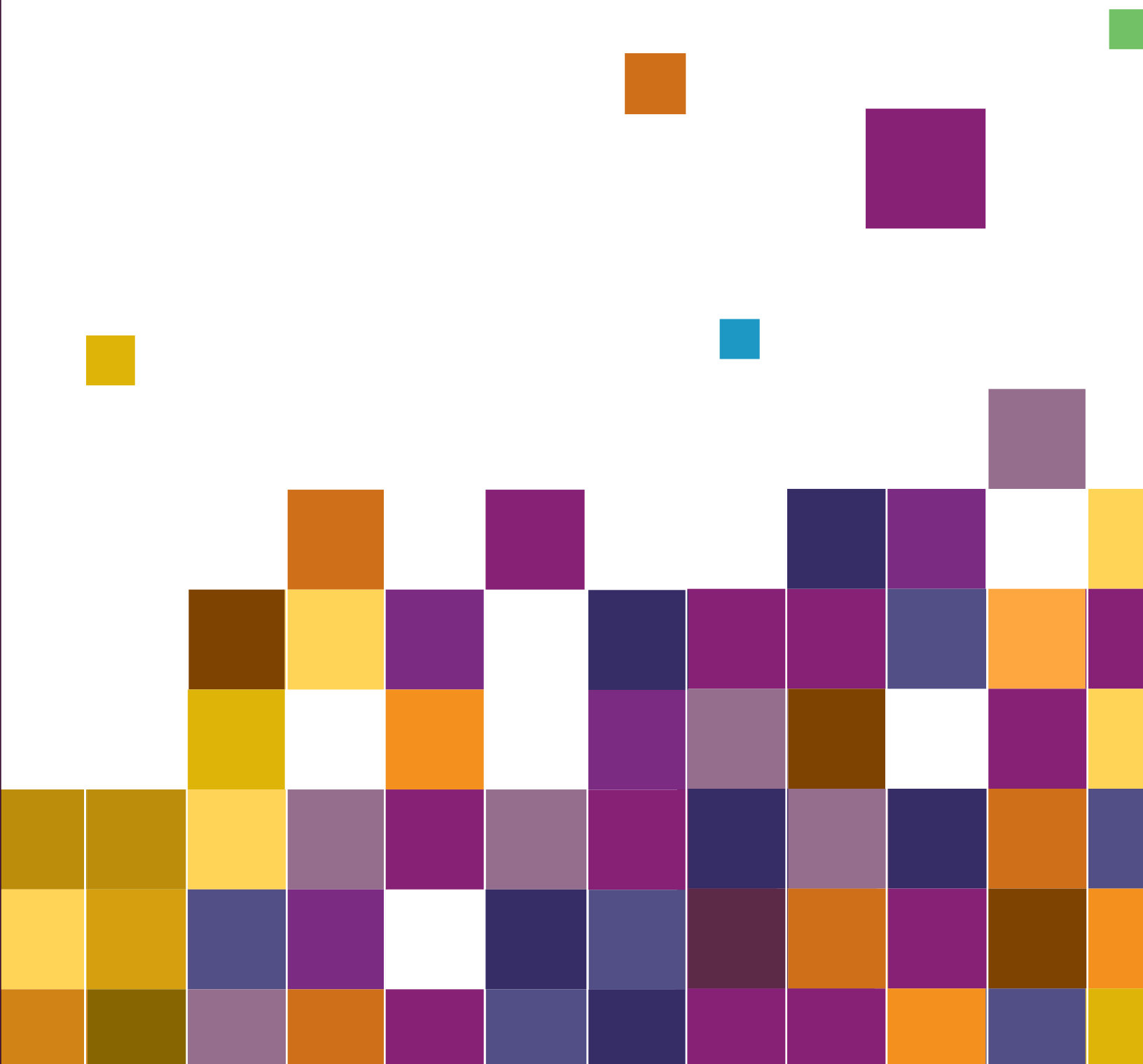
Alberta Innovates – Health Solutions KT Casebook Volume 2 2011

Interdisciplinary Teams – making research make a difference

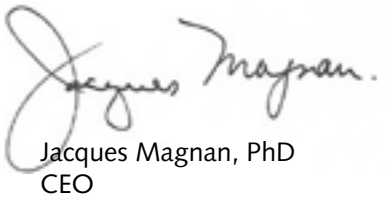


This Casebook, the second in a series produced by Alberta Innovates – Health Solutions, showcases knowledge translation activities of the Interdisciplinary Team Grant program. The program was launched in 2008 to support research addressing complex health problems. Co-funded by Alberta Health and Wellness and Alberta Innovates – Health Solutions, the program provides $50 million over five years for 10 teams. The teams are interdisciplinary and multi institutional and include nearly 600 researchers and 160 trainees, and support 147 international collaborations. Research activities of the teams cover the spectrum of basic biomedical, clinical, health services, and population health research and all encompass an integrated KT approach.

The teams have already made notable gains on all measures of knowledge translation – the teams have provided training opportunities for young researchers, leveraged $14 million in additional funding, published and hosted 439 stakeholder engagement activities, included decision makers as part of the teams, and several of the teams are pursuing technology commercialization opportunities including the creation of four spin-off companies.

The invitation to the teams to participate in this Casebook was open to any aspect of knowledge translation in their research program that they chose to highlight. The results are an impressive array of activities that show the strength and diversity of Alberta's health research and innovation enterprise.

Susan Williams
Assistant Deputy Minister
Alberta Health and Wellness



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Interdisciplinary Teams – making research make a difference

Introduction

The Interdisciplinary Team Grant program is a leading edge approach to research on priority health questions. The program developed from conversations between AIHS and Alberta Health and Wellness on what those health questions are and on identifying strategic research priorities to respond to those questions. The health questions are complex and cannot be answered by individual researchers or even teams of researchers in a single discipline. Our answer was to support collaborative, interdisciplinary, multi-institutional teams over several years with a focus on generating new knowledge but equally important, on translating that knowledge into action.

Specific objectives of the Interdisciplinary Team Grant program are:

1. To support the production of high-quality research that addresses important and complex health issues and which requires a collaborative team approach;
2. To support interdisciplinary and multi-institutional teams of talented researchers;
3. To provide superior interdisciplinary research training and mentorship;
4. To engage end-users in the production and translation of research findings to improve the health of Albertans and/or the health care system.

The program emphasizes translation of knowledge in ways that will directly impact the health of Albertans and/or the health care system. The teams have active and meaningful partnerships between institutions and end users. The guiding principle is that the end-users are influential and on-going participants in the proposed research, training, mentoring and knowledge translation activities. By being involved at the outset, we believe results will be achieved more rapidly and effectively.

The ten teams that are profiled in this KT Casebook include some of the highest quality, internationally recognized researchers in the world. The value provided by these teams goes beyond the individual researchers. It is the synergy of multiple disciplines and multiple perspectives, and the partnerships and involvement of key users of that research that is the defining quality and benefit of the teams. Some of the teams have chosen to profile a particular project within their research program while others have provided an overview of all their KT strategies. All of the cases reflect the richness of the discoveries and the successes in translating those discoveries into action.

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Integrating KT Within a Research Study: The APrON Experience

Brenda M. Leung, Bonnie J. Kaplan, Catherine J. Field, Maeve O'Beirne, Anna Farmer, Deb Dewey, David Johnston

Abstract

The Alberta Pregnancy Outcomes and Nutrition (APrON) Team represents an interdisciplinary approach to determining the effects of nutrition on child and maternal health, specifically, the impact of nutrition on maternal mental health and subsequent outcomes for the developing child. By determining these associations, results can inform parents in planning their prenatal care, healthcare providers in addressing the needs of pregnant women, and health and human services managers and government policy-makers in determining the service support needs of pregnant women. To ensure that research results can be effectively mobilized into improved care and outcomes, APrON is engaging government agencies, academic institutions, community organizations, and women who are considering or have begun pregnancy. This engagement not only sets the stage for future knowledge mobilization activities, but has contributed to a patient retention rate of 94% in the APrON study.

Background

Nutrients are essential for growth and development, as well as for good physical and mental health.[1,2] Due to the high incidence of obesity, it is often assumed that people living in developed countries consume adequate nutrients; yet deficiencies of specific micronutrients are common.[3-5] The 2006 Health of the Region report by the Medical Officer of the (former) Calgary Health Region estimated that the proportion of individuals not meeting daily nutrient requirements ranged from 72% to 87%.[6] The impact of a poor maternal diet is magnified during pregnancy, when nutritient needs increase and the fetus depletes maternal reserves.[7, 8] This suggests that a poor diet, coupled with the needs of the fetus, could affect a woman's mental health and her ability to nurture her infant as well as the growth and neurodevelopment of her baby.[9-11] The knowledge gap in this area is:

- Does nutritional deficiency affect pregnant women's mental health—in particular, mood disorders such as depression and anxiety?
- How do maternal diet and mental health affect the development of the offspring?

This knowledge gap was identified in 2007 by our researchers as a result of their knowledge of the emerging literature on nutrition and mental health. However, its importance was under-scored more recently by the Alberta Health Research and Innovation Strategy identification of child and maternal health, as well as mental health and addictions, as strategic focus areas. The adverse effects of maternal mood disorders on children's cognitive and social development are well documented.[12] The overall health of pregnant women is a public health issue with broad societal implications.

Pregnant women and new mothers regularly provide input into the development of APrON's KT activities, such as recruitment videos and newsletters.

Facing page: Dayna-Lynn Dymianiw with baby participant Braxton, Jessie Denys with APrON participant, Corinna; baby and mom in follow up assessments.

KT Initiative

The Alberta Pregnancy Outcomes and Nutrition (APrON) study wanted to determine the extent to which a woman's diet affects her mental health and her ability to nurture her infant, as well as the growth and development of her baby. Pregnant women in their first or second trimester have been recruited in Calgary and Edmonton and followed throughout their pregnancies; the offspring are being followed until age three. Specifically, APrON is evaluating:

1. women's nutrient intake and nutrient status throughout pregnancy;
2. women's mental health throughout pregnancy and the postpartum period;
3. birth outcomes and neonatal characteristics of the babies (including birth defects);
4. babies' physical and mental development up to the age of three.

By determining the association between maternal nutrition, maternal mental health, and infant development, APrON's results can inform:

- parents in their prenatal care;
- healthcare providers in addressing the needs of pregnant women;
- health and human services managers and government policy-makers in determining the service support needs of pregnant women.

Brenda Leung (APrON KT Coordinator).

Melissa Lorenzo plus APrON participant, Corina Walker; 24 hour diet recall at the APrON clinic.

Melissa Lorenzo (APrON Research Assistant).

Through the use of patient engagement, APrON has been able to maintain a 94% retention rate among their 600 study participants.

KT Objectives

APrON's main KT objectives are to raise awareness about:

- the association between maternal diet and mental health;
- the impact of mood disorders such as perinatal depression and anxiety on the health of the woman and her child.

APrON's KT initiative was part of the strategy to recruit and retain participants and project supporters by keeping them informed about APrON's progress.

A secondary objective was to sustain a network of "knowledge conduits", including:

1. a Partners' Council, consisting of governmental agencies, academic institutions, and community organizations;
2. Community Supporters such as local businesses and perinatal and children's programs; and
3. healthcare providers, lab technicians, and front-line workers in medical clinics.

The expected impact of this KT initiative is to advance knowledge on the association between maternal diet and mental health. This will be accomplished by sustaining the enrollment of pregnant women into the study, retaining participants, and maintaining our community supporters to be knowledge conduits for disseminating APrON information. Currently APrON continues to recruit pregnant women. Data from the first cohort (N=600) is being analyzed, and KT is ongoing. KT of the results will provide evidence on which to base future health promotion recommendations.

Knowledge End-Users

The audience of the current KT initiative is women considering pregnancy, pregnant women, and new mothers. As pregnant women have been the target population recruited, our knowledge of this audience is high. Throughout the study, pregnant women have provided us with input about the lack of access to research information regarding the importance of nutrition for their own physical and mental health and that of their unborn child. The feedback we have received informally from participants is that their main sources of contact - family doctors and medical clinics - provide little information about the latest nutrition and lifestyle research for optimal pregnancy and birth outcomes. This suggests that there is a significant need for knowledge dissemination.

One of the main barriers to knowledge uptake is the lack of access; women do not know where to go, and the professionals to whom they turn do not have the information they need. Women seek information from multiple sources, including obstetricians, family doctors, nurses, midwives, and other paraprofessionals. However, these resources are not always set up in ways that are easily accessible to "healthy patients." Women also search for information through various media sources, the Internet, conversations with families and friends, and their network of contacts. However, the information acquired from these sources may or may not be evidence-based.

KT Strategies

APrON has engaged pregnant women at multiple data-collection time points throughout the study. Many of these women want to be involved in discussing and disseminating the research findings to which they have contributed. A facilitator for our KT plan is the formation of a committee composed of the pregnant women and new mothers who helped develop the KT plan. By engaging our key KT audience throughout the study, utilization of the results will likely be increased.

Pregnant women have been asked what information they wish to have, and how they would like to receive that information. APrON has employed a number of tools to engage and inform our audience, from brochures in doctors' offices to social networking sites. APrON participants regularly provide content to the various KT activities. For example, pregnant women are participating in our recruiting videos and other publicity events, as well as being contributors to the APrON newsletter.

Our KT strategies are implemented using diverse tools, including:

- the quarterly newsletter "APrON Leaflet," which is emailed, posted on APrON's website (www.apronstudy.ca), and mailed to those without email. It usually includes a recipe, an interesting story about a highlighted participant, an introduction to a staff member or investigator, and an update on the research project itself;

- the APrON website, which contains information about the study, as well as fun and informational links intended to draw participants to the site;

- Facebook, Twitter, and other social networking media, which are used principally to update participants about ongoing events;

- media coverage, with the assistance of Alberta Innovates - Health Solutions, which has occurred via print, television, and radio. APrON has been featured in magazines (e.g. the Calgary-based magazine, Apple; AIHS Magazine, Research News);

- creation of a Partners' Council to help promote the study and facilitate recruitment, and of Community Supporters, who provide small incentives to participants.

Results

Evaluation of the KT activities is ongoing and consists of a number of measures, including:

- membership in our Partners' Council and Community Supporters;
- membership on our listserv contacts who receive the APrON Leaflet newsletter;
- contacts for media events; and
- tracking the number of media events, website hits, Facebook "friends," and Twitter messages exchanged.

From preliminary informal checks, the results are promising. Our Partners' Council has been consulted about methodology and KT issues, and Community Supporters (over 25 supporters) have generously continued to provide us with donations that we periodically give out to participants as tokens of our appreciation for their participation. Media coverage has resulted in features in provincial and national newspapers, and on television, radio, and Internet (13 multimedia clips and 21 articles). The APrON website has seen a steady increase in the number of daily hits (over 1,000 visits and over 5,500 page views in a one-month period). The success of our KT initiative can also be measured by our study's retention rate; to date, only about 6% of participants have dropped out, which is remarkable for a cohort study of this magnitude.

APrON's KT strategies addressed the barriers previously mentioned. The main barrier identified was how to stimulate interest and engage individuals and organizations in the project. It was recognized early in the study that no single activity or event would capture mass interest or buy-in to our KT activity. Thus, by using multiple KT tools, we have enabled APrON's messages to reach as wide an audience as possible.

Melissa Lorenzo on left, Dayna-Lynn Dymianiw and baby Braxton.

Patient feedback has indicated that primary healthcare providers are the main source of health information for new mothers. However, these providers rarely provide information on nutrition and lifestyle choices for optimal pregnancy outcomes.

Key Messages

APrON recognized that different target audiences required different engagement strategies. APrON was able to incorporate a number of KT tools and tactics at the start of the project (from the recruitment stage onward). Thus, the earlier a KT team is able to identify the audience and incorporate them into the KT process, the more effective the KT plan will be. It was also recognized that credibility is important in carrying out the message, so APrON enlisted the assistance of organizations and individuals that have an established rapport with our key audience. APrON will continue to develop KT plans to engage various target audiences, based on the insight that it will take several KT initiatives over a period of years in order for the knowledge to be accepted and utilized.

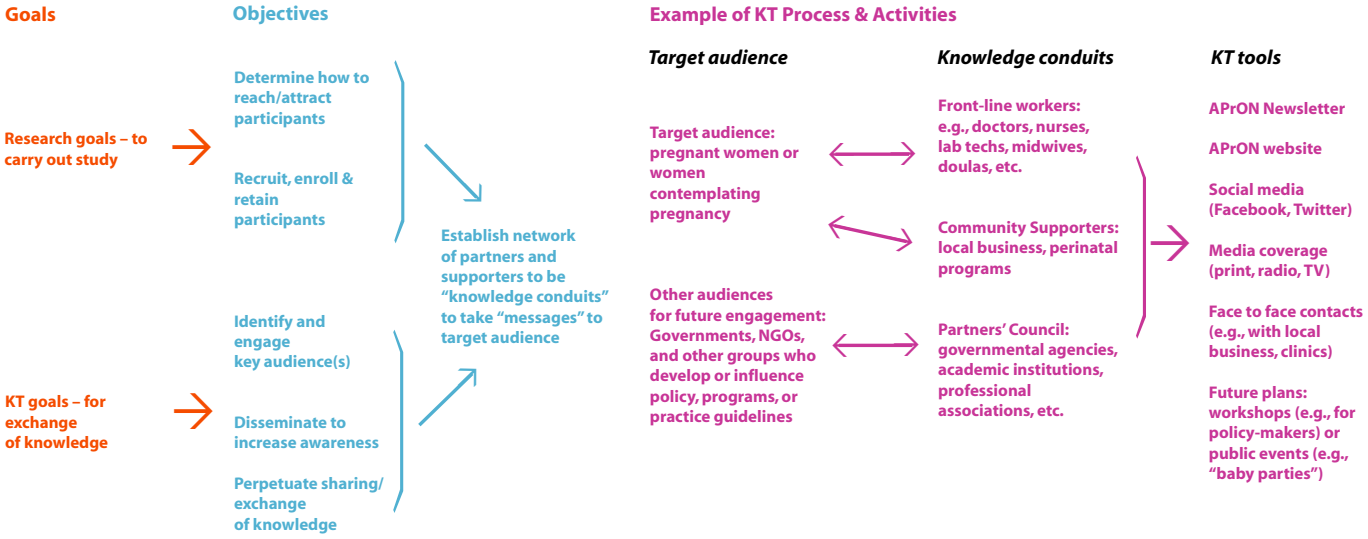
Some of the lessons learned so far through our KT initiative are:

1. Regular, consistent engagement is essential.
2. Messages must be concise and fun, yet informative and useful to the participants.
3. Multiple KT sources are needed to ensure the message is delivered.
4. The message and the mode of delivery must be audience-specific.
5. Audience engagement through the integrated KT plan helps to maintain a high retention rate in the study.

