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ACHORD

Alliance for Canadian Health Outcomes Research in Diabetes

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International Exposure for ACHORD Research & Trainees

The ACHORD Research Forum, which was held on September 24-26, 2004 at the Fairmont Palliser in Calgary, Alberta, was a tremendous success! We had 32 attendees including ACHORD investigators and collaborators, research trainees, local health policy decision-makers and representatives from advocacy and research funding agencies.

Our objectives were to discuss ongoing research in diabetes health outcomes in Alberta in the context of international studies, to establish linkages and gain input from internationally recognized investigators on our ongoing research, and to expose research trainees to these distinguished guests. The intangibles from the meeting were invaluable as it provided opportunity for attendees to network with world renowned scientists. We were fortunate to host Dr. Michael Engelgau (Diabetes Translation Unit, Center for Disease Control, Atlanta), Dr. William Herman (University of Michigan) and Dr. Jan Hux (ICES). We are already enjoying the benefits of those interactions through several initiatives.

During our poster session at the Forum, ACHORD trainees had the opportunity to share their research experiences with our guests. For example, Ms Lauren Brown, ACHORD PhD student, discussed her interests in diabetes and mental health with Dr. Engelgau. We are now making arrangements for Lauren to visit Dr. Engelgau and colleagues at the CDC in an extended work training visit for Fall 2005. Following the Forum, Dr. Bill Herman served as an external examiner for Sheri Maddigan's final examination for her PhD in December 2004. In addition, as a direct result of our Forum, Dr. Roger Thomas and Mr. Robert Lee from the University of Calgary have been in communication with Dr. Engelgau as they are looking at a project that will evaluate the cost of diabetes in the Calgary Health Region.

ACHORD will continue to build up our network with other diabetes health services researchers by hosting the 2nd annual ACHORD retreat to be held in beautiful Banff, Alberta on March 3-4, 2005.

ACHORD: Seen and Heard

Recent Publications

Brown LC, Johnson JA, Majumdar SR, Tsuyuki RT, McAlister FA. Evidence of sub-optimal cardiovascular risk management in patients with type 2 diabetes mellitus and symptomatic atherosclerosis. *CMAJ* 2004;171(10):1189-92.

Mitchell CG, Bowker SL, Majumdar SR, Toth EL, Johnson JA. Lack of correlation between patient-reported outcomes and glycemic control in type 2 diabetes. *Can J Diabetes* 2004;28 (4):362-368.

Recent Presentations

Johnson JA. Reduced Anxiety and Fear of Hypoglycemia Following Islet Transplantation Muttart Diabetes Research and Training Centre Research Seminar, University of Alberta, Edmonton, Alberta, January 10, 2005.

Johnson JA. Consensus, Cost-effectiveness and Clinical Practice Guidelines: Why can't they all just get along? Pharmacy Grand Rounds, University of Alberta Hospital, November 4, 2004.

Johnson JA. Cost-effectiveness of Preventive Strategies for Diabetes in Canada. CDA/CSEM Canadian Diabetes Association Professional Conference & Annual Meeting, October 27 – 30, 2004, Quebec City, QC.

Johnson JA. Evidence-Based Policy and Practice: Diabetes Outcomes Research and Cost-Effective Care. Regional Conference on Cost-Effective Healthcare, October 21 – 23, 2004, Singapore.

(Recent presentations continued on page 4)

Report from the Chair

Jeffrey A. Johnson

Another New Year and our ACHORD activities continue in full force, including research projects, grad student training and the active translation of our research to improve health care policy and delivery. It has been a few months since we hosted the ACHORD Research Forum in Calgary, but we are clearly reaping the benefits from that, as described on the cover article. Judging by the comments from participants, it was well worth the efforts. I thank CIHR and AHFMR for the funding support to hold that important meeting. I am particularly happy that the grad students got a lot out of the interactions and discussions.

In October 2004, ACHORD was again strongly represented at the annual CDA/CSEM meeting in Quebec City. There were plenty of posters and oral presentations from our group. I was pleased to share the podium with Dr. Venkat Narayan from the CDC in a plenary session where we discussed economic issues in the management of diabetes in Canada.

We celebrated two graduations in recent months. In October, Lauren Brown defended her MSc thesis on diabetes and depression; Lauren is now continuing on toward a PhD. Sheri Maddigan defended her PhD dissertation in December. As you can see on the next page, Sheri is staying on with us as a full-time Research Associate. This is wonderful news, as Sheri will continue to make ACHORD a productive research force.

We are now busy planning for the 2nd Annual ACHORD Retreat in Banff. This is an important meeting for our group, as we are approaching the 4th year of our 5-year NET grant. I look forward to reporting on the outcome of our retreat, where we will begin to formulate a plan for the future growth of our active research program.

