence-based synthesis: the systematic review and the meta-analysis. Most consumers of research intuitively understand the principles underlying systematic reviews, which summarize the conclusions among various published studies. The meta-analysis goes one step further and reports a statistically significant finding that is based on the combined studies.

*The modern history and application of the meta-analysis*

The first modern-era meta-analysis was published in the

psychiatric literature nearly 40 years ago.<sup>1</sup> Earlier examples have been cited, including one that was reported to have been published in the 12<sup>th</sup> century in China and in the 17<sup>th</sup> century in the British Medical Journal.<sup>1,2</sup> Healthcare disciplines have benefitted from synthesized results developed by meta-analysis over these past four decades. For example, in the early 1980's, eight studies reported on the effectiveness of streptokinase, a 'silver bullet' enzyme for breaking up blood clots in patients suffering from a myocardial infarction. Only three of the early studies reported statistically significant results, however, and even in these three studies, the treatment groups were too small to have the power to make a compelling treatment recommendation. A meta-analysis that combined the results of all of the studies produced a compelling recommendation in support of the clinical use of streptokinase. This resulted in a significant reduction in mortality and subsequent studies over the past two decades have validated the recommendation.<sup>3</sup>

The application of the meta-analysis to synthesize evidence-based recommendations has been steadily increasing over the past four decades and the standards for conducting a meta-analysis are becoming more rigorous.<sup>4</sup> In 2009, a

standards statement was updated as the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses, or PRISMA*.<sup>5</sup> Other standards have been published for evaluating observational (cohort) studies.<sup>6</sup>

The meta-analysis has been widely criticized for many reasons, including:<sup>7</sup>

- combining the results of multiple studies that employed different methodologies, in effect, 'adding apples and oranges';
- accepting the results of underpowered, poorly executed, and statistically insignificant studies, effectively artificially amplifying the weak and insignificant results to make them appear significant;
- including only published studies that have strong positive findings;
- including only studies that support the conclusion of the meta-analysis.

If these criticisms were valid, the meta-analysis would not be acceptable for developing an evidence-based clinical practice recommendation. However, the *PRISMA, Strengthening of Reporting of Observational Studies in Epidemiology (STROBE)* and other statements prescribe rigorous standards that require all of these points to be addressed when carrying out the analysis and the ways that these

(Continued on page 2)

(Continued from page 1)

## Synthesis through meta-analysis

issues were addressed are to be published in the meta-analysis paper.<sup>5,6,8</sup> Further, it is noteworthy that a well-executed meta-analysis goes even further and is actually required to also include all contrary evidence, regardless of whether the research reports were published and regardless of the sources of the evidence. Thus, it is the meta-analysis methodology that actually attempts to neutralize biases, such as authorship bias (the tendency to only submit reports that are likely to be accepted for publication), reviewer bias (the tendency for editorial reviewers to reject views that are contrary to their own set of beliefs) and publication bias (the tendency of journals to favor publication of positive results that match conventional wisdom).<sup>9</sup>

### Rationale in support of synthesis by meta-analysis

When different investigative teams set out to address one therapeutic question, differences in methodologies, techniques, and even seemingly minor details inevitably occur. For example, one research team might study a particular dosage of an antihypertensive agent with a certain size effect, e.g., a change in diastolic blood pressure of 10 mm Hg within two hours of administration and a mean duration of clinical effect of 12 hours, as well as a set of inclusion criteria, such as a history of moderate hypertension in the research subjects. Other research teams may study the same drug but design their studies to specify different

dosages, alternate forms of the drug, different effect sizes, and different inclusion criteria, such as studying those with a history of more severe hypertension. Thus, the validity question: is it valid to combine the results of such varying studies (i.e., apples and oranges) into one outcome?

The proponents of the meta-analysis methodology note the different studies have a quality of homogeneity that is found in the underlying research question and that it is in the results of that common ground that the meta-analysis specifically analyzes. Consider, too, that all of the scientific literature must be critically evaluated in the context of different study designs and investigator techniques and that conclusions about the body of knowledge is always based on the convergence of multiple sources of evidence.

Next, even if one accepts that different studies can be combined to form a single generalized result, it is not intuitively clear that combining several statistically insignificant studies allows one to infer the statistical significance of the synthesized result. This practice, however, has been empirically validated by innumerable follow-up studies that have been conducted over the past four decades.