The lessons learned from this initiative can be applied in other settings.

This KT initiative has increased our team's understanding about the practice of KT. From the start of any project, it is recommended that researchers make use of the recruitment process as part of KT. KT is not only the dissemination of research findings, but can be used to convey the importance of a study question and to help recruit and retain participants. KT for a cohort study such as the APrON study needs to be a collaborative endeavour between academic institutions, governmental agencies, professional bodies (such as front-line workers and practitioners), community members, and other pertinent groups, such as the target audience. For APrON, next steps in our KT plans are to target our "knowledge conduits," such as healthcare providers, to be the audience for future KT activities.

Integrated KT within the process of a research study – The APrOn Experience



Assumptions:
Groups and individuals who are "knowledge conduits" (i.e., vehicles or modes for disseminating information to the target audience) are also recipients of the knowledge themselves, and are a secondary audience in the KT process.

About the Authors

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Dr. Deborah Dewey (PhD) is a team co-lead of APrON, and is a professor in the Faculty of Medicine at the University of Calgary.

Dave Johnston (MA) is the project manager for APrON.

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APrON baby participant Braxton.

Alberta HEART: An Integrated Research Approach to Diastolic Heart Failure

Ryan Perry, Justin Ezekowitz, Alexander Clark, Todd Anderson, and Jason Dyck

Abstract

Progress in understanding diastolic heart failure is limited by an uncoordinated research approach into the causes and treatments of this condition. To meet this challenge, the Alberta Heart Failure Etiology and Analysis Research Team (Alberta HEART) was created to bring together 24 scientists and clinicians from across Alberta to research this condition. Based on their experience with Alberta HEART, the authors conclude that interdisciplinary research teams: 1) are key to understanding, diagnosing, and treating complex diseases; 2) are effective at bridging the bench-to-bedside-to-community gap; 3) lead to unforeseen research opportunities in other disease areas; and 4) must have an active KT component for effective internal and external translation of the team's activities and outcomes.

Background

Heart failure (HF) is a modern day epidemic that has a significant impact on patients, their families, and health systems. It affects 1.5% to 2.0% of Canadians (including more than 80,000 Albertans), incurs $3 billion in annual hospital costs, and becomes more common with increasing age.[1-2] While significant advancements have been made in the management of heart attacks, these advances have further contributed to the incidence and prevalence of HF.[3-5] In addition, despite measured improvements in hospitalization rates for HF, this condition is emerging as one of the leading causes of hospital admissions, accounting for half of all hospitalizations in older adults.[5-7] HF also has the worst effect on quality of life of any chronic medical disease,[8] and, given our aging population, prevalence is expected to double over the next 20 years.[9-11] These indicators underscore the importance of developing new strategies to treat this debilitating condition.

Although complex, HF can be simply defined as a progressive condition where the heart weakens and cannot pump blood efficiently for the needs of the body. The weakening of the heart can occur during the systolic (contraction) or diastolic (relaxation) phase of the heartbeat. Accurately diagnosing diastolic heart failure (DHF) is difficult because a traditional physical feature associated with HF that is, a decrease in the blood pumped from the heart with each heartbeat, is not present in DHF patients.[12] Notwithstanding difficulties in diagnosing DHF, there is a high prevalence of DHF in the Canadian HF population. Coupled with an associated high mortality and increased morbidity, a focused approach to improving our understanding of this condition is warranted.[13,14] In Alberta, the research and clinical activities for understanding DHF were isolated and created a barrier between the generation of new knowledge and its translation to clinical utility for improved diagnosis and treatment of DHF. The Alberta Heart Failure Etiology and Analysis Research Team (Alberta HEART) brings together 24 scientists and clinicians from across Alberta to bridge the gap between knowledge and practice.

Facing page, left to right: Ian Paterson, MD, Richard Thompson, PhD, Marleen Irwin, RRT/C (Alberta HEART Clinical Research Coordinator), Mark Haykowsky, PhD, and Ryan Perry, PhD. The machine in the background is a Cardiac Magnetic Resonance Imaging machine.

KT Initiative

Effective translation of research discoveries requires an integrated flow of information across disciplines to validate, refine and ultimately implement new approaches to the diagnosis and treatment. Alberta HEART addresses this need. Alberta HEART focuses on the increasing prevalence, lack of accurate diagnostic criteria and therapies, and fragmented research and clinical activities for DHF. An interdisciplinary team provides a dynamic and iterative approach to developing new research models, diagnostic criteria, and therapeutic options for DHF by bringing together:

- biomedical scientists (those striving to understand the basic mechanisms of DHF)
- clinicians, epidemiologists and clinical researchers (those investigating the pathogenesis, therapeutics, and epidemiology of DHF)
- decision-makers (those setting policies and guidelines)

The overall cardiovascular research environment in Alberta is highly specialized and has high impact on the world stage.[15] This environment has provided a solid foundation from which to build an interdisciplinary DHF team.

One of the key recommendations from the recently released Canadian Heart Health Strategy Action Plan is to build the knowledge infrastructure to enhance prevention and care by ensuring we have more accurate, timely information and that we efficiently share it. An expected outcome of the strategy is to realize a 25% decrease in hospitalizations for the treatment of HF by 2020.[16] Identification of the importance of this health issue by multiple agencies illustrates that stakeholders are prepared to engage in the exchange of DHF knowledge with researchers. Alberta HEART provides a mechanism for this, through an integrated research approach focused on achieving these critical goals.

Knowledge End-Users

To improve the transfer of knowledge from bench-to-bedside and, ultimately, to the community. Alberta HEART works closely with additional key stakeholders beyond the core interdisciplinary team. These stakeholders include decision-makers and end-users from industry, academia, government, healthcare, and funding agencies. Finally, a key tenet of Alberta HEART is to include our patients as participating partners of our research program. The "patients as partners" philosophy builds upon the mission of Alberta HEART to incorporate a patient-centric approach to DHF research.

In Alberta, research and clinical activities for understanding heart failure were isolated and created a barrier to the generation of new knowledge and its translation to clinical utility. Alberta HEART brings together scientists and clinicians from across the research and health spectrums to address this issue.

Knowledge-to-Action Gap

The median time frame from an initial biomedical discovery to the earliest highly cited clinical study, a "translation lag", is 24 years.[16] While information sharing across pillars has been attempted, simply sharing and exchanging knowledge is not sufficient, because the languages and contexts associated with various stakeholders can be radically different. One strategy to decrease translation lag is to create meaningful interactions and coordination between knowledge generators and knowledge users.[17,18] Alberta HEART has adopted an integrated knowledge translation (KT) strategy and the interdisciplinary team incorporates the spectrum of DHF research (knowledge generators) and clinical activities (knowledge users) from bench-to-bedside.

KT Strategies: Interdisciplinary Research

An immediate impact of Alberta HEART has been the coordination of clinical and research activities for DHF in Alberta. The team employed a patient-centric approach and developed the following three main research themes:

1. Diagnostics and Risk Assessment - to develop diagnostic criteria as well as assess the risk factors associated with DHF.
2. Outcomes - to develop a registry and infrastructure to aggregate Alberta HEART's research and clinical information at local and provincial levels.
3. Basic Research - to identify molecular mechanisms involved in regulating diastolic function as well as to test novel treatment strategies in pre-clinical models.

As a result, patient Diagnostics and Risk Assessment (Theme 1) for DHF is now linked to Outcomes (Theme 2) and Basic Research (Theme 3), and allows for the development of improved diagnostic parameters and the ability to test new therapies on more appropriate animal models of DHF.

KT Strategies: Knowledge Exchange

To actively coordinate KT and exchange between the three research themes of Alberta HEART, KT was designated as a theme on the interdisciplinary team agenda. The KT component connects the research theme leaders, on a monthly basis, with a dedicated KT specialist to continually monitor, assess, and integrate results across the core research themes as they become available. To further guide this process, a Team Impact Group (TIG) was also created to act as an external advisory board to the team's KT theme, consisting of the following core membership:

- team co-leads
- theme leads
- six external members to Alberta HEART representing national and international stakeholder groups from industry, academia, government, and healthcare

The mandate of the TIG is to provide advice and recommendations to Alberta HEART; to ensure that the overall research objectives and activities are integrated and aligned with external stakeholder interests. Ad hoc membership on the TIG from additional stakeholder groups (that is, patients and public) will be sought to provide advice and guidance to the core TIG. Since the TIG comprises relevant end-users who stand to benefit from the research outcomes of Alberta HEART, it is well positioned to function as an additional conduit for translation, exchange, and dissemination of research results.

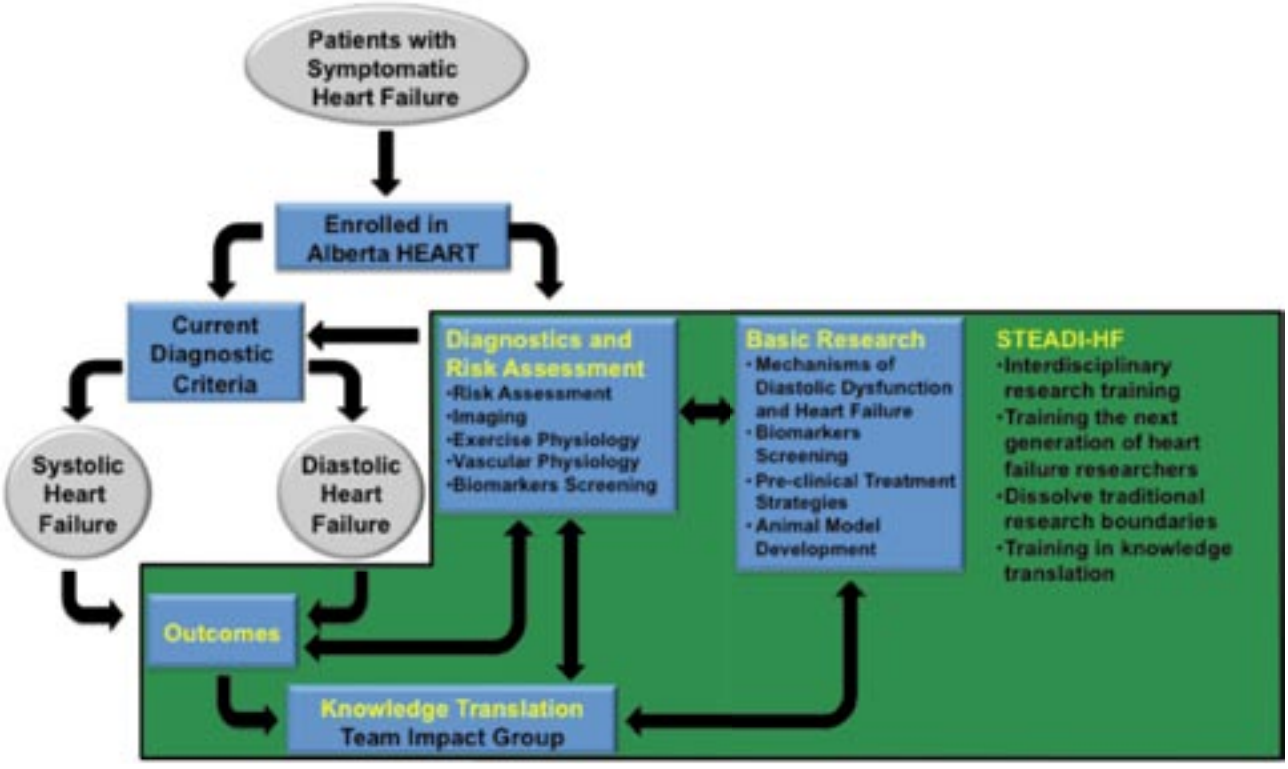
KT Strategies: Capacity Building

Alberta HEART has developed the Supporting Training Encompassing All in Diastolic Heart Failure (STEADI-HF) interdisciplinary training program to develop future interdisciplinary research leaders in DHF. Overall, STEADI-HF aims to build this capacity by dissolving traditional research boundaries, and allows Alberta HEART trainees to participate in KT activities within and beyond their own principle research areas. This intra-team exchange program allows Alberta HEART trainees to transfer between the three research themes to gain "hands-on" experience and develop skills outside their traditional research discipline. STEADI-HF also facilitates building interdisciplinary partnerships among team members.

Results

Prior to the formation of Alberta HEART, research and clinical activities focused on DHF were isolated. The isolation of researchers (knowledge generators) from clinicians (knowledge users) was identified as a key contributor to translation lag time.[17,18] Alberta HEART created a structure that integrates these activities both locally and provincially, and it is anticipated that this will greatly improve the translation of new biomedical and diagnostic discoveries for DHF into clinical utility (see Figure 1).

Figure 1. Alberta HEART Integrates Diastolic Heart Failure Research, Clinical, and Training Activities

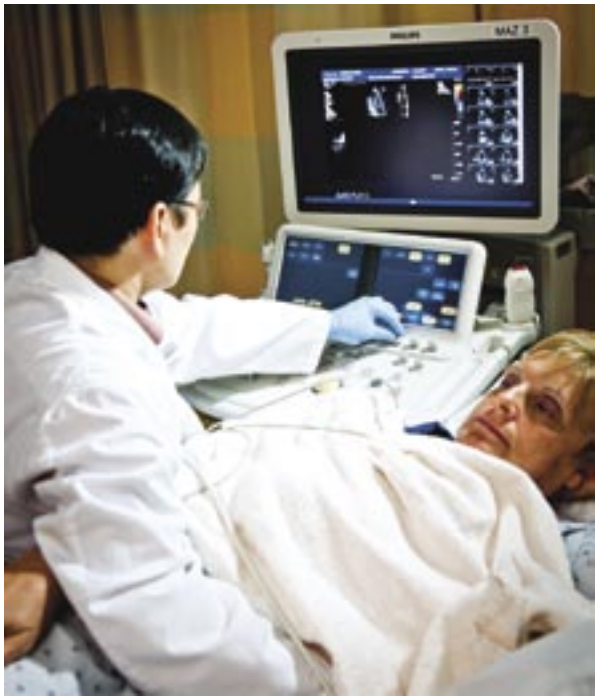


As a result of Alberta HEART, the clinical activities and knowledge users for DHF care from five specialty HF clinics located in Edmonton and Calgary, along with six rural HF clinics were identified. Development of the six rural HF clinics was facilitated through collaborations with the HF Subgroup of the Alberta Cardiovascular Access Collaborative (ACAC). In addition to coordinating clinical activities, Alberta HEART created a central DHF registry of all patients enrolled into our program from the 11 HF clinics located throughout the province. With appropriate patient consent, we are able to link patient information with administrative data from Alberta Health and Wellness.

The two distinct datasets (the clinically rich Alberta HEART province-wide prospective DHF registry and the Alberta Health and Wellness administrative database) provide comprehensive and complementary information to characterize DHF in newly diagnosed patients within a single geographic region and healthcare system. To our knowledge, no such resource currently exists anywhere else in North America. Finally, Alberta HEART also created an electronic platform to facilitate sharing and exchange of echocardiography and cardiac MRI images from both the Edmonton and the Calgary sites. The consolidated imagery database allows for integration with the clinical and administrative datasets, adding to our developing matrix for new diagnostic criteria for DHF.

Development of Alberta HEART's DHF registry has also led to collaborations with additional interdisciplinary organizations, such as the Centre of Excellence for the Prevention of Organ Failure (PROOF). PROOF is a not-for-profit organization focused on developing and implementing biomarker tests to better manage patients with conditions such as DHF. Alberta HEART has formally partnered with PROOF to begin to identify and test novel biomarkers for DHF based on the patients enrolled in our program. Identification of these biomarkers will further add to our developing HF registry, to aid in the development of more accurate diagnostic criteria for this condition.

Participation in Alberta HEART has also led to unexpected KT and exchange activities for some team members. The breadth of research interests brought together by the 24-member team served as a catalyst for the creation of new interdisciplinary research teams (IRTs). For example, an emerging interdisciplinary Cardio-Oncology Group was formed between a subgroup of Alberta HEART investigators and their colleagues at the Cross Cancer Institute, to investigate how certain cancer treatments lead to HF in patients.



Allen He, RDCS and patient, Mrs J. Noble in the Alberta Cardiovascular and Stroke Research Centre (ABACUS), located in the Mazankowski Alberta Heart Institute.

Key Messages

Alberta HEART has changed the healthcare landscape in Alberta by bringing isolated research and clinical activities together to create a unified approach to studying DHF. The interdisciplinary research approach provided by Alberta HEART:

1. is key to understanding, diagnosing, and treating complex diseases.
2. is effective at bridging the bench-to-bedside-to-community gap.
3. can lead to unforeseen research opportunities in other disease areas.
4. require an active KT component for effective internal and external translation of activities and outcomes.

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The two distinct datasets (the clinically rich Alberta HEART province-wide prospective DHF registry and the Alberta Health and Wellness administrative database) provide comprehensive and complementary information to characterize DHF in newly diagnosed patients within a single geographic region and healthcare system. To our knowledge, no such resource currently exists anywhere else in North America.