Project Highlights: Pharmacoepidemiological Assessment of Medication Adherence Rates and Clinical Outcomes in Type 2 Diabetes Mellitus

Our adherence study highlights potential risks associated with sulfonylureas for diabetic patients.

Poor adherence to prescribed drug regimens is a challenge for health care professionals. Patient decisions to take less than the prescribed dose can have a significant impact on clinical and economic outcomes. For example, poor adherence to proven efficacious therapies in heart disease is associated with an increased risk of hospitalization and mortality. These observations have led some clinicians to hypothesize that there is a "healthy adherer" effect: good adherence to drug therapy – even placebo therapy – may be a marker for good overall health behaviour.

Our study was designed to measure the relationship between adherence to oral antidiabetic drug regimens and risk of mortality. An adherence rate was estimated using the number of tablets dispensed and the interval between dispensations. Subjects were dichotomized based on an adherence rate above or below 80%. Multivariate Cox proportional hazard models, stratified by monotherapy treatment group, were used to calculate the mortality risk of good compared to poor adherence for each agent studied. Contrary to our expectations, a higher risk of mortality was associated with good adherence to both first generation sulfonylureas (adjusted hazard ratio 2.5, 95% CI 1.1-5.3) and glyburide (HR 1.3, 95% CI 1.2-1.5). This association was not observed with metformin use (HR 1.0, 95% CI 0.8-1.3).

On careful re-evaluation, our observation is actually consistent with information generated out of the University Group Diabetes Project over 30 years ago. This study suggested that sulfonylurea use may be associated with an increased risk of cardiovascular events and mortality. In our study, we observed a possible dose-response relationship, whereby subjects using higher doses of sulfonylureas were at higher risk of adverse drug effects.

Our results are incongruous with a "healthy adherer" hypothesis raised earlier. However, if the drug therapy is potentially harmful, then good adherence would increase the risk of harm. This phenomenon has been seen in adherence sub-studies of both the UGDP and Cardiac Arrhythmia Suppression Trial (CAST). Good adherence to tolbutamide in the UGDP was associated with a 2.6 fold increase in mortality risk. Similarly in the CAST study, a 10% increase in the adherence rate to active therapy was associate 3.5 fold increase in risk of mortality.

Clinicians should carefully assess the need for sulfonylurea therapy in subjects at high risk of cardiovascular events, especially at this time when other classes of oral antidiabetic drugs are available.

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Recent Literature:

Brown LC, Johnson JA, Majumdar SR, Tsuyuki RT, McAlister FA. Evidence of suboptimal management of cardiovascular risk in patients with type 2 diabetes mellitus and symptomatic atherosclerosis. CMAJ 2004;171:1189-1192.

What was the study about?

This study evaluated the extent to which medications proven to reduce cardiovascular mortality were prescribed for patients with type 2 diabetes and symptomatic atherosclerosis, including coronary artery disease (CAD), cerebrovascular disease (CBVD), and peripheral arterial disease (PAD). Administrative records from Saskatchewan Health were used to evaluate the use of antiplatelet agents, statins, and ACE inhibitors in people with type 2 diabetes, with and without CAD, CBVD, and PAD.

What were the results of the study?

There were 12,106 people with diabetes identified in this study; fewer than 25% received a statin or an antiplatelet agent, and fewer than 50% received an ACE inhibitor. Although patients with CAD were significantly more likely to receive ACE inhibitors, statins, and antiplatelet agents compared to people without CAD, the overall usage of these medications was low (60%, 29%, and 37%, respectively among patients with CAD). Similar rates of usage of medications were found in patients with CBVD and PAD. All three proven efficacious therapies were prescribed to only 11% of patients with CAD, 22% with CBVD, and 12% with PAD. Patients with PAD who had undergone lower limb amputation were no more likely to subsequently receive antiplatelet agents or statins compared to individuals without amputation. Overall, the usage of these three medications to reduce cardiovascular risk and mortality in patients with type 2 diabetes, regardless of presence of cardiovascular disease, was low.

What are the implications of the study?

Diabetes is associated with a mortality rate that is approximately double the rate of people without diabetes, and the majority of the excess mortality is attributable to cardiovascular disease. Medications proven to reduce cardiovascular risk and mortality are systematically underused in patients with type 2 diabetes, regardless of whether they have established atherosclerotic disease. The results of this study suggest a "glucocentric" view of the treatment of people with diabetes. Given that the majority of the morbidity and mortality associated with diabetes is related to cardiovascular disease, and little evidence is available to suggest reducing blood glucose decreases cardiovascular risk, it is essential that people with diabetes and risk factors for cardiovascular disease are receiving medications proven to reduce cardiovascular risk. Programs to improve the quality of cardiovascular risk reduction in these high-risk patients are needed.

