THE DRUG SAFETY AND EFFECTIVENESS CROSS-DISCIPLINARY TRAINING (DSECT) PROGRAM

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ABSTRACT

Clinical therapeutics are a cornerstone of treatment for most medical conditions. Pharmacotherapy research is a substantial worldwide enterprise. There are too few researchers who are flexible enough to understand how molecules move from bench to bedside and how their own work transcends conventional boundaries. The Drug Safety and Effectiveness Cross-Disciplinary (DSECT) Training Program has been designed to provide a training environment for future scientists in Canada to generate new knowledge that is focused on integrative thinking about the discovery and use of effective and safe medications.

This one-year program fosters cross-domain learning and collaboration using a multi-pronged approach to encourage development of both content-focused and research methods knowledge related to drug safety and effectiveness, as well as practical skill and capacity building. The curriculum consists of: an annual symposium, development of an individualized learning plan, one-to-one mentorship, a series of on-line sessions on integrative concepts in drug safety and effectiveness, on-line self-study modules and discussion sessions, a series of practical research skill-building sessions, practicum/exposure opportunities, a seminar series, an Objective Structured Knowledge Translation Experience (OSKTE) and a Book Club. This innovative curriculum is poised to broaden and strengthen the competency and culture of drug safety and effectiveness research while capitalizing on the benefits derived from knowledge pursuit that crosses multiple domains of the scientific academy.

Key Words: *Medication safety, training, cross-disciplinary, program overview, Canada*

The pharmaceutical and biotechnology industries in Canada have experienced excellent growth in the past few decades.[1] It has been identified, however, that trainees most suited to work in these industries and academic institutions - those in the primary and associated fields related to pharmacology, therapeutics and related health services research fields - are too highly focused and lack flexibility in understanding how molecules move from bench to bedside. Consequently, these trainees may be less well equipped for the variety of industry, government, academic and other types of positions that require in-depth knowledge of pharmacotherapy.[2] It has also been noted that currently there are too few trained researchers to take on substantial additional research into the real world safety and effectiveness of medicines, and few programs exist that specifically train individuals to conduct this type of work.[3]

There are a number of salient examples that demonstrate the complexity and urgency for developing a cadre of trainees who are able to view challenging medication-related issues in a comprehensive manner. An illustrative example of statins and rhabdomyolysis described below can be replicated for many other medications and associated medical conditions.[4-10] Statin use is

common and effective at lowering cholesterol and preventing vascular events; but, rhabdomyolysis is known to be a rare, but very serious adverse effect.[11] There are excellent models in basic science that have examined muscle physiology and pathophysiology, pharmacology of the various statins, and pharmacokinetics and pharmacogenetics that may help to identify the few people at risk of rhabdomyolysis with statins.[5,6,9] However, these models need further development and validation in humans before they can be translated into practice. In the meantime, clinicians struggle with understanding the clinical meaning of muscle symptoms and receive confusing messages about the value of testing muscle enzyme levels. As well, despite recent evidence about the cost effectiveness and benefit of statins for both men and women, translating this evidence remains challenging on clinical and health policy fronts.[4,12] In terms of harm, improved understanding of metabolic pathways in muscle and various leading statins, and their genetic determinants, may prevent these serious adverse events. Predicting which patients will experience serious muscle-related harm is a clinical and research priority. Further, statins are the number one cost to formularies worldwide; in Ontario, this is now about 0.5 billion dollars yearly.[7] This example demonstrates how understanding a drug safety and effectiveness issue requires incorporating research from across scientific domains.

Given the advances that have occurred within the biosciences, population health, clinical, and health policy arenas, the development of a cross-disciplinary training program is now possible as a strategy to foster a broadened perspective in junior researchers. The goal of DSECT is to encourage researchers from different domains of science to gain a broader perspective on drug safety and effectiveness, interact with researchers from different domains of science and thus encourage activity and innovation in the drug safety and effectiveness arena. Training within and across a variety of disciplines, including molecular and clinical pharmacology, epidemiology and biostatistics, clinical domains, health services research, behavioural sciences and health technology assessment, could produce synergies to stimulate the type of innovative research to further the areas of drug discovery, improving clinical practice, and implementing sound drug policy in Canada and around the world. Research training that offers opportunities for trainees across this broad spectrum of disciplines to learn together and from each other is a key impetus for filling the critical void of skilled, knowledgeable researchers. Further, it is expected that the program will produce scientists who have an enhanced understanding of how their work crosses traditional scientific boundaries and so will be better poised to generate innovative discoveries that can be applied to improve health outcomes.