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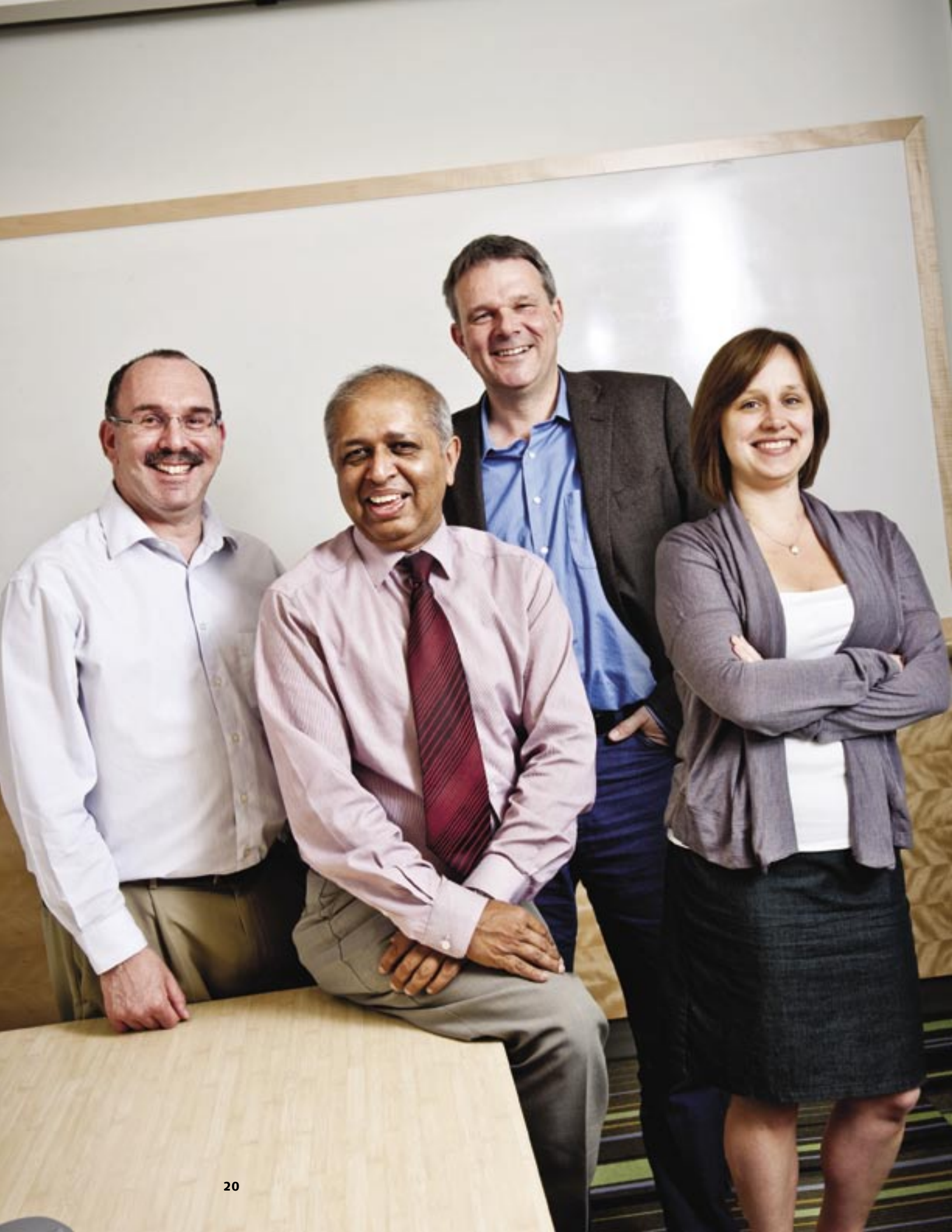


Toward Patient-Focused Research: Integrated KT in Action

Christina Heinrich, Subrata Ghosh, Keith A. Sharkey, Herman Barkema

Abstract

The Alberta Inflammatory Bowel Disease Consortium (IBD) is an interdisciplinary team of clinicians and scientists that studies the role that genetic, microbial, and environmental factors play in the development of Crohn's disease and ulcerative colitis. Through partnership with the Crohn's and Colitis Foundation of Canada, the Alberta IBD Consortium conducted a series of patient consultations across Alberta to solicit input into its research activities. This engagement lays a foundation of partnership with patient and community groups that will inform the consortium's overall KT and program strategy. By including patients in every step of the research process, from developing and prioritizing research questions to interpreting and disseminating research findings, scientists will be better positioned to develop novel studies which may in turn lead to breakthroughs in disease prevention and/or treatment that are more likely to be adopted by end-users.

Background

The patient is increasingly seen as an important partner in healthcare and medical research,[1] however, very limited work has been done on how and when it is best to involve patients in the research process. If done appropriately, the participation of disease sufferers in the design of research programs can help produce a more robust research framework, as patients and family members can provide specific and valuable insights into their conditions that can help direct questions and analyses and that might otherwise go unnoticed.[2] The research priorities of scientists and healthcare professionals have also been shown to be quite different from the priorities of patients when those priorities are directly compared.[3] By including patients in every step of the research process, from developing and prioritizing research questions to interpreting and disseminating research findings, scientists will be better positioned to develop novel studies that may in turn lead to breakthroughs in disease prevention and/or treatment that are more likely to be adopted by end users.

The Alberta Inflammatory Bowel Disease (IBD) Consortium is an interdisciplinary team of clinicians and basic scientists from across the province who have joined together to study the role that genetic, microbial, and environmental factors play in the development and perpetuation of IBD[4]. The team comprises specialists from a wide spectrum of fields including medicine, epidemiology, microbiology, veterinary medicine, genetics, and other health sciences disciplines who are working together in a novel, collaborative manner to address this complex family of diseases. A main focus of this collaborative model is to integrate the perspectives and input from a wide range of stakeholders, including partner organizations, healthcare professionals, and patients.

Through partnership with the Crohn's and Colitis Foundation of Canada (CCFC), we conducted a series of six structured patient input sessions across the province to solicit patient and family feedback on a variety of topics related to their research interests, priorities, and desire to become involved in the research process.

Facing page, left to right: Dr. Keith Sharkey, Dr. Subrata Ghosh, Dr. Herman Barkema, and Christina Heinrich.

KT Initiative

The primary objective of this initiative is to integrate patient input into our research activities within the Alberta IBD Consortium. We will use this data to inform our research questions and study designs, and will also share the data with other IBD researchers external to the team. In addition, we looked to build the foundation of a partnership with patient and community groups to inform our KT and overall program strategies.

We hope from these sessions to expand our knowledge regarding IBD patient research interests and increase specificity of topics. Through the life cycle of the initiative we also aim to increase the ability of our researchers within the Alberta IBD Consortium to undertake integrated KT in their individual research designs, as well as increasing the capacity of the patient community to engage researchers in meaningful dialogue around research into their disease.

The first round of patient input sessions has been completed and the data has been analyzed and is currently in the first stages of dissemination. We are now working to integrate the data into our planning/design processes, as well as planning next steps to continue this dialogue with patients.

KT Strategies

The use of facilitated workshops as a consultation strategy was selected as face-to-face interactions have been shown to be most effective when working with the public to identify and prioritize research topics.[5] Because the patient input sessions are intended to act as the initial guide for future integrated KT activities within the Alberta IBD Consortium, it was also important to begin to build relationships through personal interaction. Building these relationships and establishing trust are vital when working with IBD patients, because they experience intimate and embarrassing symptoms that can be challenging to discuss. A systematic and thoughtful approach is required to uncover and understand their needs.

Patient input sessions were held in six locations across the province of Alberta (Calgary, Edmonton, Lethbridge, Grande Prairie, Medicine Hat, and Red Deer). Sessions were held as part of regularly scheduled member information sessions for the CCFC. Participation was solicited through the websites of the Alberta IBD Consortium and the CCFC, through e-mails to the CCFC mailing list, and through CCFC publications. In total, over 150 individuals took part; participants included patients, family members, and front-line healthcare workers who specialize in working with IBD patients.

Sessions highlighted the integrated nature of the KT philosophy of the Alberta IBD Consortium. Each session began with an IBD overview and research update by one or two members of the team. Following these updates and a question-and-answer period, there was a facilitated workshop. Participants were led through a large group activity and were asked key questions regarding their awareness of research in general and of IBD research in particular, as well as their interest in being involved in research.

After 15 minutes of large group discussion, participants were split into small groups. A facilitator was assigned to help them work through specific IBD research concerns and priorities. Participants were asked to list a minimum of three topics related to their disease; topics in which they would like to see more research. The small groups were then asked to discuss the topics provided by each member and to group them into one of nine key topic areas as identified by Welfare et al[1] in their work with ulcerative colitis patients.

A main focus of this collaborative model is to integrate the perspectives and input from a wide range of stakeholders, including partner organizations, healthcare professionals, and patients.

As a group, the participants prioritized seven specific research topics from most important to least important. These research topics included specific areas of interest for the Alberta IBD Consortium, as well as general topics currently the focus of IBD research:

- food/diet
- pollution
- gut microbes
- genetics
- new treatment targets
- disease progression
- extra-intestinal symptoms

To conclude the session, the large group was brought back together to discuss areas of concern that were uncovered during the session and next steps, and to reiterate our commitment to them regarding follow-up and confidentiality. A Level 1 evaluation was then conducted by the CCFC to determine patient attitudes to the sessions. These evaluations revealed a very high degree of enthusiasm among participants for the material presented and the format for engagement, and a willingness to continue the dialogue with researchers in the future.

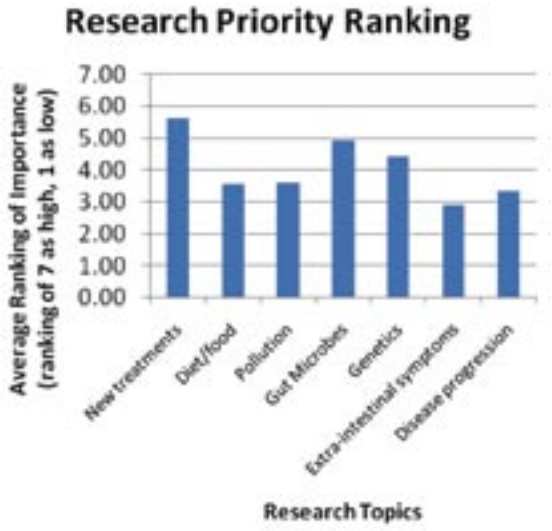
Christina Heinrich addressing group.

Patient input sessions through facilitated workshops can provide valuable research ideas, as well as build trusting, bidirectional researcher–patient relationships that can benefit both parties.

Results

The following graph illustrates how the patients who participated in the sessions prioritized the seven topics of IBD research. Not surprisingly, patients and family members ranked "new treatments" as their most pressing research priority, although there was large variability between locations and groups on this topic. From the verbatim comments collected, most participants expressed a greater desire to find a cure or prevention than a treatment. Patients also consistently rated "diet/food" fairly low (ranked sixth out of the seven topics), as they felt that this was something they could control through trial and error, and they would like to see researchers concentrating on topics that are more difficult for patients to control (for example, gut microbes).

When identifying individual topics of interest, the greatest focus was on finding the cure and on service delivery (particularly the long wait to see a gastroenterologist). From participants' responses it can be inferred that they possessed a very high level of understanding of their disease and familiarity with the research being conducted. Responses also reflected many areas of ongoing research including probiotics, pollution, stress, tobacco use, and genetics.



These results are being used to help inform the next stages of the KT strategy for the team and have also been published in the CCFC national newsletter. Based on the initial evaluation and feedback received, the sessions were viewed very positively and have accomplished the goals of building trust and awareness within the patient community, as well as within our own team, and of building patient input into every stage of the research process. The appetite for continued partnership from the CCFC, the patient community, and from members of the Alberta IBD Consortium is high, and can help model productive patient–researcher collaboration.

Although this format was useful for initial consultation and involvement and to build trust, there are several drawbacks to this methodology. From a data validity standpoint, the responses collected were influenced by the presentations that were given immediately preceding the workshop and by the focus of the individual researcher speaking. However, it is useful to note that messages provided in the research update were being assimilated as new knowledge, at least in the short term. One example of this is that genetics showed up as a low priority in early sessions, as participants reported confusion over how genetic research could help lead to cure or treatment. When the research update presentation was altered to contain specific information related to that question, genetics moved up in the results. This kind of face-to-face session is resource-intensive and only allows for relatively limited reach at each session.

Based on the session results, the team is now working on developing an online patient survey. This survey will utilize many of the same questions as did the face-to-face sessions, but will also build additional demographic, quality of life impact, and awareness questions. It is hoped that the survey will allow for more detailed results, as well as help to reach a broader audience across the province. The combination of face-to-face and survey methodologies will help support more robust findings and may address several of the weaknesses of using either strategy in isolation.

The data collected will also be used throughout this initiative to build our team's Knowledge Transfer Plan. This plan will outline a strategy to help direct future dialogues with patients and to ensure that projects undertaken by team members under the auspices of the Alberta IBD Consortium (and using team funds) are relevant and responsive to the priorities of people with IBD.

The evaluation of the patient consultations revealed a very high degree of enthusiasm among participants, and a willingness to continue the dialogue with researchers in the future.

Key Messages

Patient input through facilitated workshops can provide valuable research ideas, as well as build trusting, mutually beneficial researcher–patient relationships. This strategy has provided a solid foundation for a dynamic and progressive integrated KT strategy for the IBD Consortium. It has prompted plans for an online patient survey that will utilize many of the questions from the workshop. This will potentially increase our reach and generate a stronger data set.

We are impressed with the consistently high quality of patient input; their strong commitment to being involved in addressing their disease which has fostered a sense of co-ownership with researchers in findings and breakthroughs.

About the Authors

Christina Heinrich (MBA) is a senior advisor, organizational development with Alberta Health Services and a former knowledge transfer and exchange specialist with the Alberta IBD Consortium.

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Dr. Subrata Ghosh (MD, FRCPC, FRCP(E)) is a professor of medicine and head of the Department of Medicine at the University of Calgary, as well as regional clinical department head for Alberta Health Services – Calgary Zone and co-leader of the Alberta IBD Consortium.

Dr. Keith Sharkey (PhD) is a professor of Physiology, Pharmacology, and Medicine at the University of Calgary, Crohn's and Colitis Foundation of Canada Chair in IBD Research, deputy director of the Hotchkiss Brain Institute and member of the Alberta IBD Consortium.

The Alberta IBD Consortium is an interdisciplinary team comprising more than 30 clinicians and research scientists with a mission to improve the lives of IBD patients and their families and to reduce the impact of IBD on the health system by better understanding the causes and determinants of IBD.

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Improving the Care of Patients with Diabetes Within Primary Care Networks

Braden Manns, Marcello Tonelli, Anita Kozinski, Jianguo Zhang, Dave Campbell, Jeffrey Johnson, Peter Sargious, Richard Lewanczuk, Andreas Laupacis, Kerry McBrien, Brenda Hemmelgarn

Abstract

Although the optimal way to deliver care to patients with diabetes is unknown, Primary Care Networks (PCNs), introduced to Alberta in 2005, may offer some advantages to this population. The Interdisciplinary Chronic Disease Collaboration (ICDC) team conducted an evaluation of the impact of PCNs on patients with diabetes, and described PCN activities and programs in diabetes care. The potential users of this knowledge at a system level had a significant role in creating the research questions. A survey process also identified the key end users of the knowledge within the PCNs. A variety of strategies were used to present the research results to the end users and there is evidence that this has already had an impact on policy decisions.

Background

Diabetes is the leading cause of end-stage kidney disease and a major contributor to heart attack and stroke.[1-2] Safe, efficacious, cost-effective interventions for diabetes are available, including antihypertensive medications, cholesterol lowering treatments, and glycemic control.[3-10] However, these treatments are underutilized as diabetes care is complex and sustained behavior change is required to optimize care.[11-12]

In order to optimize care of patients with diabetes, comprehensive multidisciplinary chronic disease care (sometimes called chronic disease management, or CDM) is often required. Several different CDM programs have been tested for the care of people with diabetes. In 2006 a systematic review confirmed that most CDM programs were effective at improving glycemic control, although some types of CDM were more effective than others.[13] Programs that included team changes and case management were most effective.[13]

Primary Care Networks (PCNs) were first established in Alberta in 2005, and are one strategy for improving diabetes care. A PCN consists of primary care physicians (from one or more clinics in a geographic area) and other healthcare providers such as nurses, dietitians, and pharmacists, working together to provide primary healthcare to patients. While the major objective of PCNs is to improve quality of and access to primary healthcare, specific objectives are relevant to chronic diseases, including "health promotion, care of patients with medically complex problems, and care of patients with chronic diseases."[14] While each network has the flexibility to focus on any aspect of care that it feels will benefit patients, chronic disease management programs for patients with diabetes have been identified as a priority for most PCNs.[14]

KT Initiative

In 2007 and 2009 meetings were held with assistant deputy ministers at Alberta Health and Wellness (AHW) to establish research priorities for the Interdisciplinary Chronic Disease Collaboration (ICDC). After discussion with AHW and decision-makers at Alberta Health Services (AHS), it was determined that a comprehensive report describing current PCN activities in diabetes care and a quantitative evaluation of the impact of PCNs on patients with diabetes would inform decisions in 2011 about whether to continue, expand, or refine the model of care for PCNs.

Facing page, left to right: Dr. Marcello A. Tonelli, Department of Medicine, Faculty of Medicine & Dentistry, University of Alberta, Dr. Brenda Hemmelgarn, Division of Nephrology, Foothills Medical Centre, and Dr. Braden J. Manns, Division of Nephrology, Faculty of Medicine, University of Calgary

Those same discussions helped to identify knowledge gaps related to PCNs such as the types of chronic disease management programs being used by Alberta PCNs for patients with diabetes. In addition, the impact of PCNs on the care and outcomes for patients with diabetes was unknown.

KT Objectives

Short-term objectives:

1. To inform primary care networks and Alberta primary care physicians regarding their current management of patients with diabetes, including what types of CDM programs are offered across Alberta's PCNs.
2. To inform PCNs about which types of CDM programs should be offered, given the various budget constraints that might exist across Alberta's PCNs.

Long-term objectives:

1. To support PCNs in choosing an optimal mix of CDM services to enhance diabetes care.
2. To improve the care and outcomes of Albertans with diabetes who are cared for within PCNs.
3. To improve health system efficiency in diabetes care.

To address the knowledge gaps and to provide the evidence needed to meet our KT objectives, we first conducted descriptive and quantitative research. We also wanted to determine the effectiveness and cost effectiveness of CDM programs for diabetes to inform best practices regarding CDM programs.

To determine how care of patients with diabetes has changed since the establishment of PCNs, including the types of CDM programs offered, we surveyed the 30 PCNs in Alberta that were established as of January 2009. CDM programs were classified into 10 categories of delivery that differ by resource intensity and effectiveness (such as clinician reminders, patient reminders, patient education, team changes)

To determine whether care has changed for patients with diabetes managed in PCNs, we studied patients with diabetes (including a subgroup of newly diagnosed patients) before and after PCNs were established. We assessed several outcomes of interest including:

- hospitalization or emergency room visits for diabetes-specific ambulatory care-sensitive conditions (ACSC) (that is, events that might have been prevented by high quality outpatient care) primary outcome
- markers of high-quality outpatient diabetes care (that is, glycemic control as assessed using A1C, and use of indicated medications (that is, use of statins, angiotensin blockade in patients with proteinuria, and metformin among those requiring oral hypoglycemic agents)
- visits to primary care and specialist physicians

These outcomes have been identified by a Canadian expert panel as evidence-based quality-of-care indicators for patients with diabetes.[15]

KT Strategies

A critical part of our KT strategy has been building relationships with the relevant end-users. We involved key decision makers from the outset, including those at AHS and AHW. These knowledge users had a significant role in creating the research questions, ensuring their interest in the research results.