Last, as noted above, some have criticized the meta-analysis methodology for including only those studies that support the final outcome, or 'cherry picking' the evidence for inclusion. However, the opposite is true. A well-conducted rigorous meta-analysis does include *all* obtainable evidence, including any contrary evidence, occult

evidence (e.g., research that was never submitted for publication), grey literature (e.g., papers that were presented at conferences but not published, technical reports), and even papers published in obscure (e.g., non-indexed, no ISSN, or non-peer-reviewed) journals. Thus, a well-conducted meta-analysis is the only methodology that critically evaluates every source of data and from an unbiased perspective.

### Conclusion

A well-executed meta-analysis provides a definitive practice recommendation that is based on a statistically significant result. The result of a well-executed meta-analysis that meets PRISMA and other published standards includes all of the evidence available from every source. The rationale for conducting or accepting a meta-analysis recommendation is the importance of deriving a clinical recommendation although there may only exist several weakly powered and statistically insignificant research reports. The consumers of meta-analyses should be familiar with the rigorous standards for executing and evaluating meta-analyses and they should be able to critically evaluate the validity of the reports and their findings in order to make valid and defensible practice recommendations.

### References:

1. Russo MW. How to review a meta-analysis. *Gastroenterol Hepatol.* 2007;3(8):637-642.
2. Nordmann AJ, Kasenda B, Briel M. Meta-analysis: what they can and cannot do. *Swiss Med Wkly.* 2012;142:w13518.
3. Stampfer MJ, Goldhaber SZ, Yusuf S, Peto R, Hennekens CH. Effect of intravenous streptokinase on acute

myocardial infarction: pooled results from randomized trials. *N Engl J Med.* 1982;307:1180-1182.

4. Brand RA. Standards of reporting: the CONSORT, QUORUM, and STROBE guidelines. *Clin Orthop Relat Res.* 2009;467(6):1393-1394.
5. Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. *Lancet.* 1999;354(9193):1896-1900.
6. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009;6(7):e1000097.
7. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, STROBE Initiative. The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol.* 2008;61(4):344-349.
8. DeCoster J. Meta-analysis Notes. <http://www.stat-help.com/meta.pdf>. Accessed June 1, 2014.
9. Mahoney MJ. Publication prejudices: an experimental study of confirmatory bias in the peer review system. *Cognit Ther Res.* 1977;1(2):161-175.

## Grants Boot Camp Workshop Series Concludes

By Barbara Bittner, M.A., Beth Herr, M.P.A., C.R.A., David Cloutier, M.S., M.B.A.

The Center for Health Services Research and Patient Safety (CHRP) in partnership with the Office of Research and Compliance Services concluded the second offering of the Grants Boot Camp Workshop Series on April 10, 2014 with a session on Post-Award Management.

The series sessions addressed key events through a typical grant lifecycle: locating funding opportunities, grant writing tips and tricks, reading and interpreting funding guidelines, formatting a proposal and using language effectively, budget preparation, scientific or peer review process, grants submission process and website tools, and post-award management.

The series also provided the

opportunity for attendees to meet with key representatives of Creighton University's pre-award and post-award support services.

The success of the Grants Boot Camp series is due to the expertise provided by the presenters and discussion leaders, to whom we give thanks:

- Barbara Bittner, M.A., Senior Communications Manager, Sponsored Programs Administration
- Michon Bowen, Manager, Accounting Services
- David Cloutier, M.S., M.B.A., Director, Research Center Management and Development
- Laurie Cook, Finance

Manager, School of Dentistry

- Kimberly Galt, Pharm.D., Ph.D., Assistant Vice Provost for Multidisciplinary Health Sciences Research
- Beth Herr, M.P.A., C.R.A., Director, Sponsored Programs Administration
- Sonia Rocha-Sanchez, Ph.D., Associate Professor, Department of Oral Biology
- Patrick Swanson, PhD, Professor, Department of Medical Microbiology & Immunology

The sessions were open to faculty, staff, students, and members of the community. Each of the Creighton Schools and Colleges were

represented in the audience during the series.

Attendees provided valuable suggestions for additional material and interest areas to address in the next Grants Boot Camp series. Several participants recommended facilitated workgroup sessions to review specific funding opportunities and share ideas for proposal responses.

Please visit the CHRP website for more information about the workshop series and to access materials from the presentations: <http://spahp.creighton.edu/departments-offices/chrp/grants-boot-camp>.

## Student Reflection on IPE 410 Interprofessional Foundations in Patient Safety

By Kellye Oishi

My enrollment in IPE 410, Interprofessional Foundations in Patient Safety, familiarized me with patient safety issues and precautions and how they are applicable to various health professions and settings.