A glucocentric view of type 2 diabetes results in under use of proven effective medications to reduce CV risk.

Meet the Staff:

Sheri Maddigan, PhD

Sheri Maddigan completed her Bachelor of Science in pharmacy at the University of Alberta in 1995. She practiced as a community pharmacist for several years before returning to the University of Alberta to pursue a Masters of Science in Pharmacy Practice, which she completed in 2001. Her Masters thesis focused on predictors of older adults' capacity for medication management. Upon completion of her M.Sc., Sheri entered into a Ph.D. program in Public Health Sciences in the Population Health stream, under the supervision of Dr. Jeff Johnson. Her area of research was clinical and population-based applications of generic health-related quality of life measures in type 2 diabetes. During the course of her studies, she was a part-time Research Associate with ACHORD and the Institute of Health Economics. She recently completed her Ph.D. and now joins us full-time. Her current research projects include a number of epidemiologic and cost studies in diabetes using the administrative dataset from Saskatchewan Health (1991-2001).

ACHORD

Alliance for Canadian Health Outcomes Research in Diabetes

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Institute of Health Economics

Staff & Research Trainees

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Ms. Lauren Brown
Mr. Dean Eurich
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Ms. Jackie Lewyk
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Recent ACHORD Presentations (*continued from front cover*)

CDA/CSEM Canadian Diabetes Association Professional Conference & Annual Meeting, October 27 – 30, 2004, Quebec City, QC:

Simpson SH, Eurich DT, Majumdar SR, Johnson JA. Adherence to Sulfonylureas May Increase Risk of Mortality. *Can J Diabetes* 2004;28(3):260.

Johnson JA, Kotovych M, Ryan EA, Shapiro, AMJ. Reduced Fear of Hypoglycemia and Anxiety in Successful Islet Transplantation. *Can J Diabetes* 2004;28(3):280.

Eurich DT, Simpson SH, Majumdar SR, Johnson JA. Progressive Management of Glycemia in Type 2 Diabetes. *Can J Diabetes* 2004;28(3):298.

McDonald C, Majumdar SR, Johnson JA. The effects of beta-blockers after myocardial infarction in type 2 diabetes. *Can J Diabetes* 2004;28(3):305.

Supina AL, Feeny DH, Carroll L, Johnson JA. Construct Validity of Health Utilities Index Mark 2 and Mark 3 in Adults with Type 1 Diabetes. *Can J Diabetes* 2004;28 (3):309.

Maddigan SL, Feeny DH, Johnson JA. Health Related Quality of Life Deficits Associated with Diabetes and Comorbidities in the National Population Health Survey. *Can J Diabetes* 2004; 28(3):308.

Bowker SL, Mitchell CG, Majumdar SR, Toth EL, Johnson JA. Lack of Correlation between Patient-Reported Outcomes and Glycemic Control in People with Type 2 Diabetes Not Managed by Insulin. *Can J Diabetes* 2004;28(3):310.

Maddigan SL, Majumdar SR, Johnson, JA. The Structural Relationships Between Patient-Provider Interactions, Self-care Behaviors, and Health-Related Quality of Life in Type 2 Diabetes. *Can J Diabetes* 2004;28 (3): 311.

Brown LC, Majumdar SR, Newman SC, Simpson SH, Johnson JA. Increased Prevalence of Depression in People with New-Onset Diabetes Mellitus. *Can J Diabetes* 2004;28(3):314

Johnson JA, Majumdar SR, Toth EL, Bowker SL, Edwards A. Improved Financial Access to Diabetes Test Strips is Not Associated with Improved Glycemic Control in Type 2 Diabetes: Results of a Randomized Controlled Trial of Reimbursement Policy. *Can J Diabetes* 2004;28(3):260.

Why this Newsletter?

The purpose of the ACHORD Newsletter is to keep you updated on the activities of the ACHORD group and to provide reviews of recent, relevant diabetes literature. The newsletter is published three times a year.

You can expect to see the following in every issue:

- *Report from the Chair*
- *Meet the Staff/Trainee*
- *ACHORD Project Highlights*
- *ACHORD Seen and Heard*
- *Review of Recent Literature*

If you have any questions about the newsletter, please call Jeffrey Johnson or any of the ACHORD staff at the Institute of Health Economics at (780) 448-4881.

ACHORD Events

ACHORD Banff Retreat
Banff, Alberta, February 3-4, 2005