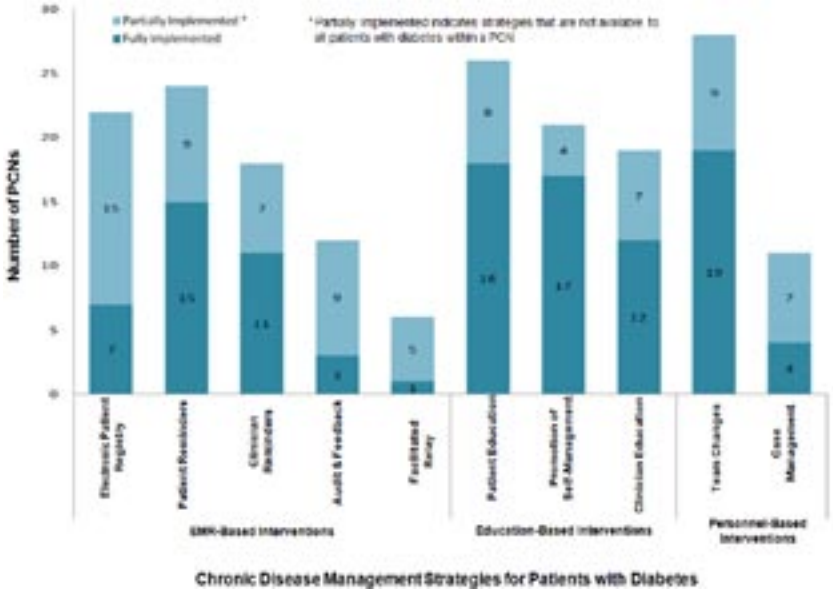
Engaging the PCNs was challenging given the number of networks, but contacts made during the process of surveying the PCNs enabled us to establish relevant contacts within each of them. Specifically, after completion of the research, we also involved key end-users at the Primary Care Initiative Committee, including leads of the PCNs themselves.

In addition to building relationships, our integrated knowledge translation strategy has involved end-users in developing optimal communications vehicles and other KT tools.

Research Results

Twenty-nine of the 30 PCNs established by January 2009 completed our telephone survey in August 2010, and of these, 28 offered at least one type of chronic disease management program for diabetes (see Figure 1). Some PCNs provided these CDM programs to all patients treated in the PCN; others offered them to a subset of patients. The two most common CDM programs offered to at least a portion of patients were "team changes" (in 28 of 29 PCNs) and "patient education" (in 26 of 29 PCNs). Fewer than half of the PCNs (12 of 29) had programs where members of the multidisciplinary team other than the primary physician had the authority to alter prescription medications. CDM programs that required significant resources (for example, case management) to operate were just as likely to be offered as CDM programs that required fewer resources (for example, clinician or patient education) to establish and operate. Of note, an effective strategy that can be facilitated by an electronic patient registry (that is, physician audit and feedback) was one of the least commonly used strategies in Alberta's PCNs.

Figure 1: Chronic Disease Management Strategies Used in Alberta Primary Care Networks



Compared to people with diabetes who were managed outside a PCN, patients with diabetes managed in a PCN had a 19% lower rate of hospitalizations or emergency room visits for diabetes-specific ACSCs, as well as better glycemic control (a mean reduction in A1C of 0.2). Patients with a new diagnosis of diabetes managed by physicians in PCNs in 2007, compared with those managed outside of PCNs in 2007, had similar rates of hospitalization and emergency room visits for diabetes-specific ACSCs, but better glycemic control and greater use of statins and metformin. Only approximately 50% of patients with diabetes were using statins (inside or outside of PCNs), which have been shown to be very effective in reducing cardiovascular risk among patients with diabetes. While patients with diabetes managed within PCNs received higher quality care and had better clinical outcomes, the differences were very small in magnitude and the observational nature of our data does not permit us to establish causality.

KT Results

To date, the following have been accomplished:

1. Presentation of project proposal to Alberta Health and Wellness: after collaboratively developing the study questions for this project, we presented the draft research proposal for their feedback at an Alberta Health and Wellness Lunch and Learn Session. Feedback strongly supported an ongoing collaborative research effort between AHW and ICDC.

2. **Presentation of results to all stakeholders:** Key results of this research were presented to decision makers at AHW, AHS, and the Primary Care Initiatives Committee Forum.

3. **Creation of a working paper and other KT tools:** The final working paper included an executive summary and a covering letter outlining key points, both of which were developed in consultation with the end users at AHW and AHS. This was subsequently distributed to all relevant stakeholders at AHS, AHW, PCNs and the AMA.

4. **Drafting of manuscripts for peer-review:** Two manuscripts based on the working paper were written: "The Use of Chronic Disease Management Programs for Diabetes by Alberta's Primary Care Networks," is in print at the Canadian Family Physician journal; and "Association between enrolment in a Primary Care Network and quality of care for patients with diabetes" which is currently under consideration by the Canadian Medical Association Journal.

5. **Involvement in Diabetes Clinical Advisory Group:** On behalf of the ICDC, Dr. Manns has been invited to sit on an Alberta Health Services Diabetes Clinical Advisory Group, which will oversee strategic development of care and evaluation for patients with diabetes across Alberta. The work conducted within this project will assist this group in determining what quality indicators can be tracked using available data within Alberta.

The true test of whether our KT strategy has been effective is whether this information has impacted decision-making in Alberta with respect to PCNs. Discussions with the decision-makers at AHW and AHS have been very encouraging, suggesting that this information helped inform the decision to extend the trilateral PCN agreement. Furthermore, we are aware that this information has been used by the AHS chronic disease group to refine the current trilateral agreement governing PCNs, specifically with respect to recommendations around how CDM programs are used by PCNs.

Another sign that our strategy has been effective is the ongoing willingness of decision-makers to work with the ICDC, including a third invitation to present to AHW in Sept 2011, which will be another opportunity for us to re-elicit future research priorities.

To continue to meet our goal of improving the care and outcomes of Albertans with diabetes who are cared for within PCNs, further research and KT activities are planned:

- Continue evaluation of the effectiveness and cost-effectiveness of the different types of CDM programs in diabetes, with completion expected in late 2011.
- Resurvey of PCNs on their use of CDM programs, and to re-examine the care and outcomes of patients with diabetes at the end of the project.

Future planned KT activities:

- In late 2011 we will disseminate to PCNs the results of the updated systematic review of CDM programs for diabetes, through presentations and a variety of KT tools deemed to be appropriate by end-users.
- Through involvement with the Diabetes Clinical Advisory Group, our research will be used to develop a quality improvement framework to track outcome changes for patients with diabetes associated with PCN implementation and changes.

Key Messages

- KT is a deliberate process that requires significant cognitive and human resources.
- When decision-makers are involved from the outset and, in fact, pose the overall questions, they are much more likely to be interested in the results, and to act upon them.
- Meeting with decision-makers on an ongoing basis is an effective method of maintaining their engagement.
- It is important to provide small information packets and concise messaging, and to have decision-makers involved in determining the key messages.
- Making KT a component of all of ICDC's research is a priority, but to make this a reality, it is critical that a KT person be hired who makes this their daily job.

About the Authors

Dr. Braden Manns is an associate professor of Medicine and Community Health Sciences at the University of Calgary. He is a co-lead of the Interdisciplinary Chronic Disease Collaboration team.

Dr. Brenda Hemmelgarn and Dr. Marcello Tonelli are co-leaders of the Interdisciplinary Chronic Disease Collaboration team.

The Interdisciplinary Chronic Disease Collaboration (ICDC) is a motivated team of researchers whose overall objective is to improve the health of patients living with (or at risk of developing) chronic disease. This novel collaboration between healthcare decision-makers, scientists, and educators from 14 key disciplines was formed to examine issues related to treating patients who have (or who are at high risk of developing) hypertension, diabetes, chronic kidney disease, and vascular disease.

The ICDC Team wishes to thank Susan Williams, Assistant Deputy Minister, Health Policy and Service Standards, for her contributions as Alberta Health and Wellness liaison with the team.

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Approach to KT in Development of Disease Diagnostics

H. John Crabtree, Nana Yaa A. Boadu, Erin L. Navid, Edna F. Einsiedel, Jason P. Acker, Stephanie K. Yanow, Linda M. Pilarski

Abstract

Team Microfluidics (TM) is creating new miniaturized technology for testing to screen for the presence of infectious agents (for example, malaria, influenza) and cancers in patient samples. While the idea is simple, developing a "sample in, answer out" device is far from simple. The scientific research and technology development are very challenging, but alongside these are the equally important knowledge translation (KT) activities. The team's KT plan comprises research, IP protection, collaboration, commercialization and dissemination activities, and building partnerships is a key aspect of the plan, tailoring the technology to end user needs. Partnerships are equally critical for product acceptance in developing countries, where the complexities of technology adoption, less skilled operators and a much harsher physical environment come into play.

Background

Most diseases involve genes carried either by the host or by the cells, molecules, or pathogens that cause the disease. Genetic testing involves identifying important segments of genetic material and amplifying them from one or a few copies to many millions of molecular copies, in what is essentially a molecular copying machine. This is called nucleic acid amplification and is critical for molecular testing - tests that detect genes or the products of genes as a measure of disease. Screening for infectious diseases and cancers is a critical component of diagnosis and treatment. The most effective technique for detecting infectious agents is molecular testing for their genes. Although accurate and sensitive, molecular testing is rarely done due to its complexity and expense.

Nanotechnology platforms that can carry out cost-effective molecular testing allows us to create hand-held laboratories with the potential to significantly decrease these costs, while allowing molecular testing to be deployed even in remote and underdeveloped areas. This has the potential to improve health outcomes on a global scale and also to bring significant benefits to Alberta through intellectual property (IP) protection and technology commercialization. Miniaturized devices that provide "sample in, answer out" capability offer substantive social and economic benefits by enabling rapid testing while the patient is still in the clinic. The majority of clinical laboratories however, lack the capability for molecular testing, usually some type of polymerase chain reaction (PCR), the most widespread strategy for genetic amplification.

Despite its sensitivity, accuracy and speed, molecular testing currently suffers from several problems that restrict its use in many medical testing labs, including:

- cost
- complexity
- variability in sample processing and purification
- variability in sensitivity and accuracy
- requirement for highly trained personnel
- expensive infrastructure needing regular upgrading or replacement
- increasing strains on space in clinical testing laboratories

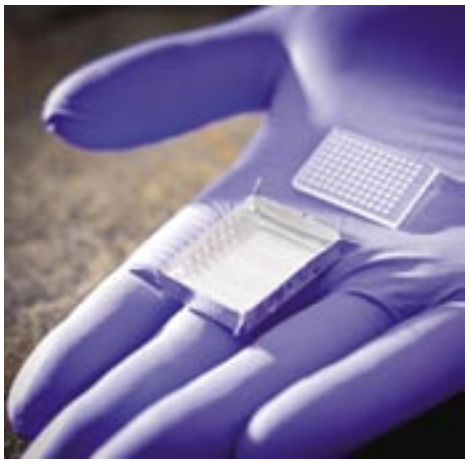
Facing page, left to right: Hashim Mohammad, Jason Acker, Dammika Manage, John Crabtree and Jana Lauzon .

Shipping samples for batch processing in centralised testing facilities is either not feasible or introduces delays in implementing treatment. Molecular testing, despite its emerging value for medical decision-making and therapeutic tailoring for personalized medicine, is almost completely inaccessible. For vulnerable populations in rural, remote, or impoverished areas, even simple types of medical testing can be compromised by a lack of refrigeration, basic sanitation, and/or clean water.

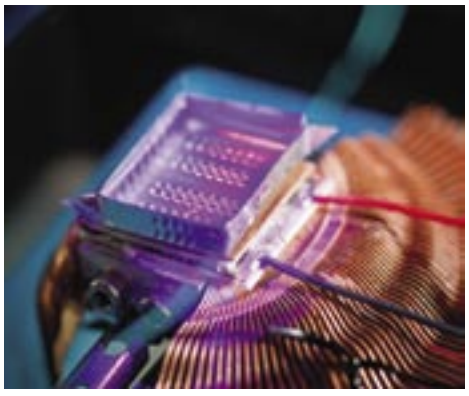
Sustainable and accessible molecular testing requires robust testing platforms with standardized sample delivery and on-board reagents stored at room temperature. Such platforms could be used in local medical centres, rapid response laboratories, or even rudimentary health facilities in under-resourced locations, and would allow for "on the spot" high quality medical testing for infectious diseases, ongoing or emerging epidemics, and chronic or acute diseases.

Miniaturized devices able to perform many molecular tests at once offer immediate one-at-a-time testing when the patient first presents in the clinic, with none of the delays inherent in centralized PCR strategies that must accumulate hundreds of samples for batch processing. At the time each sample is collected, our in-gel PCR technology platform1 for molecular testing carries out inexpensive PCR amplification of a whole series of molecules important for a given disease or set of symptoms. It consists of an array of moulded polymer gel pillars with a consistency somewhat like that of Jello™. Gel posts contain all of the chemicals needed for PCR, requiring only that the patient's sample containing genetic material be applied to the surface of the gel posts.

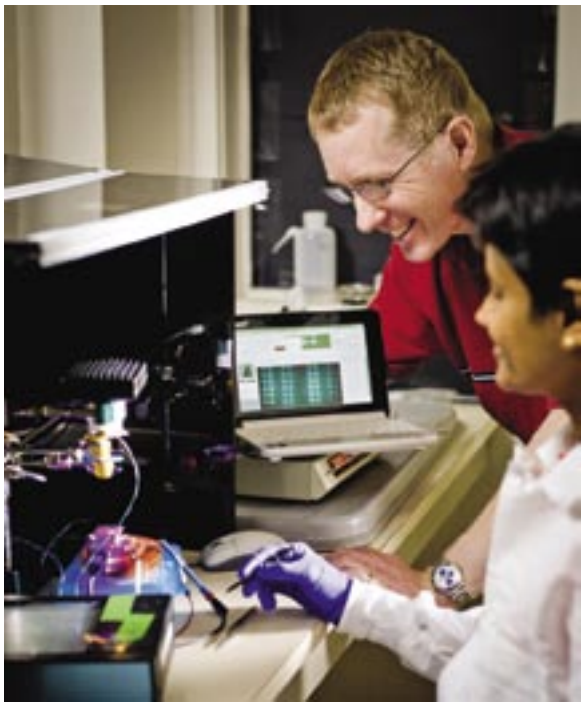
Miniaturized devices that provide "sample in, answer out" capability offer substantive social and economic benefits by enabling rapid testing while the patient is still in the clinic.



A gel post array immersed in oil sits in an aluminum pan, with the mould to form the posts above.



Pan with gel post array is mounted atop Peltier heater with a copper heat sink and is illuminated by the instrument's violet laser.



John Crabtree observes while Dammika Manage performs a PCR sample analysis on the gel post array.

Our in-gel PCR system directly addresses the above-mentioned challenges facing molecular testing, as needed for a viable point-of-care (PoC) diagnostic. It provides discrete gel post reaction vessels that are inexpensive and semi-automated, and require minimal patient samples. Operation of the instrumentation for molecular testing using PCR is, at this stage, simple in the hands of a research technician; it will be easily performed by a minimally trained PoC field assistant once a fully developed system is available.

Knowledge of the social contexts for which this technology is being developed is crucial to its eventual acceptance. The technology readily lends itself to different disease applications that are relevant in very different geographical locations. Thus, depending on the application, a detailed understanding of the status quo, principle advantages, and barriers inherent in our technology's use in the developed and developing world is a primary underpinning to its success.

KT Objectives

Briefly put, the primary objective of TM's KT initiative is to build relationships with suitable commercial partners in order to enable technology transfer and subsequent product development. The impact of successfully transferring our disease diagnostic technology to a suitable receptor company will be:

- first, a successful launch of a disease diagnostic product built on the technology
- eventually, the widespread use of this product and technology to address the healthcare challenge presented by the disease(s)

More broadly, the impact will be to see our technology dramatically reduce the diagnostic challenges that presently impair the provision of healthcare in several critical disease areas.

Examples of solutions to challenges that could be provided by our technology are:

- the reduction of both time to diagnosis and the likelihood of misdiagnoses
- rapid turn-around to inform a medical professional with respect to an appropriate response
- the facilitation of diagnoses in sophisticated urban hospitals, local health clinics, and remote locations, or in the harsh environments that are typically home to many serious diseases in the developing world

KT Strategies

Our team must consider two principle audiences for knowledge translation purposes.

1. The various end users for whom the technology platform is being designed: for diagnostic applications in the developed world, this is likely to be a nurse, lab technician, or other health care worker working in a fairly controlled environment. For applications in the developing world, this is likely to be a minimally trained field worker at a clinic or mobile clinic working in rugged conditions. In all cases, the end-user requires that technology be:

- simple and easy to operate—insert sample, press "run," and receive test results approximately 15 to 30 minutes later
- robust, reliable and independent—given the infrastructure and typical environment in both developed and developing world settings, the system will need to operate robustly and efficiently in dusty, hot (~40°C) settings, and on battery power with sporadic access to main power.

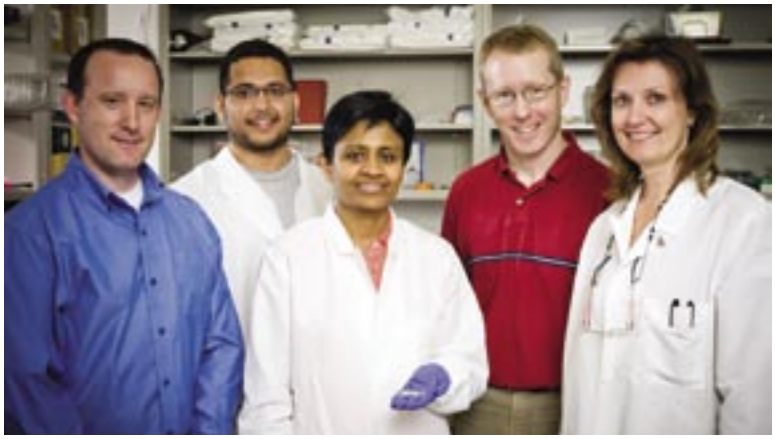
2. The receiving commercialization enterprises who aim to incorporate our technology into their products. These companies comprise the more immediate audience, with barriers to technology transfer varying somewhat, depending on the type and maturity of the private enterprise.

