

FH Canada:
Increasing Awareness, Targeted Screening, Empowering Patients, Saving Lives

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Principal investigator:

Dr Jacques Genest, MD FRCPC Cardiologist
Professor, Faculty of Medicine, McGill University
Research Institute of the McGill University Health Center
1001 Decarie Blvd, Bloc E, Office EM12212
Montreal, Quebec, Canada H4A 3J1
Tel: (514) 934-1934 ext 34642
Jacques.genest@mcgill.ca

Collaborators:

Dr Daniel Gaudet, ECOGENE-21 Clinical Research Center, University of Montreal, Montreal, QC, Canada

Dr Robert A. Hegele, Robarts Research Institute, University of Western Ontario, London, ON, Canada

Dr Gordon Francis, Healthy Heart Program Prevention Clinic, University of British Columbia, Vancouver, BC, Canada

Dr Brian McCrindle, The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada

Dr James Brophy, Epidemiology and Biostatistics, McGill University, Montreal, QC, Canada

Abstract

FH Canada: Increasing Awareness, Targeted Screening, Empowering Patients, Saving Lives.

The overall goal of the project is to increase awareness of familial hypercholesterolemia (FH) among health care professionals (HCP), their patients and family members through the creation of educational resources and web-based applications to simplify FH diagnosis and treatment. We will leverage the Canadian FH Registry and its website (www.FHCanada.net) to achieve these goals. The project will combine **1)- the creation of educational resources for health care professionals (HCP)** across Canada (accredited teaching slide kits, revised book on lipoprotein disorders, peer-reviewed position statements, FH Canada 2016 Reunion); **2)- the design of apps for Canadian FH diagnosis criteria and treatment;** and **3)- educational FH Canada-based resources for patients.** These interventions align with the mission of the FH Canada registry initiative and, once implemented, will directly improve the care of Canadian FH patients, a population at high risk of cardiovascular events. The 3 principal objectives of the proposal are to 1- increase awareness of FH among HCP in Canada; 2- increase ease of diagnosis for family physicians and cascade screening through simplified Canada FH definition and apps, and 3- increase awareness of FH for Canadian patients, family members and Health Care Providers. We expect to improve the precision of FH diagnosis, increase the number of diagnosed FH patients and family members and provide them access to expert care, on-going clinical trials and novel therapies.

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C. Reviewer Comments

1- In your full proposal, it is important to include sufficient information to justify your full budget. Please review the attached Full Proposal Guidance document for details.

Please refer to **Section G, Detailed Budget**.

2- Proposals should describe the means of evaluation and how project outcomes will be measured.

Please refer to **Section D - 5. Evaluation Design**.

3- Please clearly define the education component of the project. Specifically, the educational design of proposed projects should demonstrate how clinician performance will be supported, beyond the acquisition of knowledge. Please describe any tools that will be used to support the learning and that will help achieve the objectives of the project.

Please refer to **Section D - 4. Project Design and Methods** for a complete description of the educational project proposed.

D. Main Section of the Proposal

Familial hypercholesterolemia (FH) is a genetic lipoprotein disorder characterized by elevations in low-density lipoprotein cholesterol (LDL-C) >95th percentile for age and gender. Affected individuals may show clinical manifestations (xanthomas, xanthelasmas and premature arcus corneus) although these manifestations are seen less frequently with early diagnosis and treatment. As an autosomal dominant genetic disorder, the transmission of the affected allele is 50%. Left untreated, men develop atherosclerotic cardiovascular disease (CVD), primarily CAD, in the third to fourth decade of life and women, ten years later on average [Nordestgaard 13]. When identified and treated early, life expectancy is normal.

There are at least three accepted definitions for FH, based on absolute LDL-C levels (MedPed criteria)[Williams 93], the Simon-Broome criteria include a fixed cut-point for LDL-C, the presence of DNA mutations and xanthomas [Marks 03], and the FH Dutch Criteria (the Netherlands) [Fouchier 01]. While each classification stands on its own merit, there is no real “gold standard” for an unequivocal diagnosis of FH. Rather, lessons learned from family studies and molecular genetics have taught that FH represents a wide spectrum of clinical manifestations that depend, in part, on the impact that the gene mutation has on the phenotype.

The FH Canada initiative, instigated in fall 2014, is aimed at creating a Canada-wide registry of FH patients and to identify Canadian patients with FH and their family members in order to improve health and healthcare delivery. FH Canada is characterized by a well-developed and extensive network of 17 lipid clinics specializing in FH in Canada (www.FHCanada.net). Over 65 experts in lipidology, endocrinology, cardiology, pediatrics, public health and epidemiology participate in this project.

1. Overall Goal & Objectives

The overall goal of the project is to increase awareness of FH among HCP, their patients and family members through the creation of educational resources and web-based applications to simplify FH diagnosis and treatment. We will leverage the Canadian FH Registry and its website (www.FHCanada.net) to achieve this goal.

The **3 principal objectives** of the proposal are to:

- 1- Increase awareness of FH among HCP in Canada;
- 2- Increase ease of diagnosis for family physicians and cascade screening through simplified Canada FH definition and apps;
- 3- Increase awareness of FH for Canadian patients and their family members.

We expect to improve the precision of FH diagnosis, increase the number of diagnosed FH patients and family members and provide them access to expert care, on-going clinical trials and novel therapies.