Health care involves a very complex system, which contains many opportunities for error, especially since many individual professionals are responsible for a designated and limited part of the entire process. In IPE 410 we learned of many areas within health care systems that could contribute to better patient safety

outcomes. One of these areas involved filling in health care gaps by working as a team.

Team-oriented health care delivery involves health professionals working together - even though they are in different professions. By working as a team, health care providers act as a comprehensive unit to deliver the necessary care to patients and ensure there are no gaps in care. We also learned that the practice of open discussion between the different professions leads to better patient outcomes and can lead to fewer lawsuits.

These are just a few of the many topics we covered over the semester that truly sparked my passion of helping to improve access, quality, cost, and satisfaction of care through focusing on patient safety and becoming a patient-oriented pharmacist in the evolving health care world.

I believe that my exposure to current, successful methods of practicing patient safety and to the issues of patient safety will be highly beneficial to me when I am a pharmacist. IPE 410 offers valuable information that informs students on how to improve safety as a health

professional as well as raises awareness on how to be a better consumer/patient of health care. This course is highly beneficial for current or future health care professionals and even students with a non-health care focus. I am and will be forever grateful for my gained knowledge and awareness of patient safety that IPE 410 has provided.

*Kellye Oishi graduated from Creighton University in 2014 with a Bachelors of Science in Health Administration and Policy. She is interested in pursuing a career in the profession of pharmacy.*

Center for Health Services  
Research and Patient Safety  
2500 California Plaza, Boyne 143  
Omaha, NE 68178

Phone: 402.280.4411

Fax: 402.280.4809

E-mail: [chrpinfo@creighton.edu](mailto:chrpinfo@creighton.edu)

<http://chrp.creighton.edu>

#### Editorial Committee

##### Editors-in-Chief

Amy Abbott, Ph.D., R.N.

Kevin Fuji, Pharm.D., M.A.

##### Contact for Contributions

402.280.4411

[chrpinfo@creighton.edu](mailto:chrpinfo@creighton.edu)

The Creighton University Center for Health Services Research and Patient Safety was founded to coordinate and support research and training efforts among faculty within an interdisciplinary and collaborative research environment. Faculty and staff serve the research interests of governmental agencies, health care facilities, employers, health care industry companies and educators.

Mission Statement: The Center for Health Services Research and Patient Safety conducts health services research to improve quality, safety and efficiency of patient care through the discovery, translation and dissemination of new knowledge.

**Creighton**  
UNIVERSITY  
Center for  
Health Services Research  
and Patient Safety

## Publications

- Dr.'s Kevin Fuji and Amy Abbott had their publication cited in the Agency for Healthcare Research and Quality (AHRQ) Electronic Newsletter – AHRQ in the Professional Literature column, April 15, 2014, Issue #420. The publication cited is: Fuji KT, Abbott AA, Norris JF. Exploring care transitions from patient, caregiver, and health-care provider perspectives. *Clin Nurs Res.* 2013;22(3):258-74.

## Presentations

- Abbott AA, Fuji KT, Galt KA. Adaptation vs. Adoption: A Qualitative Study of Nurses Engagement with Electronic Health Records (poster presentation). AcademyHealth 2014 Annual Research Meeting, June 8-10, San Diego, CA.
- Siracuse MV, Galt KA, Abbott AA, Fuji KT, Bramble JD, Paschal KA. Perceptions on Electronic Health Record Safety and Quality in Rural Ambulatory Clinics (poster presentation). AcademyHealth 2014 Annual Research Meeting, June 8-10, San Diego, CA.
- Abbott AA, Fuji KT, Galt KA. Adaptation vs. Adoption: A Qualitative Exploration of Nurse Engagement with Electronic Health Records (podium presentation). Nebraska Healthcare Quality Forum, June 4, La Vista, NE.

## Announcements

- Dr. Kim Galt has been asked by Agency on Healthcare Research and Quality AHRQ to serve again and continue as a federal grant review member of the Health Care Research and Training (HCRT) study section through 2015.
- Dr. Mark Siracuse has been serving as an ad hoc special emphasis panel federal grant reviewer for the Centers for Disease Control and Prevention during this 2014 spring cycle.

**Creighton**  
UNIVERSITY

Center for Health Services Research and Patient Safety  
2500 California Plaza, Boyne 143  
Omaha, NE 68178