- For a larger, more mature enterprise, the principle challenges are to convince them of the value in expanding their technology base to include ours based on the benefits conferred, and assist in defining a viable product vision.

• For a smaller start-up enterprise, the greater barrier to KT may be raising funds that enable them to fully develop the product and business model. The creation of a functional prototype device and a sound business plan are therefore crucial to attract investment capital and remove this barrier.

Facilitators to KT with either type of commercial receptor are:

1. Sound technology development must lead to a functioning prototype device that demonstrates the concept with robust performance.
2. Establishment of preliminary IP protection or secrecy is a necessary underpinning for commercialization.
3. Although more in the purview of the commercialization partner, social context and/or product acceptance research in relevant environments.



Jason Acker, Hashim Mohammad, Dammika Manage, John Crabtree and Jana Lauzon.

Results

At present, despite some early stage challenges, the team has achieved significant KT successes with several commercial partners, with gains in several key areas:

1. Technical development: The development of an innovative gel-based platform. Proof-of-principle is complete; effort is now focused on improving engineering controls and refining the overall design for enhanced reproducibility, performance and portability.

2. IP protection: Two US provisional patents, filed to protect platform IP and several implementation patent submissions, are in preparation.

3. Social context: Research thus far has underlined a number of end-user needs, existing government healthcare policies, and treatment practices that must be considered for the diagnosis of different diseases in both developed (Canada) and developing (Ghana) countries. Significant findings have been distilled regarding social contexts and end user acceptance in both world settings, relevant to products harnessing our disease diagnosing platform.

4. Dissemination: Although secondary to the team's need for IP protection, we have published and presented team research at conferences and public speaking events.

5. Outside partnerships: Several collaborations have been established for the application of our technology to malaria diagnosis with researchers in Colombia, Denmark, and Uganda, and commercial interest in our platform is being demonstrated. Aquila Diagnostic Systems (Edmonton) has established a technology platform licensing agreement and close working relationship with the team to define its product vision.

Evaluation of our initiative's effectiveness is primarily demonstrated through successful technology transfer to a (or several) commercial entity(ies) and, ideally, helping and observing them proceed to product launch.

Key Messages

We have learned several lessons through the implementation of our KT plan, some of which are fairly novel and/or seldom implemented in the context of academic scientific research.

1. Ensure that technology is extensively vetted with applications (and not technology development) users. This entails a strong focus on robust function and reproducibility since these are prerequisites for technology commercialization.

2. Establish IP protection at the earliest stage, and ensure the team understands the "protect first, publish second" philosophy to enable commercial success.

3. Foster commercialization partnerships at an early stage as well, as this affords the best chance for both the research team and the commercial development partner to learn from each other and to tailor their activities to assure mutual success.

4. Foster academic collaborations that are as close to the end-user as possible, and that specifically target social aspects of acceptance. Although they are not targeted at creating commercial linkages, they provide invaluable information regarding the potential barriers and pathways to a product's commercial success.

About the Authors

Dr. John Crabtree (PhD, PMP), Department of Oncology, University of Alberta, is project manager for Team Microfluidics and the founder of HJC Consulting.

Nana Boadu is a PhD student studying global health at the School of Public Health, Department of Public Health Sciences, University of Alberta.

Dr. Edna Einsiedel (PhD) is a professor in the Department of Communications and Culture, University of Calgary.

Erin Navid, of the Department of Communications and Culture, University of Calgary, is a research associate in the Einsiedel Group.

Dr. Jason Acker (PhD, MBA) is an associate professor in the Department of Laboratory Medicine and Pathology, University of Alberta, and also a senior scientist with Canadian Blood Services.

Dr. Stephanie Yanow (PhD) is an assistant professor at the School of Public Health, University of Alberta, and also a program leader with the Alberta Provincial Laboratory for Public Health.

Dr. Linda Pilarski (PhD) is professor in the Department of Oncology, University of Alberta, and is the team leader of Team Microfluidics.

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Our in-gel PCR system provides discrete gel post reaction vessels that are inexpensive and semi-automated, and require minimal patient samples.

A Holistic Approach to Pressure Ulcer Prevention

Nichola Wilson, Vivian Mushahwar, Ming Chan, and Lisa Kawasaki

Abstract

Pressure ulcers are highly prevalent in acute, chronic, and home care centres. In Canada, their treatment is estimated to cost $3.5 billion annually. Individuals suffering from pressure ulcers are also susceptible to complications such as sepsis, localized infection and, in extreme cases, death. In its aim to prevent deep tissue injury and the development of pressure ulcers, the team has developed Smart-e-Pants which utilize a novel electrical stimulation approach to induce contractions in muscles subjected to persistent pressure. Engagement of end-user groups, through an invitation to caregivers and members of the community, was sought in the very early stages to test and evaluate design prototypes, and has directly influenced product development. This engagement of stakeholders and end-user groups at the grassroots level has proven to be a critical factor in the design and acceptance of the Smart-e-Pants system.

Background

Pressure ulcers are a serious side effect of immobilization or loss of sensation. Populations susceptible to the formation of pressure ulcers include:

- people with spinal cord injury (SCI), stroke, multiple sclerosis, and bone and joint conditions
- people who are confined to bed
- people who are dependent on wheelchairs for their daily mobility

Pressure ulcers are highly prevalent in acute, chronic, and home care centres. In Canada, the treatment of pressure ulcers is estimated to cost $3.5 billion annually (Ferguson-Pell, unpublished data), and in the United States, $11 billion.[1]

To date, specialized mattresses and wheelchair cushions have been the main interventions used to prevent the formation of pressure ulcers. The majority of these specialized surfaces provide static relief of pressure, which increases the length of time body regions can be subjected to pressure; however, these durations are limited to a few hours at best. Dynamic relief is necessary for the prevention of pressure ulcers and is normally achieved by repositioning patients. Despite the continual advancements in support surfaces and repositioning methods since the 1950s, the incidence of pressure ulcers has not changed.[2,3]

Pressure ulcers are divided into two categories: those that form on the surface of the skin and progress inward and those that form at deep bone – muscle interfaces, termed "deep tissue injury" (DTI), and progress outward. Despite the substantial deleterious effects of DTI, no methods currently exist for its early detection. The Mushahwar group has proposed and tested a novel electrical stimulation approach – intermittent electrical stimulation (IES) – for the prevention of pressure ulcers and DTI. Tests have shown that IES-induced contractions redistribute pressure around bony prominences and increase oxygenation levels in loaded and deformed deep tissues. Coined "Smart-e-Pants", this smart neural prosthetic system for delivering IES patterns to people with reduced mobility or sensation may prove to be the next generation of technology in the clinical arsenal for the prophylactic prevention of pressure ulcers.

Facing page, left to right: Lisa Kawasaki, Dana Schnepf, Joy Scott, Vivian Mushahwar, Anita Clarke, (front) participant Sandy Brooks-Scott; members of the Pressure Ulcer Group at the Allen Gray Continuing Care Center.

KT Initiative

The ultimate goal of the Smart-e-Pants project is to provide clinicians and end-users with an effective means of prevention of pressure ulcers that can be used in conjunction with current interventions such as specialized cushions and mattresses. If effective, it may alleviate the labour/time intensive repositioning methods that consume valuable clinical resources. At present, human prototypes of the Smart-e-Pants garment have been developed, and their feasibility, acceptability, and safety are currently being tested in the clinical environment. Industrial partnerships are also being formed and a commercialization strategy is actively being developed as a vehicle through which the Smart-e-Pants system can be marketed to caregivers and end-users in the future.

KT Strategies: Linkage and Exchange

To tackle this perilous clinical problem, a diverse group of engineers, neuroscientists, clinicians, caregivers, and regulatory and industrial experts have joined together to design and test a smart neural prosthetic system that is accepted and effective in the prophylactic prevention of pressure ulcers. Like a puzzle, the components of Smart-e-Pants required the individual expertise of many participants to put the pieces together; however, melding this diverse group into a cohesive team presented challenges.

The basic technology development and clinical implementation involved negotiation and interaction between many organizations, and overcoming the barriers that exist between institutions. These hurdles have been successfully tackled by the team through extensive open communication between group members and by identifying the clinical and industrial liaisons necessary for the successful development and testing of the Smart-e-Pants system.

Regular interaction between trainees, principal investigators, and clinical personnel was facilitated through monthly focus group meetings. Clinical liaisons were identified from the outset of the project and charged with setting up and facilitating interactions with CEOs and senior administrators in the clinical centers. Linkages with existing commercial entities were pursued to provide component development and to assist in evaluating target markets and the commercial viability of Smart-e-Pants. Extensive communication between these diverse groups has been fundamental to the successful development of Smart-e-Pants, as team members joined together to contribute their unique perspectives to the system's development, usability, and acceptability. If realized, this will be the attainment of a major goal of the team: to break down barriers between biomedical engineering technical development, clinical acceptance, and the delivery of a new technology to patients at the bedside.

Left to right: participant Sandy Brooks-Scott, Dana Schnepf, and Vivian Mushahwar assess the Smart-e-Pants garment.

Knowledge End-Users

Engagement of end-user groups was sought in the very early stages of Smart-e-Pants development through community workshops designed to both inform participants about this pressure ulcer intervention and to invite clinical and industrial partners and patient groups to test and evaluate design prototypes. This feedback influenced early prototype designs, as modifications to the system were made based on end-user response. Through these workshops, industrial and clinical partners were also exposed to neural prosthesis technologies and applications, while researchers were at the same time acquainted with patient needs. Collaboration across the spectrum of research, development, and deployment has been a mandate of the team and key to the success and acceptance of the Smart-e-Pants system.

Clinical centres have also been engaged to test various design prototypes and to assess the feasibility of their deployment across the continuum of care (intensive care/acute care units; rehabilitation; long-term care; home and community care). Partnerships have been formed with the Foothills Intensive Care and Acute Rehabilitation Units, the Glenrose Rehabilitation Hospital, the Allen Gray Continuing Care Hospital, and with Home & Community Care Services. To date, nursing staff at the Allen Gray and the Glenrose Rehabilitation Hospital have received training in the administration of the Smart-e-Pants system, and nine patient volunteers have undergone staged testing. These tests have provided valuable input regarding the system's clinical friendliness and sustainability, and the garment's aesthetics, comfort, and construction. Input from workshops and from clinical testing also determined the need for multiple prototypes to meet the requirements of different clinical centers and individual end-users.

This iterative process, whereby technical prototypes are developed with the input of clinical liaisons and end-user stakeholders, will continue to be assessed in various clinical environments. Modifications will be incorporated and retested as technologies are implemented. We believe that this process will lead to a neuroprosthetic system that is accepted by end-users and that integrates seamlessly into the clinical environment.

Engagement of end-user groups was sought in the very early stages through community workshops designed to both inform participants about this pressure ulcer intervention and to invite clinical and industrial partners and patient groups to test and evaluate design prototypes.

Dr. Ming Chan.

Results and Next Steps

Smart-e-Pants continues to be positively received by the nursing staff and volunteer patients who work with the system through clinical trials. The cooperation and willingness of patient volunteers to take part in the study and to provide valuable input is vital in improving the system. Collaboration amongst team members continues to focus on the sharing of information and on feedback from end-user stakeholders. The safety, feasibility, and acceptance of the Smart-e-Pants system are continually being re-evaluated through questionnaires, focus group meetings, and face-to-face communication with end-user groups. Frequent workshops led by team scientists and clinicians also help to maintain knowledge exchange between groups and to ensure that the future development of the Smart-e-Pants system is a true partnership between all stakeholders. These workshops led to the team looking into a new garment material to improve breathability.

With the support of AIHS funding, the Smart-e-Pants project will move ahead with expanding trials in diverse clinical environments such as at the Foothills Hospital Intensive Care Unit, which will allow testing on subjects more acutely ill than those at the Allen Gray Continuing Care Hospital and the Glenrose Rehabilitation Hospital. We will also be implementing a testing program for independent community dwellers who use a wheelchair for daily mobility. Prototypes for the closed loop Smart-e-Pants system will be tested in able-bodied volunteers and in a limited set of end-users at our partner clinical sites. The Phase Two prototype has been built for the wireless system, which would have a local receiver that can monitor operation of the stimulator, store relevant information, and deliver alarms as required. It will also relay alarms to a nursing station to notify staff, so that they can respond appropriately.

Key Messages

Our inter-disciplinary team has a continuing desire to work collaboratively with end-user stakeholders by sharing expertise, ideas, and experiences. This has been central to the project's KT practices. At times, interaction and communication between multiple organizations and team members presented challenges; but a dedicated drive to maintain connections through focus groups, team meetings, and workshops has proven to be key in overcoming those barriers.

These cycles of constant refinement through active participation and establishing a meaningful dialogue amongst all stakeholders have helped improve the quality of the end product and its versatility to meet demands in different clinical settings. Those steps are also crucial in transitioning key insights attained through basic science research in the laboratory to applications at patients' bedsides and in the community.

Our ultimate goal is to commercialize the Smart-e-pants system and make it available to patients everywhere. This requires us to engage industrial partners at an early stage. Those multi-directional interactions represent knowledge transfer at its best. If realized, our hope is that the intended technology will not only benefit a narrow segment of patients, but will also benefit individuals who are at high risk of developing pressure ulcers worldwide. Collaborative practice has also allowed the Smart-e-Pants group to engage the resources and knowledge of a diverse range of specialists to achieve project goals, and has increased our understanding of pressure ulcers, DTI, and their causes.

Coined "Smart-e-Pants," this smart neural prosthetic system may prove to be the next generation of technology in the clinical arsenal for the prevention of pressure ulcers.

About the Authors

Nichola Wilson is the project manager's assistant for the Alberta Innovates – Health Solutions Interdisciplinary Team in Smart Neural Prostheses.

Dr. Vivian Mushahwar, team lead and member of the Pressure Ulcer group, has pioneered the use of electrical stimulation to prevent the development of pressure ulcers. Dr. Mushahwar is an Associate Professor at the University of Alberta and receives funding from AIHS.

Dr. Ming Chan is lead clinician for the Pressure Ulcer group and is in charge of the clinical application of the Smart-e-Pants system for the Edmonton region. Dr. Chan is an Associate Professor of Physical Medicine and Rehabilitation at the Glenrose Rehabilitation Hospital.

Summer student Lisa Kawasaki works directly with participants at the Glenrose Rehabilitation Hospital and the Allen Gray Continuing Care Hospital, testing and conducting data analysis of the Smart-e-Pants system.

The AIHS Interdisciplinary Team in Smart Neural Prosthesis would like to acknowledge the contributions of the following individuals who have dedicated to much time and energy to the Smart-s-Pants project: Anita Clarke, Alisa Ahmetovic, Dana Schnepf and Ryan Sommer. Thank you for your time, expertise and commitment.

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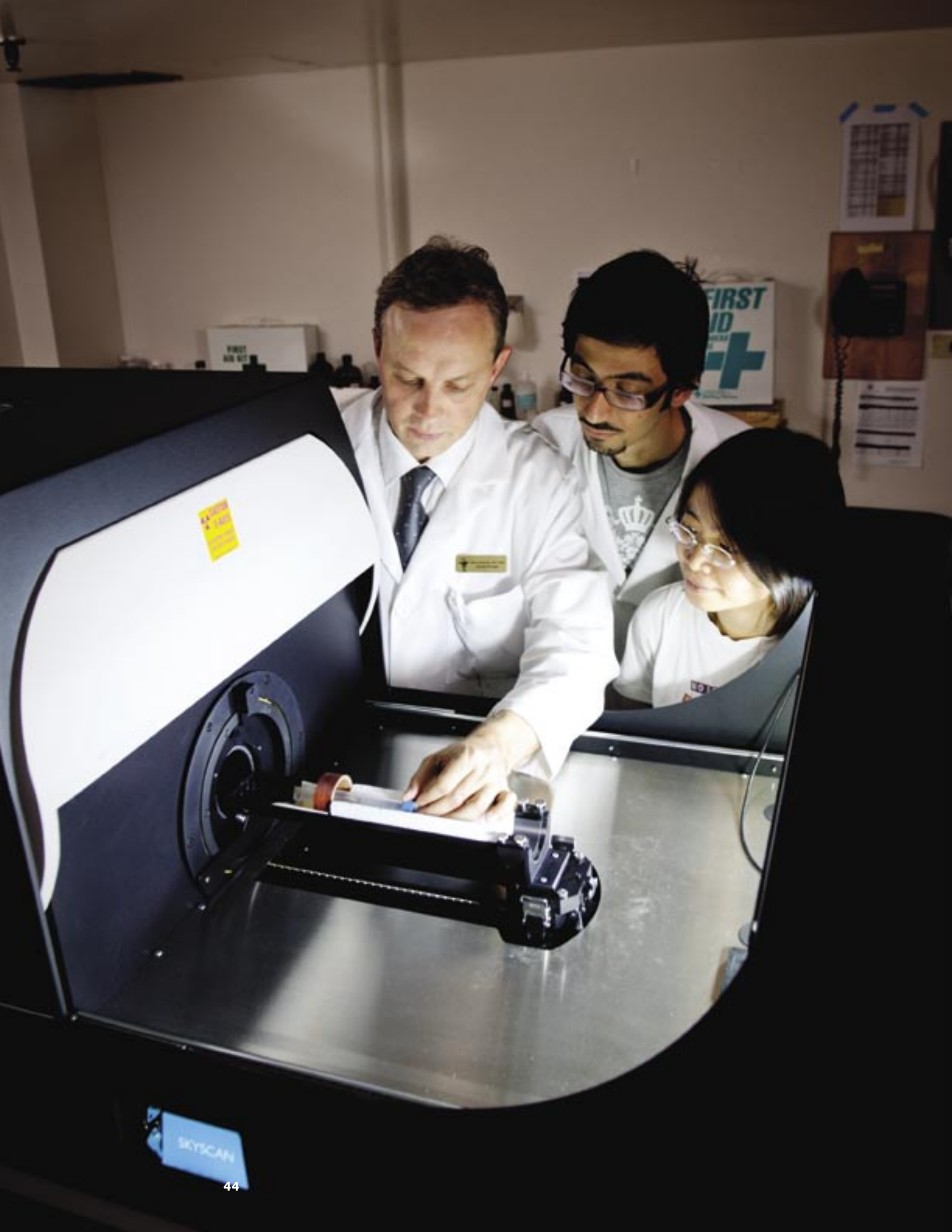
FIRST
SKYSCAN

Bone Trek—The "Next Generation" of Drugs for Osteoarthritis

Mike Doschak

Abstract

In our aging Albertan population, osteoarthritis (OA) is a common source of debilitating pain, loss of mobility and, ultimately, quality of life. An estimated 4.5 million Canadians, including approximately 450,000 Albertans, suffer from OA—a bone and joint condition characterized by the progressive destruction of the shock-absorbing articular cartilage in our joints. Currently, no disease-modifying treatments are available for OA, meaning that the drugs currently being used to treat patients with OA will not stop the disease from progressing further. Thus, for now, all our medical system can offer patients is conservative pain management and moral support as the joint tissues and structures continue to deteriorate. Novel drug-delivery research at the University of Alberta, led by Dr. Mike Doschak, with the Edmonton arm of "Team OA Alberta," has its sights firmly set on interrupting the OA disease process and providing novel drug treatment options for OA sufferers. Dr. Doschak's research efforts have resulted in the recent pharmaceutical synthesis and characterization of what many consider to be the "next generation of bone drugs."

