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ACHORD

Alliance for Canadian Health Outcomes Research in Diabetes

Inside this issue:

ACHORD Lives! CIHR Team Funding

Since 2002, the ACHORD Group has been supported by a $1 million New Emerging Team (NET) grant from the Canadian Institutes of Health Research (CIHR) NET Chronic Diseases program. This grant was co-sponsored by the Canadian Diabetes Association, Heart and Stroke Foundation of Canada, and Kidney Foundation of Canada in partnership with the CIHR Institutes of Circulatory and Respiratory Health (ICRH), and Nutrition, Metabolism and Diabetes (INMD). This grant enabled ACHORD to establish itself by recruiting and training highly skilled graduate students. Many different research projects were developed which led to numerous successful collaborations provincially as well as nationally and internationally. The original NET grant was for 5 years, so this important infrastructure funding was quickly running out.

We were recently informed that we were successful in obtaining an additional 5 years of funding through an Emerging Team grant from the CIHR Obesity and Related Diseases competition sponsored by CIHR-INMD. This award will provide $2.4 million over the next 5 years, ensuring ongoing support for the administration and coordination of collaborative research efforts. The funding will further establish ACHORD's strong research and training environment. These efforts include regular investigator meetings, as well as support for research trainees, and an extended circle of collaborators in diabetes health outcomes research. Dr. Jeff Johnson is the Principal Investigator for this grant with Co-Investigators Dr. William Ghali, Dr. Sumit Majumdar, Dr. Scot Simpson and Dr. Doreen Rabi. As in the past, the ACHORD Group includes core investigators as well as a broad circle of collaborators and stakeholders, including research trainees. This funding will help to ensure that ACHORD's successes live on and will continue growing and establishing itself further as an international leader in diabetes health outcomes research.

ACHORD Seen and Heard

Recent Publications

Plotnikoff R, Karunamuni N, Johnson JA, Kotovych M, Svenson L. Health-Related behaviors in adults with diabetes: Associations with health care utilization and costs. *Can J Pub Health* 2008:99(3):227-231.

Rabi DM, Edwards AL, Svenson LW, Sargious PM, Norton P. Larsen ET, Ghali WA. Clinical and Medication Profiles stratified by household income in patients referred for diabetes care. Cardiovasc Diabetol. 2007 Mar 30;6:11.

McAlister FA, Eurich DT, Majumdar SR, Johnson JA. The risk of heart failure in patients with Type 2 diabetes treated with oral agent monotherapy. Eur J Heart Fail. 2008;10(7):703-8.

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Report from the Chair

Jeffrey A. Johnson

Here we are with half of the year behind us and the other half to look forward to! The ACHORD Team has continued to work hard and as you can see from the rest of the newsletter reports, our hard work is paying off in terms of new grants and contracts. In addition to the major funding through the CIHR Team Grant and the ABCD Project, we also received a CIHR operating grant for our ongoing research on the role of antidiabetic medications and cancer outcomes.

We also continue to be successful in our ACHORD trainee program. I am pleased to announce that Lauren Brown was awarded a CIHR Fellowship Award for her continued work in the area diabetes and mental health. Connor Low has joined us as a summer student; Connor hails from Southern Alberta and has just completed his first year of Medical School here at the U of A. JM Gamble successfully defended his MSc thesis in July, and is now starting a PhD with Dr. Dean Eurich. On another happy note, congratulations go to Stephanie Vermeulen on her recent marriage to Justin Balko; we wish you all the best.

I have been travelling a fair bit this spring attending meetings for various committees and professional or scientific conferences, including CPhA in Victoria, CAHSPR in Ottawa, and ADA in San Francisco. JM Gamble, Samantha Bowker and Scot Simpson also attended the ADA Conference. JM had a poster presentation and Samantha and I completed oral presentations.

We continue to be busy with our active dissemination for ADSS. Stephanie Vermeulen, Greg Hugel and I travelled to Westlock on June 23 for two presentations; the first was video-conferenced to a number of sites across the Aspen Health Region, followed by a presentation to the Primary Health Care Committee and invited guests. We also held our annual ADSS Steering Committee Meeting on June 24 which was very productive, providing us with an excellent framework for ongoing ADSS activities.

I hope everyone has a great summer and is able to take some time to relax and enjoy the outdoors. I look forward to reporting on our ongoing activities in our next newsletter!