The Drug Safety and Effectiveness Cross-Disciplinary (DSECT) Training Program

The Drug Safety and Effectiveness Cross-Disciplinary (DSECT) Training Program has been designed to provide a training environment for future scientists in Canada to generate new knowledge that is focused on integrative thinking about the development and use of effective and safe medications. The DSECT Program crosses four domains of science:

1) Biosciences, including molecular pharmacology, biopharmaceutics, pharmacogenetics, biotherapeutics and biopopulations, which are beginning to emerge as mechanisms to make drug choices based on a patient's genetics profile;[13-16]
2) Clinical therapeutics, including soliciting patient preferences and values, evidence-based therapeutics and knowledge exchange to providers and patients;
3) Population health and epidemiology, including the collection and interpretation of primary data on drug safety and effectiveness from patients, using this data to develop predictors of benefit and harm and statistics to provide the foundation of proficiency needed for design and analysis of research studies as well as the advancement of biostatistical capacity building in drug safety and effectiveness in the real world; and,
4) Health services and policy research, including interdisciplinary collaboration to improve medication prescribing and use, understanding the effects of different policy choices or health services on drug

prescribing and use, and health economics and evidence synthesis including decision analytic techniques for incorporating drug safety and effectiveness data.

Trainees from all four areas are brought together in a stimulating and innovative learning environment. DSECT has been funded mainly by the Canadian Institutes of Health Research (CIHR name: CIHR Training Program in Bridging Scientific Domains for Drug Safety and Effectiveness) as a Strategic Training Grant in Health Research (STIHR) and trainees are given the title of "CIHR Strategic Training Fellow".

Program Objectives

The main objectives of the DSECT program are to:

1) provide a foundation in the basic concepts of drug safety and effectiveness within multiple domains of science;
2) bridge scientific domains by linking complementary domains at both the trainee and investigator level;
3) increase the use of cross-domain approaches in research conduct;
4) provide a rich learning environment that is content and research methods focused;
5) provide tangible opportunities for trainees to develop collaborative research skills;
6) provide direct opportunities for trainees to learn and practice research skills; and
7) incorporate knowledge translation learning and activities at all stages of the program.

DSECT Overview

This one-year innovative program fosters cross-domain learning and collaboration using a multi-pronged approach to encourage development of both content-focused and research methods knowledge related to drug safety and effectiveness, as well as practical skill and capacity building. Eligible trainees include those enrolled in a graduate (Masters, PhD), or post-doctoral program, with demonstrated academic excellence and an interest in or experience related to medication. Trainees remain situated within their graduate training program and are expected to continue to develop their expertise in their primary focus of study through continued work on one or more central research projects. Trainees participate in DSECT face-to-face and on-line training experiences in conjunction with their primary graduate work. Stipend support is available for some trainees.

The DSECT Program has a Steering Committee, a Program Advisory Committee, an Applications Review Committee, and an Administration Committee. A key aspect of the DSECT Program are its faculty mentors who represent varied disciplines and span in expertise from basic sciences to community-based applied research. Faculty mentors are from academic institutions across Canada and over time will include those from other parts of the world. A program logic model is being used to guide evaluation of the program. The DSECT Program is strongly supported by the host institutions of McMaster University and St. Joseph's Healthcare, Hamilton as well as other organizations with an interest in optimizing medication use.

Program Design and Curriculum

Key program components were refined through iterative dialogue and consensus at a series of meetings with experienced program mentors representing the four primary scientific domains included in this program. Literature reviews and mentor surveys were conducted by the research team to identify competencies to be reached by trainees and to inform curriculum development. Results were presented to a core group of (seven) mentors for discussion and adaptation of findings and then review by the full mentor group. There are five areas of competency that have emerged:

1) concepts and methods from primary scientific domain,
2) conduct of research that bridges scientific domains,
3) communication across scientific domains,
4) interaction with others from other scientific domains, and
5) general research skills.