Background

As bone turnover in OA joints begins very early in the disease, it is thought to play a critical role in the progression of that disease. In addition to cartilage loss, OA results in changes to the bone beneath the cartilage and surrounding the joint margins. Accordingly, much of the pain and inflammation associated with OA can be traced back to those accompanying bony changes. In particular, OA progression will result in the formation of tender bony "growths" at the joint margins known as osteophytes, that serve as a source of pain and stiffness, along with thickened subchondral plates that end up rubbing "bone upon bone" following the full-thickness loss of the cartilage cushion in full blown, end-stage OA.

Bony growths also serve as the major cause of pain in the OA joint, because cartilage does not contain nerves and does not sense pain. Bone, on the other hand, is highly innervated and thus therapeutic strategies that target bony changes offer the opportunity to treat OA early, with the potential for modifying disease outcomes. As with any disease, early detection of OA is very important and offers the greatest hope for slowing the progression of symptoms. Currently, planar X-rays serve as the most common method by which physicians can confirm the diagnosis of OA, with evidence of joint space narrowing due to cartilage loss and the appearance of osteophytes serving as important indicators of OA-related joint pathology. Clearly, the success of newly developed drug interventions aimed at slowing or even blocking the bony changes linked with OA progression will need to be initiated as soon as possible after early diagnosis has been confirmed.

Calcitonin is a naturally occurring peptide hormone in humans, secreted by the thyroid gland, which serves to quiesce (or "rope in") uncontrolled bone turnover, to maintain bone balance, and to conserve existing bone microstructure. Calcitonin has been used historically as a therapeutic agent in diseases of low bone volume and fragility fracture, such as osteoporosis, but it has received limited attention in the treatment of other bone disease due to its lack of potency and efficacy relative to other treatment options available for controlling bone mass. Curiously, however, calcitonin further

Facing page: Team OA Alberta researcher Dr. Mike Doschak (left) loading the sample bed of the SkyScan 1176 in vivo micro-CT imager, along with Doctoral trainees Arash Panahifar (centre) and Yuchin Wu (right). The micro-CT imager is capable of producing highly magnified images from the bones of living subjects treated with novel drug therapies, in order to gauge the success of novel OA drugs in the treatment of Osteoarthritis.

possesses powerful pain-relieving effects upon nerves and has been shown to exhibit cartilage-protecting properties, leading to a renewed interest worldwide in calcitonin for the potential treatment of OA. However, current calcitonin drug formulations are quickly diluted and readily excreted by the body after administration, resulting in the all-too-common lack of potency and efficacy associated by physicians and patients alike with this naturally occurring and otherwise safe peptide medication.

KT Initiative

To challenge calcitonin's shortcomings and work toward a commercializable product, the lab under Mike Doschak at the University of Alberta developed and synthesized bone-seeking variants of calcitonin, by chemically coupling them to bone-seeking bis-phosphonate (BP) drug moieties under highly controlled reaction conditions. The novel drug compound - BP-conjugated calcitonin (or BP-CT) - directly targets and "protectively coats" bone tissue after administration by its specific binding to bone hydroxyapatite mineral, eliminating the problem of systemic drug dilution and side effects when native calcitonin is administered at very high doses.

One of the most effective ways to test novel bone drugs is to conduct safety and efficacy trials in small rodent models, such as lab rats. To visualize the changes in the amount and strength of newly formed bone in the rat after drug dosing regimens, non-invasive X-ray imaging technologies such as micro-computed tomography (or micro-CT) are utilized. Micro-CT is a rapidly developing technique used to image and quantify bone and other mineralized materials, non-destructively, in three dimensions (3D). In contrast to other 3D imaging techniques (for example, MRI), micro-CT is ideally suited for the imaging of dense matter such as mineralized tissues and materials. Recently, technology has been developed that enables the "in-vivo" imaging of living laboratory animals by micro-CT. Designed for use with small laboratory animals (such as mice and rats), the detailed imaging of bone micro-architecture can now be assessed at multiple time-points in the same animal over time, thus greatly increasing the ability to test hypotheses related to bone adaptation by direct "cause and effect" measurements.

In order to capitalize on that novel technology, Dr. Doschak secured the necessary funding to establish the Pharmacy Micro-CT Imaging Facility (PMCT; http://www.pharmacy.ualberta.ca/Doschak_lab/facilities.htm), which has an aim to non-invasively quantify bone and mineral adaptations in living animals, after pharmaceutical interventions. Since the arrival of the Canada Foundation for Innovation (CFI)-funded SkyScan 1076 micro-CT imager at the University of Alberta in April 2007, Dr. Doschak and the lab staff have established world-class in vivo micro-CT imaging and data analysis protocols with over 20 investigators across campus, for the benefit of the university academic community, as well as the Canadian biotech sector.

Imaging technician Jillian Chapman monitors a vivo micro-CT scan image, while graduate student Arash Panahifar reconstructs data sets in order to visualize and quantify the effectiveness of a drug regimen that is being trialled.

That infrastructure was utilized to conduct the necessary pre-clinical safety and efficacy trials of the new BP-conjugated calcitonin formulations, using micro-CT imaging of bone mass and mineral density according to FDA standards. Currently, the Doschak lab has developed and characterized several formulations of BP-CT conjugates, containing from one to three water-soluble bone-targeting moieties. In preclinical safety and efficacy studies in laboratory rats, BP-CT was measured to significantly outperform currently available commercial formulations of calcitonin, offering the enormous promise of a novel drug therapy for OA and many other bone diseases.

Furthermore, to date, more than 12 pharmaceutical sciences graduate students have utilized the micro-CT imager as part of their basic science research, leading to a new generation of highly qualified personnel trained with this novel imaging modality for application to novel research findings. Those outcomes fit into the "KT cycle" of the Alberta Health Research and Innovation Strategy (AHRIS), developed to respond to the policy and health system needs identified by the government of Alberta. Specifically, "innovative platforms" are identified as a major enabling strategy for improving health and health system outcomes, in order to "enhance targeted technology and product development programs and support innovative preventative, diagnostic, and therapeutic technologies and health products." (AHRIS)

KT Strategy

With the aim of bringing the novel BP-CT bone drugs nearer to human clinical trials, Dr. Doschak and his research team have established a university "spin-off" biopharma in Edmonton—Osteo-Metabolix Pharmaceuticals Inc. (OMX). OMX constitutes a start-up company focused on the development, formulation, and evaluation of bone-targeting biologics for bone conditions such as OA, osteoporosis, and Paget's disease. OMX is now in the process of seeking a strategic co-development partnership with the established pharmaceutical industry for lead optimization of the BP-CT compound, toward drug "scale-up" and first-time-in-human (FTIH) evaluation of this unique bone-targeted therapy for bone disease.

BP-conjugated calcitonin is unique to Alberta's OMX Pharmaceuticals. While there is some activity in the area of BP-conjugated drugs in general, no other research groups are currently investigating BP-CT as a targeted anti-resorptive therapy. This means that BP-CT is highly marketable as a significantly improved treatment for a wide range of bone diseases, including OA and osteoporosis. This puts OMX Pharmaceuticals in a very strong intellectual property (IP) position. Based on this, they have successfully filed a US patent (and related Patent Cooperation Treaty, or PCT) to protect the value of their novel BP-CT conjugates, functional bioassays, and methods for applying the new drugs for treatment of bone disease.

One of the enabling events leading to the KT breakthrough, from research idea to a novel pharmaceutical as a deliverable, was inclusion of Dr. Doschak's research team as part of the Alberta Innovates – Health Solutions Osteoarthritis Interdisciplinary Team Grant initiative, also known as "Team OA Alberta" (http://www.oarthritis.com/). The bringing together of highly skilled teams of new and established researchers in both Calgary and Edmonton, to focus on osteoarthritis research in Alberta, helped fund and guide the necessary research in the Doschak lab that resulted in the generation of several bone drug candidates that now offer new hope for patients suffering debilitating OA pain. The KT process was further made possible by guidance and co-development from TEC Edmonton, the business commercialization arm of the University of Alberta. TEC Edmonton's company development program was a valuable resource in helping develop a business plan for OMX, as well as in providing the services of market analysts, business strategists, and seasoned executives-in-residence with extensive networks and experience, in order to develop a viable strategy for the further commercializing of OMX's therapeutic OA compounds.

It is anticipated that successful commercialization of the BP-CT compound will yield economic, health, and societal value benefits on several fronts. These compounds hold potential not only to reduce the economic costs of OA, but also to improve patient outcomes. In addition, the KT process will provide economic benefit in the form of the development and retention of high-quality personnel, and new industry partnerships with players in the pharmaceutical and biotechnology industries, both locally and internationally. Such relationships are beneficial to the Canadian and Albertan economies through product innovation, bringing funds into the economy, and building a pro-entrepreneur environment.

Key Messages

OMX Pharmaceuticals Inc. specializes in the development of novel bone-targeted therapies with a broad spectrum of applications in bone disease. Bisphosphonate-conjugated calcitonin is unique to OMX, putting this Alberta biopharma company in a very strong IP position with excellent market potential. BP-CT has improved therapeutic efficacy in increasing bone density and reducing systemic side effects when compared to conventional, unconjugated calcitonin, with the enormous promise of improving pain and disease outcomes for OA patients.

Strategic partnership with established corporations in the pharmaceutical industry will result in shortened product development times and an improved patent position, as BP-CT will serve as a natural follow-on from existing drug development programs with those partner companies, whilst further supplying access to specialized expertise and testing methodologies for drugs acting on bone cells.

Faculty of Pharmacy & Pharmaceutical Sciences technician Vishwa Somayaji loading novel drug samples in thin glass vials in preparation for NMR-mass spectroscopic analysis of the newly synthesized products.

The bringing together of highly skilled teams of new and established researchers in both Calgary and Edmonton has resulted in the generation of several bone drug candidates that now offer new hope for patients suffering debilitating OA pain.

About the Author

Dr. Mike Doschak was recruited as an assistant professor to the Faculty of Pharmacy and Pharmaceutical Sciences at the University of Alberta in September 2005, based on his promise to deliver a drug delivery research program for the mineralized connective tissues of the body, namely the bones and teeth. That discovery followed on from his in-depth research efforts at the University of Calgary in understanding the mechanism of action of the bisphosphonate class of anti-resorptive drugs, particularly with non-traditional therapeutic and/or diagnostic applications.

Team OA Alberta, with co-leads Drs. Cyril Frank and Walter Herzog, are conducting research on novel, non invasive diagnosis of OA; developing novel OA prevention strategies; broadening the therapeutic window for treatment options; and improving outcomes for patients with mid- and end-stage OA.

Dr. Doschak and his research team have established a university "spin-off" biopharma in Edmonton—Osteo-Metabolix Pharmaceuticals Inc.

Partnering in Research on Maternal and Child Health to Inform Practice and Policy: The Preterm Birth and Healthy Outcomes Team

Suzanne Tough, Shoo Lee, Karen Benzies

Abstract

Between 8% and 9% of Alberta infants are born preterm and are at risk of chronic health problems, developmental delay, behavioral problems, and academic underachievement. The Preterm Birth and Healthy Outcomes Team (PreHOT) brings together a diverse group of researchers to study how to prevent preterm birth and improve outcomes for children and their families. PreHOT initiatives include the Care by Parent Study, which is piloting a model of care based on greater parental involvement in neonatal care, the Fathers and Babies Study, which provides fathers with home visits and education to enable them to better support their infants, and the All Our Babies Cohort Study, which is following 3,300 women from pregnancy to early parenthood, to better understand the causes of preterm birth and the impact of prenatal care programs. The authors conclude that successful knowledge mobilization benefits from building trusting relationships with knowledge end-users, engaging them throughout the research project, and ensuring that results are relevant to their needs.

Background

Between 8% and 9% of Alberta infants are born preterm, at less than 37 weeks gestation.[1,2] Alberta has the highest rate of preterm birth among Canadian provinces; the province's rate is surpassed only by rates in the Territories.[1] Babies born preterm are at risk of chronic health problems, developmental delay, behavioural problems, and failure to achieve academically.[3-7] Can preterm birth be prevented? [8]

Researchers from different disciplines have some ideas about why babies are born preterm, but no one can really predict which pregnant women will deliver preterm. Strategies to prevent preterm birth have often formed within single disciplines. Population health experts may target risk factors, such as obesity and smoking. Clinical researchers may examine the role of infection. Genetics researchers may emphasize the identification of genetic risk markers. Yet these discipline-specific strategies have not solved the problem and preterm rates are increasing. Meanwhile, there is limited understanding of how primary healthcare and interventions might improve birth outcomes and outcomes for children born preterm. This provides an opportunity to address the issue of preterm birth using different kinds of strategies.

Interdisciplinary Team Research

The Preterm Birth and Healthy Outcomes Team (PreHOT) brings together 17 researchers with a variety of expertise and perspectives to study how to prevent preterm birth and to improve outcomes for children born preterm and for their families. PreHOT includes diverse investigative approaches to the problem of preterm birth, including identification of genetic markers, animal models of risk factors, analysis of uterine contraction in labour, the impact of parenting techniques on outcomes, and the evaluation of different models of prenatal care. This interdisciplinary research approach includes internal knowledge translation, as animal models have informed human studies,

Facing page, left to right: Home visitor Dr. Karen Benzies video recording a father, Vic Rutherford, as he plays with his baby, Alex.

and team members are developing methods for connecting psychosocial questionnaire data to biological data. Working together across disciplines, PreHOT has designed a research program to understand the relative contribution of health service delivery, clinical services, demographics, and lifestyle, as well as genetic, biologic, and physiologic risks to the problem of preterm birth in order to target interventions for maximum impact.

KT Initiatives

The following are just a few of the projects undertaken by PreHOT members that demonstrate the ability of the research team to work across disciplines, build relationships, and integrate knowledge translation throughout a research project. These projects are jointly funded through Alberta Innovates – Health Solutions' Interdisciplinary Team Grant to PreHOT, as well as by other funding partners as noted in the acknowledgements at the end of this article.

The Care by Parent Study is based on international evidence suggesting that when preterm infants are cared for primarily by their parents they gain weight faster, have fewer challenges with their health, and have shorter hospital stays.[9] While caring for their infant under the guidance of hospital staff, these parents meet other parents who are also caring for a preterm infant, creating opportunities for parents to support each other in their journeys. The Care by Parent research team understood the importance of connecting with those who would ultimately receive, provide, and oversee this model of care, so they gathered substantial local input from the Parent Advisory Board, nurses and nurse managers, and senior level hospital administrators. The result was the construction of a nursery that allowed parents and babies to be together in a way that resembled a home environment, and the implementation of a pilot study of this model of care. Parents are grateful to be able to participate in the pilot study and to provide care for their infant. Some mothers have even shared their stories publicly about the benefits of this type of care.

The Fathers and Babies Study begins with evidence indicating that the foundations of all future social, emotional, cognitive, and physical capacities are established in early childhood, and that parents are the most important influence in the growth and development of their young children. However, there are significant gaps in what parents know about child development.[10] Parents consistently say they need opportunities to learn about child development and to normalize their experiences.[11]

Now, imagine you are the father of a preterm infant. Your baby is in an intensive care nursery and attached to specialized machines. While in the hospital, you try to support your baby's mother with breastfeeding and care, but it is tiring because you also need to work to support your new family. After discharge it is time to get to know your baby … but how? You are invited to participate in the Fathers and Late Preterm Babies Study, designed for fathers of preterm babies. In this intervention, a skilled home visitor comes out to your home and video-records you playing with your baby. You review your video with the home visitor and get individual pointers about how to understand your baby's cues and respond more effectively. Whenever you want to review the pointers, you can look at your video again via the Internet. Within months, you notice your confidence has improved and your baby has benefitted from the high quality of play that you have provided. This type of intervention is consistent with the state of the science in early brain development that focuses on the importance of quality early relationships. By linking a unique combination of technology and video techniques, the team has been able create specialized supports for the fathers of late preterm babies.

The All Our Babies Cohort Study research team has expertise in community-based research, epidemiology, obstetrics, genetics, nursing, psychology, economics, and biostatistics. This large cohort began gathering data from about 3,300 women during pregnancy through to four months after birth. All women completed three questionnaires and provided consent for access to their medical record information. About 1,800 women also provided biological samples. The use of a questionnaire and of biological data will allow the interdisciplinary research team to gain an understanding about the gene-environment interactions that contribute to preterm birth, and the impact of prenatal care programs on health outcomes.

In the only randomized trial of group prenatal care, Centering Pregnancy demonstrated promising results, including improved prenatal knowledge, increased readiness for labour and delivery, higher

rates of breastfeeding initiation, and increased satisfaction with care.[12] Of particular interest was the reduction in preterm delivery rates observed in women who received group prenatal care (9.8%versus 13.8%).[12] The All Our Babies Cohort will allow the research team to compare outcomes of mothers and infants who received group prenatal care to outcomes of mothers and infants who received standard prenatal care.

KT Strategies: Building Relationships

The reason many researchers gravitated to a research career is because their nature and skills often include independence, reflection, and introspection. The idea of meeting new people and explaining things in a colloquial manner, without using precise terms and profuse detail, can be unfamiliar and uncomfortable. However, those outside a research office often have skills in building relationships, programs, and policies. These skills can be incredibly beneficial when one is eager to see research findings used to support practice and policy. Developing partnerships with these people has enhanced PreHOT's collective ability to achieve a common goal.

KT Strategies: Integrated KT

PreHOT KT initiatives such as organizing a healthcare setting to better meet the needs of parents and infants, understanding models of service delivery, and engaging fathers in parenting an infant born preterm intersect directly and naturally with the interests of a community of stakeholders. These projects have included program planners, parent advisory boards, focus group consultations, community stakeholders, and policy- and decision-makers in the design of projects, resulting in a research agenda that applies to issues that are relevant to the province. When research demonstrates improved outcomes for parents and children, these relationships between researchers and other stakeholders facilitate the implementation of effective programs and policies to help children and families reach their potential.