Alberta's Caring for Diabetes (ABCD)

The ACHORD Group recently announced funding for a major collaborative project unique to Alberta that will improve quality of care for people with diabetes and other chronic diseases. Alberta Health and Wellness is providing over $5 million over the next 5 years for the Alberta's Caring for Diabetes (ABCD) Project. The funding is arranged through a partnership between Alberta Health and Wellness and the Institute of Health Economics. The ACHORD Group will run this project, led by Drs. Jeff Johnson and Sumit Majumdar out of the University of Alberta. The ABCD team will include physicians, pharmacists, nurses and dieticians.

How will ABCD work?

The ABCD team will collaborate with the regional health authorities and primary care networks which serve as appropriate vehicles to implement this service. A key element of the ABCD project will be performance measurement and benchmarking within the health care system. As both Edmonton and Calgary have fully developed diabetes care programs, they would serve as hubs for the outreach intervention. The main goal of this intervention will be enhanced care by local primary care health professionals with particular focus on vascular protection, including control of blood pressure, lipids, use of antiplatelet agents, and renal protection, in addition to glycemic control. The ABCD team will also work with the regions and PCNs to develop and evaluate interventions for other non-glycemic outcomes, such as mental health and eye care.

How will we know if ABCD is accomplishing what it should?

The impact of ABCD will be assessed through the already established Alberta Diabetes Surveillance System, including measurement of population-level outcomes and patient-level indicators of quality of care. Examples of the latter type of data include: laboratory data, fasting lipids and renal function; physical measures, such as blood pressure, height and weight, as well as patient-reported information, such as health-related quality of life, patient satisfaction, and self-care behaviors. Patients would then be followed on an annual basis to track progress of diabetes and cardiovascular risk factors, health outcomes, and quality of life indicators.

Recent Literature:

The Action to Control Cardiovascular Risk in Diabetes (ACCORD) Study Group. Effects of Intensive Glucose Lowering in Type 2 Diabetes. N. Engl J Med 2008;358:2545-59.

The ADVANCE Collaborative Group. Intensive Blood Glucose Control and Vascular Outcomes in Patients with Type 2 Diabetes. N Engl J Med 2008;358:2560-72

What were the studies about?

The ACCORD (Action to Control Cardiovascular Risk in Diabetes) and ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation) trials were multi-center randomized factorial trials designed to assess the efficacy of various treatment strategies such as glycemic, blood pressure, and lipid control in people with type 2 diabetes. The aim of the glycemic therapy arm in both the ACCORD and ADVANCE trial was to evaluate the effect of an intensive glucose lowering strategy compared to a standard glucose lowering strategy on cardiovascular (CV) events in people with type 2 diabetes. Over 10,000 patients with type 2 diabetes at an increased risk of a CV event were randomized to either intensive glucose lowering therapy (an A1C target <6% in ACCORD and <6.5% in ADVANCE) or standard glucose lowering therapy (A1C target 7-7.9% in ACCORD and ≈7% depending on local guidelines in ADVANCE). The primary outcome in the ACCORD trial was a composite of cardiovascular events (nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes). A primary composite outcome was also used in the ADVANCE trial defined as major macrovascular events (death from CV causes, nonfatal myocardial infarction, or nonfatal stroke) and major microvascular events (new or worsening nephropathy or retinopathy).

What were the results of the studies?

In the ACCORD trial 352 (6.9%) people experienced the primary outcome in the intensive therapy group versus 371 (7.2%) people in the standard therapy group (Hazard ratio (HR) 0.90; 95% confidence interval (CI) 0.78 to 1.04; P=0.16).

The glycemic arm of the ACCORD trial was stopped early due to a 22% increase in mortality among the intensive therapy group compared to the standard therapy group (HR 1.22; 95% CI 1.01 to 1.46; P=0.04). In the ADVANCE trial 1009 (18.1%) people in the intensive therapy group experienced the primary outcome compared to 1116 (20.0%) people in the standard therapy group (HR 0.90; 95% CI 0.82 -0.98; P=0.01). Major macrovascular events considered separately did not show a significant difference between groups (HR 0.94; 95% CI 0.84 to 1.06; P=0.32); however, major microvascular events were associated with a significant difference between treatment strategies (HR 0.86; 95% CI 0.77 to 0.97; P=0.01).

What are the implications of the studies?