There are many components to the curriculum. There is an annual symposium that presents details of the program to the new trainees and provides an opportunity for trainees to be introduced to one another and the program faculty. Trainees are expected to develop an

individualized learning plan and receive one-to-one mentorship. There are a series of on-line synchronous (i.e., everyone participates at the same time) sessions on integrative concepts in drug safety and effectiveness, on-line self-study modules and on-line discussion sessions about basic concepts in drug safety and effectiveness. Practical sessions include a series of research skill-building sessions, a practicum or exposure opportunities, and an Objective Structured Knowledge Translation Experience (OSKTE). There is also a Book Club. Each component is described in more detail on the program website (www.safeandeffectiverx.com). The program aims to provide a foundation for fundamental drug safety and effectiveness concepts. The approaches used by the program to help trainee's bridge scientific domains are listed in Table 1. It also aims to foster and support more advanced training in specialized areas in collaboration with other groups such as the Canadian Network for Observational Drug Effect Studies (CNODES**),** a Canadian Drug Safety and Effectiveness Network (DSEN) centre.

TABLE 1 Approaches used by the DSECT program to help trainees bridge scientific domains

DSECT trainees complete an individual learning plan that addresses program competencies including competencies related to the conduct of research that bridges scientific domains and communication and interaction across scientific domains. Trainees identify activities they will undertake to meet the competencies.
Each DSECT trainee is assigned a secondary mentor, often from another scientific domain.
Specific discussion questions posed during on-line sessions prompt responses that encourage thinking across scientific domains.
Trainees are paired with trainees from a different scientific domain for certain activities.
Self-study learning materials covering basic drug safety and effectiveness concepts from different scientific domains can be accessed by trainees to improve their understanding of other domains.
Some trainees become involved in research connected to a program faculty member who is focused outside the trainee’s primary scientific domain.

Some examples of integrative on-line sessions are: (1) statistical concepts related to drug safety and effectiveness data; and (2) the basic, clinical, population health and health policy levels, real world drug safety and effectiveness in relation to clinical practice and health policy. Self-study modules consist of on-line audio and video lectures and there are basic foundational topics within each represented scientific domain, intended to familiarize trainees with important introductory concepts from outside their primary domain. Examples include:

1) basic principles in genetics and genomics,
2) drug metabolism,
3) regression analysis,
4) an introduction to health technology assessment and,
5) the process for selecting or modifying drug therapy (from a clinical perspective).

The OSKTE is a formative experience in researcher-decision maker knowledge transfer, modeled on the clinical Objective Structured Clinical Examination (OSCE).[17-19] In the OSKTE, each trainee delivers a 5 minute presentation on a research study (choices from across all domains of science) and its implications for a simulated scenario to a panel of real clinical and health policy decision makers. The panel provides constructive feedback and unique insights from their perspectives and provides a real life example of knowledge transfer and exchange with decision makers.

Technology Platform

The DSECT Program website (www.safeandeffectiverx.com) contains general program information, an on-line admissions and applications review portal, trainee and faculty mentor profiles, announcements and news, and research resources. DSECT also has a separate online learning platform that houses current and previous program curriculum including video archives from our annual symposium, archived course sessions that have already been delivered in a synchronous manner, self-study video modules that focus on basic concepts in drug safety and effectiveness, as well as accompanying resources (i.e., websites, journal articles, and presentation slides). The learning platform also supports trainee asynchronous (i.e., everyone participates at a different time) and synchronous communication through discussion threads. Eventually, each trainee will have their own private learning portfolio within the site's learning platform that reflects their individual curriculum plan. The self-selected nature of the curriculum site is complemented with the use of synchronous web conferencing sessions via the Elluminate platform. These Elluminate sessions enable faculty to narrate and present material in real-time, as well as facilitate discussion with and among trainees. Trainees may participate via two-way audio, text messaging, a shared whiteboard, surveys and polls, and all sessions are recorded and archived on our curriculum site.