- Engaging patient populations respects the importance of connecting with those who would ultimately be at the receiving end of models of care, while developing data collection that meets the needs of all partners. This is an undertaking that requires input and dedication from everyone. It is important to create an environment where everyone contributes, and it takes time to build trusting relationships.
- Engaging healthcare providers and clinical partners (for example, perinatal educators and nutritionists) provides expertise in such areas as working with high-risk women, assistance in finding an appropriate care setting, and assistance in developing population-based strategies to recruit pregnant women and collect biological samples.
- Engaging health systems policy-makers, through their inclusion in research and program teams, allows for the design and adjustment of research programs that will be most meaningful for end-users. It also creates relationships that will facilitate future dissemination of policy-relevant research.

Home visitor Dr. Karen Benzies, reviews a video of Vic Rutherford playing with his baby, Alex. Dr. Benzies is reinforcing the components of the father's play that will promote the baby's development and giving tips to strengthen the quality of play.

- Engaging non-governmental organizations and participating in national and international collaborations enables routine sharing of information about emerging issues and potential solutions.
- Engaging trainees in these projects invests in a future generation of researchers who will be well equipped to build relationships and integrate KT into their own research programs.

Results

We have experienced the relationship side of knowledge translation and believe that its outcomes are well beyond the traditional benchmarks of publishing and presenting. We experience success when decision-makers, health service providers, members of the community, and the media contact us to ask questions, invite us to share our findings, and want to work together to address other relevant issues. We experience success when we find ways to adapt to a changing environment and work together to keep our vision on the long-term goal: improving outcomes for women, children, and families. We know we are raising awareness when stakeholders, trainees, clinicians, and others talk about their "new understanding" of the importance of pregnancy and the early years, because we know our research is contributing to this conversation.

The Care by Parent Study has held meetings with representatives from all NICUs to inform them of progress on the project, and has obtained agreement from most to participate in a multi-centre national trial after the pilot. Several hospitals have also committed to becoming pilot sites and to providing in-kind support for facilities renovations for the project. They have communicated with government representatives in several provinces to obtain their support, and will be presenting their project to hospital executives at the Canadian Association of Pediatric Health Centres' annual conference at a plenary session in October 2011. Results of the pilot will be published when it is completed at the end of 2011.

The Fathers and Babies Study has developed specialized technology that is of interest to clinicians and researchers locally and internationally. Researchers from the Universities of Washington and New Brunswick have requested access to the technology, or assistance to set up comparable systems for their research programs. The technology has potential value for clinicians who provide similar interventions to families of children with a disability who have difficulties with social interactions. The team submitted a Report of Invention to Innovate Calgary (formerly University Technologies International). The application was assessed and deemed to have commercialization potential, given that no similar technologies were located. The technology is currently being refined, with a cost-benefit analysis planned to ensure that this "first to market" product will have value.

The All Our Babies Cohort Study has collected data suggesting that women at risk of postpartum depression can be identified early in pregnancy, and now a local maternity clinic is involved in a pilot study to identify these women so they can go on to receive support from a new program. The All Our Babies study team will continue to gather data from the 3,300 mothers and children throughout the children's early childhood. This will allow the team to build on the investment to date and identify early markers of risk to child development. That way, interventions can happen early and can reduce the impact of threats to child development. The Alberta Children's Hospital Foundation and the University of Calgary Faculty of Medicine have already partnered financially in this work, and the Alberta Centre for Child, Family & Community Research is partnering to develop a data centre in which to store the valuable data from mothers and their children.

Key Messages

1. Create an environment where everyone contributes, and build trusted relationships. This is a critical element in the development of an applied research agenda and it takes time.
2. Make it relevant by involving end-users in the development of the research questions. The ability to work collaboratively in the development of research questions enhances the likelihood that the evidence created will be used and will be relevant. Once a team can agree on what success will look like, they can work backward, linking the outcome measures to the intervention.

3. Expect the unexpected, stay flexible, and focus on the vision. Throughout our projects we have experienced changes in our clinical champions, changes in the ability of stakeholders to maintain their commitments (both time and financial), changes in the ability to access space for program delivery, changes in project staff, changes in clinical staff, and/or changes in both our research teams and our project teams. With a common vision and communication, we have worked through these times of transition.

4. Make it relevant by involving end-users in the interpretation of the data. One of our successful processes has been to have stakeholders brainstorm with the researcher about what the data says, so common messages can be jointly created.

5. Get out of the office and listen to others. The opportunity for partnership is enhanced by trying to meet people where they are at, talking enough so that there is shared understanding about the issues and concerns, and listening to ensure that the strategy or project being developed addresses core issues to the best ability of all stakeholders.

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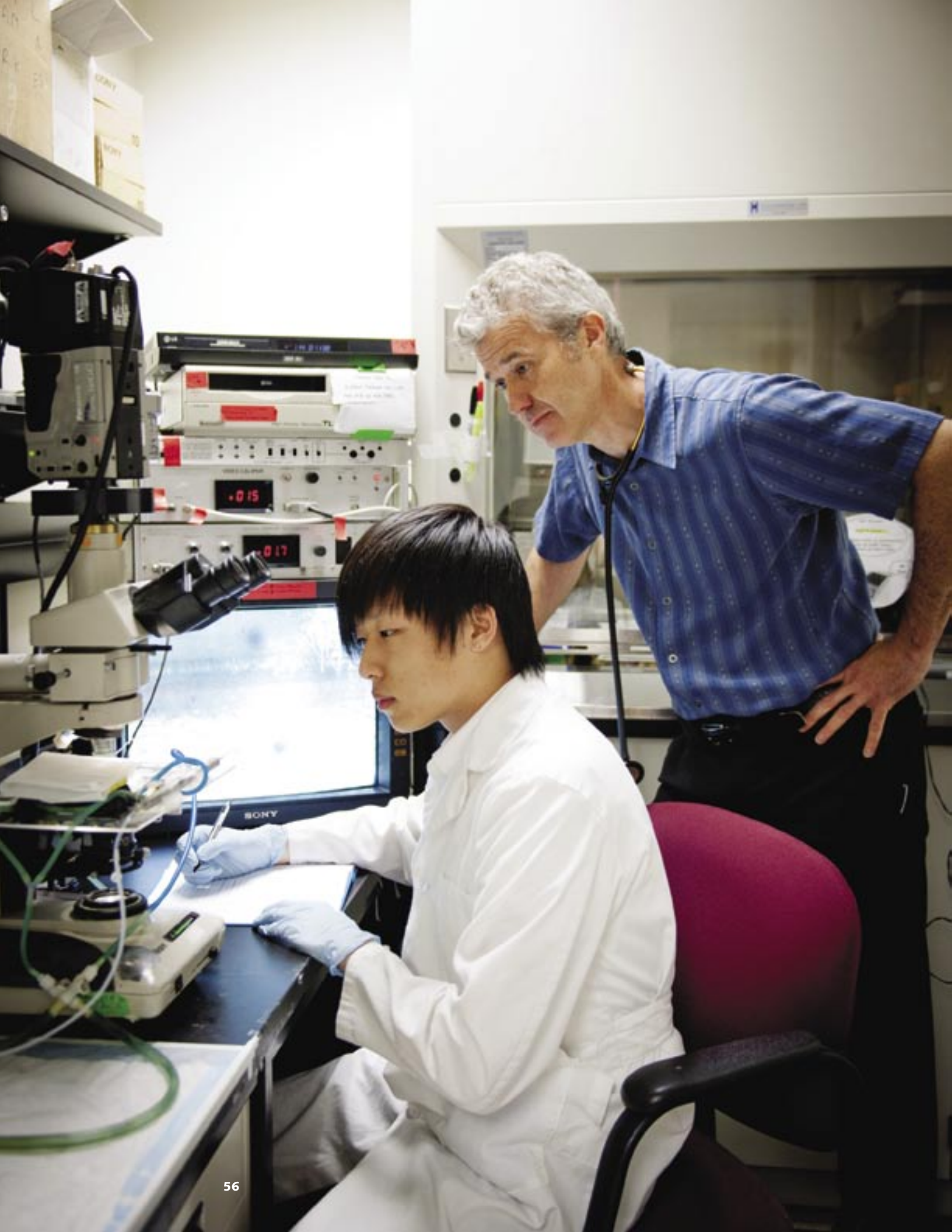
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The Alberta Sepsis Network Knowledge Translation Activities

Ari Joffe, Derrice Knight, Paul Kubes, Christopher Doig, Eddy Lang

Abstract

Sepsis is a leading cause of mortality and morbidity among adults and children in Alberta, resulting in enormous human and financial costs. The Alberta Sepsis Network (ASN) is an interdisciplinary team of basic researchers, clinical researchers, and clinicians who have come together to identify the research priorities for improving sepsis outcomes. This effort has resulted in the preliminary identification of a metabolomic profile for sepsis that has the potential to enable accurate and early diagnosis. Further, the establishment in Alberta of a comprehensive outcomes registry and tissue bank will allow for the generation of knowledge about long-term outcomes and evaluation of interventions in sepsis care. A unique part of the KT strategy is engaging a marketing firm to develop branding around sepsis as a prerequisite to greater public involvement in early identification.

Background

Sepsis is a leading cause of mortality and morbidity in adults and children.[1,2] Each year 4000 Albertans are admitted to intensive care units (ICU) with septic shock. Over the past decade incidence has increased, hospital costs have grown, and mortality has remained high.[3] The basic elements of treatment have not changed since the 1960s, and emphasize antibiotics, source control (removal or drainage of an infected source), and resuscitation with volume and vasoactive drugs.[3] Delays in diagnosis and treatment have a significant impact on patient outcomes; for example, for every hour that antibiotics were delayed after the onset of septic shock, there was an 8% increase in mortality.[4-6] Mortality for those admitted with septic shock to adult ICU is 30% to 40%; for children admitted to pediatric ICU it is 10%.[1,2] Attributable deaths and loss of cognitive and functional abilities have been found for years after the sepsis event.[3]

The Alberta Sepsis Network (ASN) is an interdisciplinary team of basic researchers, clinical researchers, and physicians who are developing methods for the early identification of sepsis, investigating the relationship between pathogenesis and clinical trajectories, and studying the long term neurocognitive outcomes of adults and children who have had severe sepsis.

KT Objectives

1. Identify knowledge needs that may change practice through engagement with researchers, clinicians, and policy makers.
2. Identify research priorities through exchange among a multidisciplinary partnership of researchers and clinicians stakeholders, with mutual control over decisions.
3. Develop a comprehensive outcomes registry to evaluate the long-term outcomes of sepsis; this will facilitate awareness, interest, and future assessment of the impact of mobilizing research knowledge.

The impact of these objectives should ultimately be to advance knowledge, inform decision-making, and impact health and social outcomes.

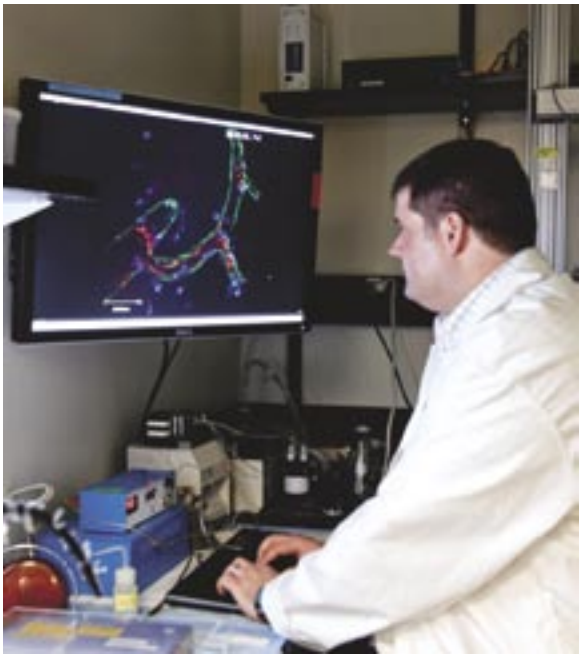
Facing page: Dr. Chip Doig overseeing summer AIHS summer student Weitong Yan in vivo imaging.

KT Strategies: Interdisciplinary Research

The ASN brings together a collaboration of multidisciplinary end-users: basic science researchers in immunology, microbiology, and metabolomics; clinical researchers in public health, epidemiology, intensive care, and infectious diseases for both adults and children; clinicians (physicians and nurses) caring for patients in emergency departments and intensive care units; and policy makers from Alberta Health and Wellness (AHW) have been integrated into the ASN at all phases of research. KT is a social process and must be seen as relevant to end-users and key stakeholders; the target audience is intentionally a wide network of colleagues, allowing co-creation of knowledge and ensuring relevance within the context of patient care.

A first priority was to assemble the interdisciplinary group of researchers and clinicians. Representation from the target audience across Alberta has been achieved. Annual face-to-face meetings of the ASN group have been held in Red Deer to facilitate participation from across the province. Several conference call and/or dinner meetings among the ASN knowledge champions have occurred. Semi-annual meetings with AHW have also taken place. Local presentations and discussions at departmental rounds and lunch hour sessions have supported dissemination and setting of research priorities. An ASN website facilitates this exchange of information. This interdisciplinary team approach allows for basic research knowledge, clinical research knowledge, and clinical practice knowledge to continuously inform both each other and new research programs.

Weitong Yan, 2011 AIHS summer student, in the vivo imaging lab.



Dr. Bjoern Petri, past AIHS postdoctoral fellow, looking at Confocal Spinning disk data in the vivo imaging lab.

ASN Graduate student, Keir Pittman, working on an in vitro neutrophil biology assay.

KT Strategies: Identifying Knowledge Needs

Through engagement of all disciplines from the start of the ASN, we identified knowledge needs priorities that may change practice. Early detection and therefore treatment of sepsis was identified, based upon the high economic and health costs of sepsis. Understanding the novel microbiology and immunologic pathophysiology of sepsis was identified as another knowledge need that has potential to change practice. Comparing this pathophysiology and host response between adults and children was identified as a potential strategy for understanding delayed resolution of organ dysfunctions and morbidity/mortality, given the difference in outcomes among these patient populations.

Exchanges among the team of researchers and clinicians identified research priorities to meet the knowledge needs. Metabolomics was identified as a priority for investigating a novel method of early diagnosis of sepsis, with the potential to inform patient triage decisions, disposition, and early treatment, and to improve outcomes.

KT Strategies: Knowledge Generation

The first step in investigating novel host responses and microbial communities in severe sepsis is the development of a comprehensive bank of patient specimens and clinical data and to develop and link that to an outcomes registry. These are necessary steps to evaluate the long term outcomes of sepsis. This will emphasize the importance of the ASN to all clinicians, inform counseling of patients and decision-makers, and allow future assessment of the impact of mobilizing research knowledge. Another priority has been to engage both adult and pediatric clinicians in order to facilitate understanding of the range of host responses to sepsis.

KT Strategies: Health Literacy

The ASN has engaged a major marketing firm to develop branding around sepsis as part of a public education campaign. This is an important prerequisite to public involvement in the early identification of sepsis warning signs, which could lead to quicker hospitalizations of septic patients and better outcomes.

Results

Early results from this KT initiative have included:

1. Engaging the appropriate audience to identify research priorities and knowledge needs and to ensure relevance. These are all important to future implementation by end users and as a catalyst for further research.
2. Developing a comprehensive Alberta outcomes registry, database, and tissue bank. This has had the added benefit that clinicians working in hospital emergency rooms and intensive care units are aware of ASN activities and of the importance of sepsis, and that they have frequent interactions with ASN research coordinators and local opinion leaders. By generating end-user interest in the ASN, the future translation of research findings to the bedside is already eagerly anticipated.
3. Engaging all end-users in the research process, including data collection and interpretation. This has enabled the preliminary identification of a microbiome of interacting pathogens in septic patients, and the preliminary identification of a metabolomic profile of septic patients during early stages of their illness. This holds promise for the development of a new diagnostic tool for sepsis.
4. Engagement of a team of researchers and clinicians that continues to be leveraged to inform ASN activities. As novel findings are developed to allow early diagnosis, prognostication, and prediction of therapeutic response, these are presented to bedside clinicians, who in turn inform subsequent research priorities.

The dynamic and iterative process of knowledge exchange among basic science and clinical researchers, adult and pediatric clinicians, and policy-makers has allowed the priorities of the ASN to be appropriate to the context of real-world patients. Several benchmarks have been achieved along the knowledge-to-action cycle. We have:

- identified the problem—inability to reliably diagnose sepsis at its early stage
- confirmed its importance in the local context—emergency rooms and intensive care units for both children and adults
- overcome barriers to knowledge use—fragmentation of activities between basic researchers, clinical researchers, clinicians, and policy-makers
- prioritized the ASN research activities—by identifying the target audience, engaging these end-users and potential adopters of knowledge, and integrating the audience into the ASN process, we have developed an interactive group to facilitate future knowledge-to-action activities.
- created an appetite and perceived need for research results—by engaging local opinion leaders in the ASN and generating local interest and participation from bedside clinicians; this will facilitate dissemination of research outcomes by involving the very groups that will be impacted by ASN findings.

Future KT activities are anticipated, leveraging the infrastructure created. These include conference presentations and publications, educational sessions with practitioners and policy-makers, media engagement to disseminate strategic knowledge to the public at risk for sepsis, potential commercialization of scientific discoveries, and interactive meetings to discuss future research directions as well as the implications and feasibility of practice change. Adoption of these efforts will need to be monitored and evaluated to document improvement in patient care and practice decisions.

An example is the upcoming ASN Consensus Conference: A Knowledge Translation Agenda in Sepsis Care. The components of a robust sepsis care pathway are not easy to implement in the hectic environment of acute patient care. Optimizing sepsis care along the continuum from the emergency environment to the intensive care unit demands collaboration and seamless integration of the transitions between both care environments. It also demands the engineering of robust systems of care that can monitor and provide effective and timely feedback on performance indicators related to sepsis. The ASN has decided to hold a joint meeting of emergency and ICU clinician and research stakeholders to define key unanswered questions and to determine future directions for sepsis care in the province. Founded on the principles of knowledge translation and exchange, this meeting is designed to foster a productive alignment between sepsis researchers and providers.