These studies were appropriately powered to detect a clinically meaningful difference in major cardiovascular events between treatment strategies, however, neither study showed a meaningful benefit in terms of CV events when an intensive glucose strategy was implemented with a goal of achieving a near normal glycemic level. The results must be kept in context of the study population which included people of 62-66 years on average with an 8-10 year duration of diabetes at baseline. Furthermore, 32-35% of patients had a history of a macrovascular disease. Therefore the applicability to people with a new diagnosis of type 2 diabetes at a low risk of macrovascular disease is uncertain. Interestingly, subgroup analysis in ACCORD found that people without a history of macrovascular disease were less likely to experience the primary outcome compared to those with a history.

Beyond not showing a benefit in terms of CV events, the results from ACCORD suggest harm is associated with intensive glucose lowering therapy. The potential reasons for the observed increased in mortality are many and the authors speculated that their aggressive approach to lower A1C rapidly or perhaps the level reached may be an explanation. Another practical implication of these trials is the difficulty in teasing out the individual effects of the medications used, independent of their glucose lowering effect. These trials were designed to evaluate the effects of two different glucose lowering strategies whereby numerous antidiabetic agents were used to achieve glycemic targets. There were several differences in the medications used to lower glucose between the trials (higher insulin and thiazolidinedione use in the ACCORD trial and high gliclazide use in the ADVANCE trial). Non-glucose lowering treatment differences were also apparent (ASA and statin use was much lower in the ADVANCE trial). Although many questions remain regarding the speed and how glucose should be lowered, the consensus from the ADA meeting was that our current A1C target of ≤7% is still appropriate provided that benefits (i.e. a decrease in microvascular complications) and risks are weighed for each individual.

These trials were designed to evaluate the effects of two different glucose lowering strategies whereby numerous antidiabetic agents were used to achieve glycemic targets.

ACHORD Chair

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Recent Presentations

Gamble JM, Simpson SH, Brown LC, Johnson JA. Insulin versus an oral antidiabetic agent as add-on therapy in patients with type 2 diabetes failing their current oral antidiabetic regimen: a meta-analysis. 6th Annual Canadian Cochrane Symposium, March 6-7, 2008, Edmonton, AB.

Vermeulen S. Alberta Diabetes Surveillance System Dissemination. Diabetes Collaborative Workshop, Palliser Primary Care Network. April 25, 2008, Medicine Hat, AB.

Lothammer R, Vermeulen SU, Johnson JA, Jonsson E. IHE Consensus Development Conference on Self-Monitoring in Diabetes. 2008 CADTH Invitational Symposium, April 28-29, 2008, Edmonton, AB.

Ohinmaa A, Lau R, Johnson JA. Projection model of the economic burden of diabetes – simultation of cost effectiveness studies to Alberta population. 2008 CADTH Invitational Symposium, April 28-29, 2008, Edmonton, AB.

Norris CM, Jensen L, Johnson JA, Hegadoren K, Ghali WA, Spertus J. Gender-based disparities in Quality of Life Outcomes among patients with Coronary Artery Disease. 9th Scientific Forum on Quality of Care and Outcomes Research in Cardiovascular Disease and Stroke Conference 2008, Baltimore, Maryland, April 30 to May 2, 2008.

Lau R, Ohinmaa A, Johnson JA. Projecting the Future Burden of Diabetes in Alberta (2006-2036). Canadian Public Health Association 2008 Annual Conference, Halifax, Nova Scotia, June 1-4, 2008.

Johnson JA, Vermeulen SU, Couch RM, Marks SD, Pacaud D, Hugel G. Increasing Incidence and Prevalence of Diabetes between 1995 and 2006 in Young Children and Adolescents in Alberta, Canada. [Oral Presentation] 68th American Diabetes Association Annual Meeting, San Francisco, California, June 6-10, 2008.

Bowker SL, Yasui Y, Veugelers P, Johnson JA. Antidiabetic Therapies and Cancer Mortality in Type 2 Diabetes: Assessing Time-Varying Exposure. [Oral Presentation] 68th American Diabetes Association Annual Meeting, San Francisco, California, June 6-10, 2008.

Gamble JM, Eurich DT, Simpson SH, Johnson JA. The Relationship between Insulin Exposure and all-cause mortality. 68th American Diabetes Association Annual Meeting, San Francisco, California, June 6-10, 2008.

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.

If you have any questions about the newsletter, please call Jeffrey Johnson or any of the ACHORD staff at the University of Alberta at (780) 492-7317.

ACHORD Events

6th Annual ACHORD Retreat
March 5 & 6, 2009
The Banff Centre
Banff, Alberta, Canada