Program Strengths

The DSECT program includes multiple modalities and opportunities for trainee interaction to facilitate growth in knowledge and skills. The program includes approaches that customize learning for the individual trainee to broaden their perspective in a manner that best suits their current research trajectory. Each trainee completes their own learning plan based on competencies predefined by the program, their own needs and opportunities within their research setting as well as what is offered by the DSECT program. The trainee will complete mandatory program activities but also select a number of sessions and activities that best align with their learning plan.

Each trainee also receives structured feedback about their learning plan and progress in the program from an assigned faculty mentor. Video-taped presentation opportunities at the beginning of the program, self-study modules, and the OSKTE all provide occasions for trainees to regularly assess learning and skill development. Trainees are linked with a secondary faculty mentor from DSECT who works with the trainee and their graduate program supervisor, encouraging links between mentors. In addition to the usual role of academic supervisor, the primary faculty mentor will provide guidance on the trainees' integration of DSECT program learning and his/her programs' academic work. The approaches to customize a trainee experience work together with methods to promote interdisciplinary team functioning. Trainees develop collaborative research skills through purposeful pairings during course activities and

dialogue with one another during face-to-face and on-line sessions as well as on each other's research projects throughout the year. These latter experiences foster cross-disciplinary communication skills, a tangible proficiency that is typically not focused on in graduate programs.

Program Challenges

Despite a number of program strengths, various challenges have been documented through the program's first year. While enthusiastic to be part of DSECT, busy faculty mentors have limited time to contribute to the development and provision of educational sessions on top of their busy teaching loads. Trainees, too, must balance time pressures and efforts need to be made so that trainees carve out time to participate in live sessions delivered by faculty so that there is enough of a critical mass of participants to have a worthwhile learning session. It is also unclear which of the varied disciplines are most essential to this program and further exploration of this question would help provide more of a focus for trainee applicants and the involvement of program faculty.

DSECT is heavily dependent on technology and this has not been without some challenges. Technology has been necessary to create a beneficial on-line learning experience; however, at times the technical aspects of the system are suboptimal including inoperable microphones, low connection speeds, and faculty or trainee unfamiliarity with strategies to communicate in an on-line environment. Most of these issues dissipated with increased frequency of use during the program.

In terms of program development, ongoing energy needs to be spent identifying what learning will be most useful for trainees coming from different domains of science, given that each domain has their own culture, approaches, and expectations on how a graduate student should spend their time. Also, there are limited resources available to support program development and implementation.

Finally, the length and scope of program may not be adequate to achieve a level of proficiency for a trainee to generate true innovation in the drug safety and effectiveness arena. Extending the timeframe of the program, including advanced level activities to accelerate the growth of researchers, and better integration of program activities into existing activities of mentors and trainees to maintain constant learning and persistence over time need to be explored to increase the opportunity of DSECT to make a long term difference in drug safety and effectiveness research.

Next Steps

Moving forward, DSECT has identified a number of areas of focus. Efforts will be focused on improving the approach to developing individualized learning plans, including an online learning portfolio. Further development of self-study modules will take place to incorporate trainee activities such as answering multiple choice and short answer questions or participating in asynchronous on-line discussions to encourage active learning while completing self-study modules. DSECT will continue to foster linkages with other organizations and stakeholders, including international collaborations, so as to grow the program in a scalable and sustainable manner. A formal evaluation of first year activities has begun including a compilation of trainee evaluations of each session and the symposium, an end of program survey for trainees and mentors, a compiled list of trainee publications and presentations, and a comprehensive assessment of the OSKTE including qualitative interviews of the participants and an analysis of OSKTE presentation evaluation forms.

CONCLUSIONS

The DSECT program aims to broaden the education of the next generation of medication safety and effectiveness researchers, scientists, and policy analysts by complementing graduate and postgraduate work with an innovative and diverse curriculum. DSECT hopes to strengthen the culture of drug safety and effectiveness research through capitalizing on the benefits derived from knowledge pursuit that crosses multiple domains of science.

Acknowledgements/ Funding

We thank Patangi Rangachari for his valuable insights and contributions to program development. Funding for DSECT is from the Canadian Institutes of Health Research.

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