The conference objective is to establish a multi-stakeholder and consensus-based prioritized agenda for improving sepsis care in the early hours after presentation in the emergency department. Specific objectives are:

1) to review the focus and accomplishments of the ASN
2) to describe the major evidence-based interventions that should guide sepsis care in the early phases of care
3) to establish how KT principles apply to approximating the gaps between knowledge and practice in sepsis care

This one-day consensus conference will attract clinician leaders, researchers, and front-line providers who are involved in sepsis care at either the institutional, regional, or provincial levels. The presentations given will provide the substrate for structured discussions in the latter half of the day that will define optimal approaches for improving outcomes in sepsis care using sustainable and measurable approaches, as well as define for the ASN the key unanswered questions that must be addressed in order to achieve comprehensive, high-quality early sepsis care.

Key Messages

We have learned several lessons from our early KT activities:

- Engagement of a multidisciplinary group of researchers and clinicians has enabled the identification of relevant knowledge needs and research priorities appropriate to the context of patient care in emergency rooms and intensive care units.
- Collaborative partnerships have been established that have overcome the major barrier to sepsis research—the fragmentation between different basic science and clinical researchers, which has prevented relevant research and rapid uptake of knowledge by end-users.
- By engaging all stakeholders early in the ASN project, collaborative, interactive decision-making has occurred. This has created interest and awareness, and facilitated KT activity.

We believe future practice change will be achievable later in the ASN project, when research results have generated the knowledge to be applied at the bedside.

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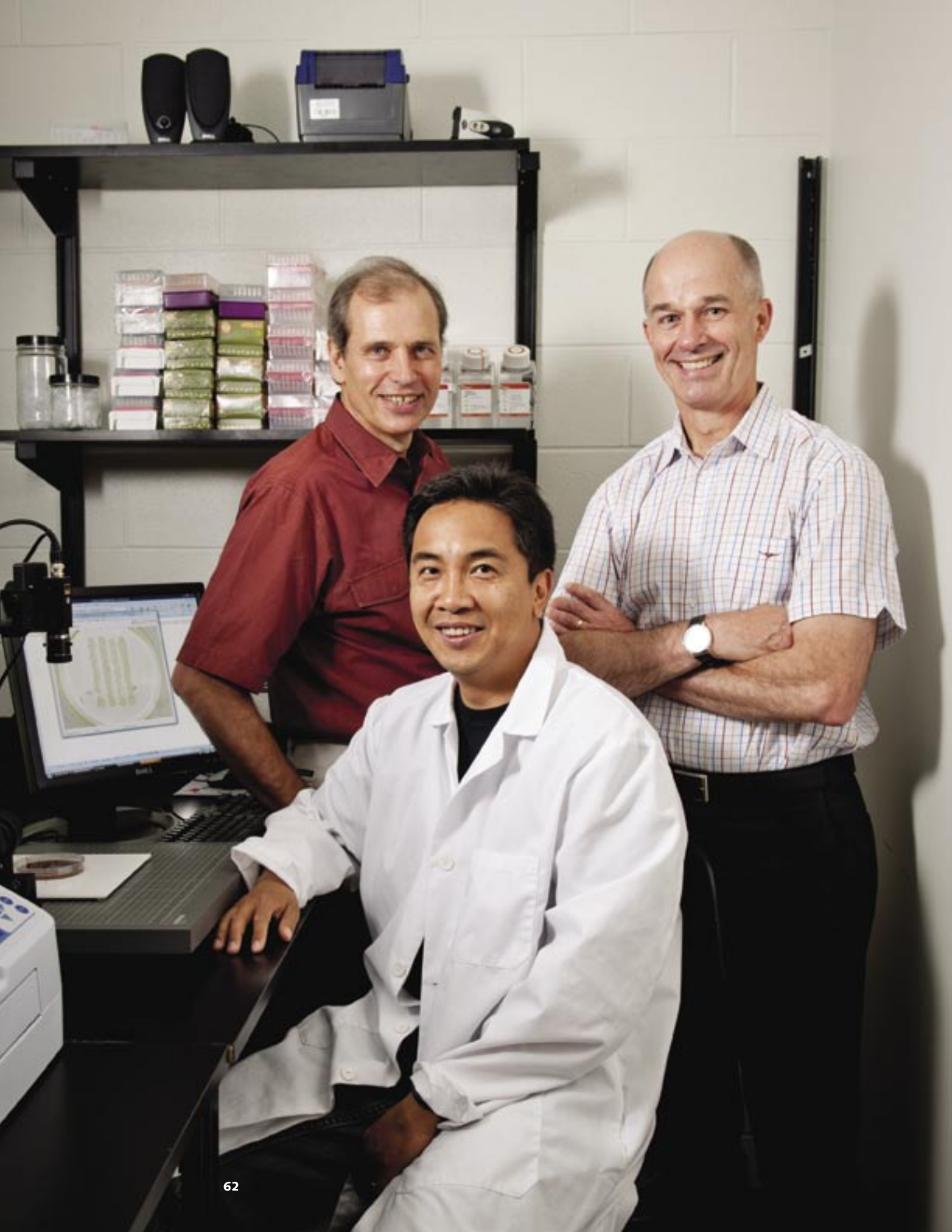


Development of Alberta as a Centre for Vaccine Design and Evaluation

Jaime Kaufman

Abstract

Despite the tremendous success of vaccinations in reducing the burden of infectious disease, many challenges still exist in this field. The objective of the Vaccine Design and Implementation Team is to support optimal vaccine utilization in Alberta and Canada; their initial work focuses on upper respiratory tract childhood pathogens. The three key initiatives of the team are to create a one-stop shop for vaccine research and evaluation studies, to develop a humanized mouse model of infection, and to engineer a single vaccine for multiple pathogens and diseases. Interdisciplinary research is key to achieving their objectives.

Background

Infectious disease continues to be the most common cause of preventable childhood morbidity and mortality worldwide. Of an estimated nine million deaths in children under the age of five in 2008, 68% were attributed to infectious diseases, over half of which were vaccine-preventable.[1] In addition to being responsible for devastating morbidity and mortality among children, infectious diseases pose a tremendous burden to the healthcare system and the economy in the absence of appropriate therapeutic interventions such as vaccines. Management of acute and chronic illness, as well as of disease outbreaks within the community, continue to create huge burdens on healthcare facilities and medical personnel.

Vaccination has been declared one of the greatest success stories in human medicine.[2] In spite of this, and in spite of advances seen in childhood vaccination programs, many challenges remain. Immunization programs face societal barriers, as well as limitations to existing knowledge and strategies in vaccine design and delivery for important childhood diseases. In order to develop a product that will reduce death and disease from key childhood pathogens such as Neisseria meningitidis and Streptococcus pneumoniae, the most appropriate vaccine targets and formulations still need to be identified.

New and better products are needed to address the changing face of vaccine-preventable infectious disease. Novel design and advanced evaluation methods will introduce vaccines that better reflect the needs and concerns of both the public and of policy-makers. The goal of the Vaccine Design and Implementation Team (part of the Alberta Innovates – Health Solutions Interdisciplinary Team Grant program) is to enhance health service delivery using an interdisciplinary team to design and evaluate vaccines for the prevention of childhood respiratory disease.

The Calgary Vaccine Research and Evaluation Centre (CVREC) will act as a "one-stop shopping" centre for vaccine research and evaluation studies accepted by regulatory agencies and policy-makers.

Facing page, left to right: Dr. Tony Schryvers, Dr. Joenel Alcantara, and Dr. Jim Kellner

The four primary objectives of the Vaccine Design and Implementation Team are:

1. To integrate the four pillars of health research into a program directed at improving social, health, and economic outcomes related to vaccine-preventable infectious disease.
2. To address existing limitations in vaccine design and delivery, such as the lack of a Canadian centre for evaluation that meets government and industry standards and incorporates relevant animal infection models.
3. To generate economic and disease models that examine the cost and effectiveness of vaccine implementation and disease prevention.
4. To provide policy-makers with research knowledge on the best use of current and future vaccines, that is, vaccine schedules, vaccine health outcomes (protection and efficacy), epidemiological impact, and health economics.

One of our team's most important program goals is to improve health outcomes through development of optimal vaccine use recommendations, both in Alberta and across Canada. Our research capabilities will help engineer the development of a single effective, economical vaccine for multiple pathogens and diseases. The potential reduction in vaccine dosages given to children may increase parental compliance with recommended guidelines, leading to improved health status, less morbidity/mortality, fewer lost educational/work days due to illness, and a reduced burden on the healthcare system.

KT Strategies: Interdisciplinary Research

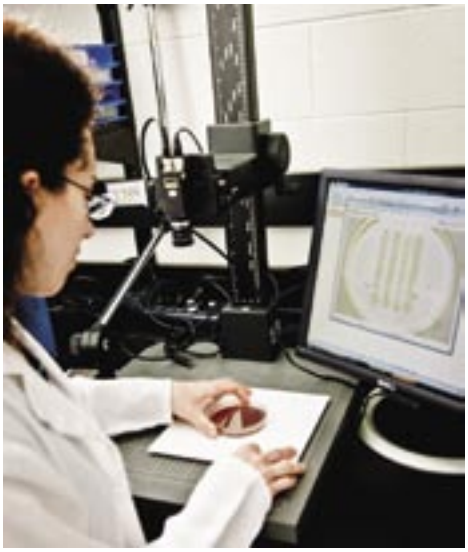
Interdisciplinary research is becoming increasingly important in addressing many of Canada's key health problems. Integrating the four pillars of health research (biomedical; clinical; health systems/services; population and public health) creates a dynamic environment in which each discipline can inform and guide research in complementary areas. This approach allows us to answer unique questions that will optimize the social, health, and economic outcomes related to vaccine-preventable disease.

As such, we will integrate basic and clinical research, using structural and molecular biology, immunology, and bioinformatics in combination with clinical data, strain collections, and patient samples. In addition to the combination of biomedical and clinical sciences, it is important to include population and public health in order to identify our vaccine targets within healthy and sick populations. This approach will further rely on the development of computer modeling and visualization tools for invasive pneumococcal disease, and will be expanded to include additional parameters that would be important to our program and could be extended to other pathogens.

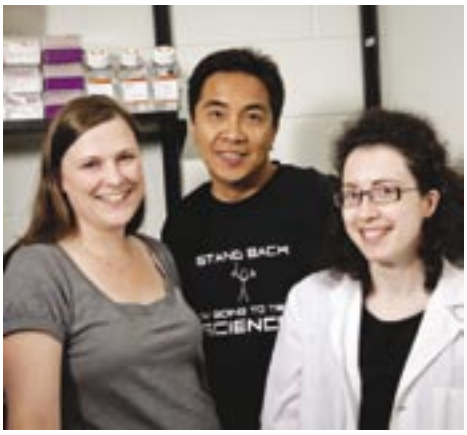
Integrating the health research pillars and incorporating many research areas will further strengthen a well-established training environment within our program. The emphasis on interdisciplinary problem solving will develop trainees who are able to approach scientific problems from a new and more progressive perspective, and will change the face of ongoing vaccine research.

KT Strategies: Policy-Informed Research

A guiding principle of the Alberta Immunization Strategy 2001–20173 (AIS) state that "immunization interventions are evidence-based and sustained over extended periods of time." and that both "research and evaluation of immunization programs are critical to ensure maximum effectiveness." Research combined with vaccine evaluation will demonstrate the economic and clinical efficacy of new and existing vaccination programs. Alberta will be at the forefront, initiating innovative approaches to improving childhood immunization programs and ensuring the most effective and successful programs are in place here in Alberta. The capacity to conduct high quality research locally will also be an asset to Alberta in terms of clinical and economic decision-making and will work toward objectives laid out in the AIS strategic plan.



Erin Brown looking at a serum bactericidal plate.



Dr. Jaime Kaufman, Dr. Joenel Alcantara and Erin Brown.

KT Strategies: Innovation Platforms

One of the issues in the development of meningococcal vaccines is the absence of a relevant animal model of infection to accurately assess the immunological response to the vaccine. By developing a "humanized" mouse model of infection that possesses specific key characteristics, we can examine the efficacy of the vaccine prior to its introduction into human trials.

Basic biological and clinical expertise will expand evaluation approaches based on need, and improve the responsiveness of current vaccine evaluation strategies to industry licensing and evaluation. Until now, there have been no vaccine evaluation centres in Canada, and only two centres worldwide, capable of examining the efficacy of N. meningitidis vaccines in accordance with industry and regulatory standards.

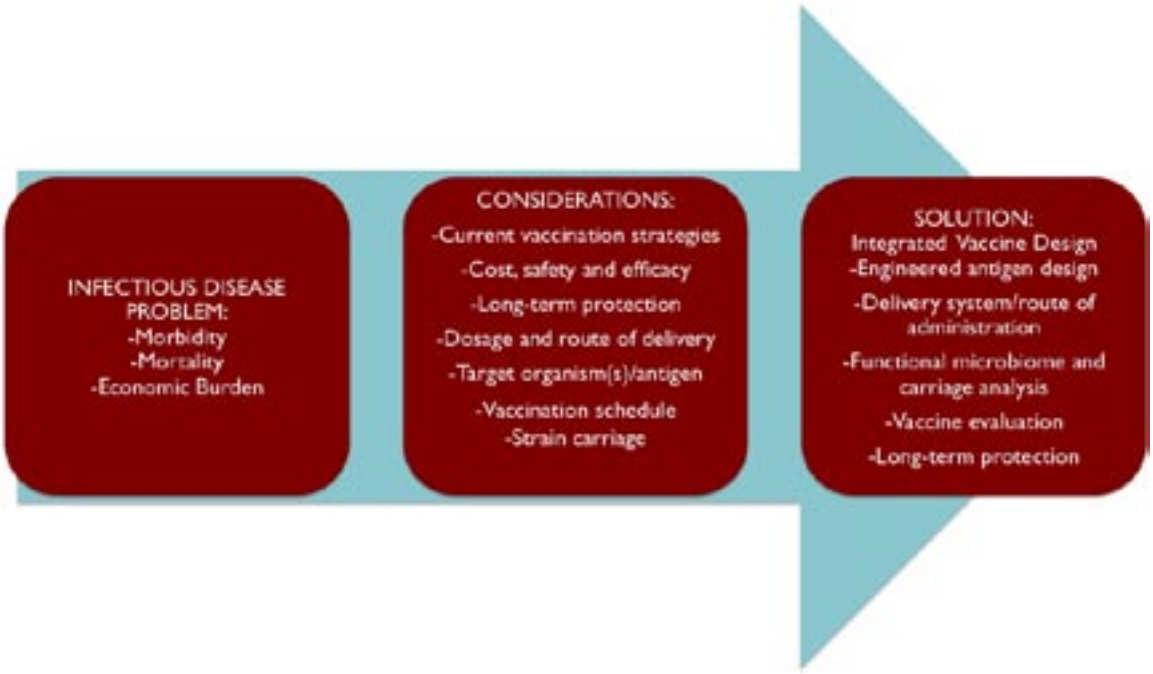
The creation of a fully functional translational research and evaluation laboratory will establish an environment in which both clinicians and basic researchers can work together. The clinical, academic, and industrial development of long-term relationships will address many questions for current and future vaccines. The Calgary Vaccine Research and Evaluation Centre (CVREC) will act as a "one-stop shopping" centre for vaccine research and evaluation studies accepted by regulatory agencies and policy-makers.

Establishment of CVREC will generate research revenue for Alberta, attracting business from major pharmaceutical companies, local businesses, and government research and regulatory agencies. Alberta will be established as the center for vaccine evaluation in Canada. Initial work is being done on childhood upper respiratory tract pathogens, but the tools being developed will be applicable to many different types of bacterial and viral vaccines, with endless applications within our province. We will be communicating our results to healthcare policy-makers to help guide changes in vaccine policy for Alberta, with local, national, and international recognition and collaborations as measures of success.

KT Strategies: Relationships

As we create world-class capabilities, the building of relationships with those involved in vaccine development, implementation, and regulation is critical. The clinical team is networked to other groups to share strain collections and clinical information. We have connected (and will continue to collaborate) with industry, for basic research in the advancement and development of meningococcal vaccines and for establishing relevant evaluation protocols for vaccine products. The development, with local biotechnology companies, of non-vaccine-related protocols will also generate revenue, validate protocols, and build capacity within Alberta.

Basic scientific and clinical expertise available within our program will not only help build optimal evaluation capacity within the CVREC, but progress made in Alberta will redefine policies as they relate to vaccine licensure on a larger scale, and will provide guidelines for provincial childhood vaccination programs. As our research and capacity for detailed vaccine evaluation grow, we will communicate the results of our research to help guide relevant vaccine policy changes as our program expands. Meetings will be held with Alberta Health and Wellness (AHW) to provide updates on the progress of the Vaccine Interdisciplinary Team Grant, to strengthen researcher/policy-maker relationships, to gauge policy needs, and to lay the foundation for future mobilization of vaccine team research discoveries.



Our fully "humanized" mouse model for our vaccine targets is nearing completion and will allow us to more accurately predict the impact of our vaccine products on their host system.

Results

In establishing translational research capabilities, key protocols have been identified and validated, and we are establishing other elements of a comprehensive program. One such CVREC study has enabled clinical and basic researchers to address fundamental questions regarding the scheduling and dosing of MenC vaccination programs in centres around Canada. This will be expanded as we optimize vaccine target candidates for key childhood respiratory pathogens.

Our fully "humanized" mouse model for our vaccine targets is nearing completion and will allow us to more accurately predict the impact of our vaccine products on their host system prior to the full development and introduction of a vaccine product in humans, saving both time and money.

As we establish ourselves as a go-to centre for integrated research and evaluation, we are developing long-term relationships with industry for vaccine studies as well as for research and support. The relationships built with industry (including with major pharmaceutical companies) for collaborative work, service provision, protocol validation, funding opportunities, and the development of new vaccine products will be integral to our program.

Further, we are ensuring that dialogue is underway with government to identify the strategic needs to be addressed within Alberta, and to creating a unique niche in Alberta and North America for vaccine development and evaluation. We continue to cultivate protocols to formally provide information to key decision-makers on the progress of our research program and the development and expansion of the translational research facility in Alberta, communicating major milestones to government.

Key Messages

Many factors must be considered in addressing healthcare needs within our province. Changes to our current systems, such as the development and implementation of new pediatric vaccination programs, should simultaneously address ongoing interdisciplinary research and the complex nature of healthcare delivery. The ability to conduct research that responds to health status, health systems, and healthcare policy needs will be extremely important to achieving improved health, social, and economic outcomes. Interdisciplinary research will be key to achieving these objectives.

About the Author

Dr. Jaime Kaufman (PhD) is the program manager for the Vaccine Design and Implementation Team.

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