2. Current Assessment of Need in Target Area

2.a) Need for this project. The prevalence of FH in Canada is conservatively estimated at 1/500 while it is approximately 1/270 among French-Canadians due to a “founder” effect [Moorjani

93]. Given a population in the province of Quebec of 7.9M and a population for Canada of 35M, the number of patients with FH in Canada is conservatively estimated ~ 83,500. Probably less than 5% of patients have been diagnosed with FH so far in Canada, meaning that there is a considerable need for HCP as well as patient education, and a need for the implementation of proper diagnostic tools. We need to fill this gap and the FH Canada registry will help us to do so. In fact, as of now, we should have a lot more patients diagnosed with FH across the country, we should be performing cascade screening among the family members of the newly diagnosed patients with FH, and we need to offer specialized health care resulting in a better management of their high cholesterol levels and in the prevention of heart disease.

2.b) Project starting point.

In 2013, Nordestgaard *et al.* published the estimated per cent of individuals diagnosed with FH in different countries/territories, as a fraction of those theoretically predicted based on a frequency of 1/500 in the general population [Nordestgaard 13]. In Canada, it was estimated that less than 1% of Canadians have been diagnosed with FH. The implementation of the FH Canada registry initiative in 2014 gave us the unique opportunity to get data on existing databases of patients with FH in Canada. With the help of our colleagues from the FH Canada registry, a network of specialists in lipoprotein disorders, we revised the per cent of diagnosed Canadians with FH to about 5%: there is still a clear need to improve detection of FH in Canada. The Netherlands, for instance, is a country with a well-established registry on FH (started in 1994) with an actual per cent of diagnosed FH patients of over 70% [Nordestgaard 13].

3. Target Audience

The targeted audience for the proposed project is HCP and community physicians across Canada. We will use a “hub and spoke” model of medical care established in the FH Canada registry so that the 17 specialized clinics (hubs) translate the knowledge to the community clinics (spokes). We estimate that over 20,000 family physicians can be reached to help increase awareness of FH in patients, improve the diagnosis of FH and provide better healthcare, which includes access to newly available therapies such as PCSK9 inhibitors. As of February 2016, we will have enrolled >4,200 patients in FH Canada, with a goal of entering 6,000 patients by June 30, 2016.

3.a) Level of commitment. With the FH Canada registry initiative, we have linked more than 90 investigators, clinicians, basic researchers and industry participants across Canada so far. The 65 physicians participating in the Canadian FH registry are recognized at the national level for their expertise in lipoprotein disorders and with advanced laboratory facilities; they are the ones to whom the patients with rare and severe lipoprotein disorder cases are referred to. They already committed to the initiative; letters of collaboration can be found at the end of the present document (**Section I. Letters of commitment**). These physicians will be our link to the family physicians across Canada, since all new information on FH will be radiating from these academic centers to the regional clinics that treat patients with FH.

3.b) Scope of target audience. There is no doubt that with the help of the implemented network of FH Canada, we will succeed in increasing awareness among a maximum of HCP and patients with FH across Canada. The network is really the key in the present project: with an easier diagnosis and implementation of cascade screening, all participants, including patients,

will be transmitting new knowledge on FH and will help disseminate new tools across the country.

3.c) Who will benefit. We expect to improve the precision of FH diagnosis, increase the number of diagnosed FH patients and family members and provide them access to expert care, on-going clinical trials and novel therapies. Therefore, in addition to the HCP working around dyslipidemic patients, who will get new knowledge on FH, a greater proportion of Canadians with FH will be discovered and will directly benefit from the project outcomes. In the end, patients will be the major beneficiaries of this initiative. The FH Canada template is being used in the Systems and Molecular Approaches in Severe Hyperlipidemias (SMASH –a registry of orphan lipoprotein diseases) to address the unmet need of rare lipid disorders.

4. Project Design and Methods

4.a) Overall strategy. In order to **increase awareness of FH among HCP, their patients and family members** through the creation of educational resources and web-based applications to simplify FH diagnosis and treatment, we intend to specifically:

Objective 1) create educational resources for health care professionals (HCP) across Canada (accredited teaching slide kits, revised book on lipoprotein disorders, peer-reviewed position statements, FH Canada 2016 Reunion);

Objective 2) design specific apps for Canadian FH diagnosis criteria and treatment;

Objective 3) create educational FH Canada-based resources for patients.

These interventions align with the mission of the FH Canada registry initiative and, once implemented, will directly improve the care of Canadian FH patients, a population at high risk of cardiovascular events.

Methodology:

Objective 1. In order to help increasing awareness of FH among HCP, we plan on using the FH Canada network to bring together Canadian experts in lipidology, endocrinology, cardiology, pediatrics, public health and epidemiology:

- To create an accredited teaching material on FH and to revise the core curriculum in lipoprotein disorders. Both educational resources will be bilingual and freely available online, and will include the latest knowledge on FH, its revised Canadian definition and diagnostic criteria, the available treatments in Canada, the results from the latest clinical trials and details on the on-going trials, including the use of PCSK9 and CETP inhibitors. They will include an update of the fourth edition of the book “Dyslipoproteinemias: The Clinical Approach”, a tool that has been used in the past by several medical students, interns, residents, doctors, HCP and basic researchers. Its revision includes the creation of different versions for the general public and patients, for primary care clinicians and professionals, and for lipidologists, medical specialists interested in lipidology or residents who wish to prepare for the *American Board of Clinical Lipidology* exams or HCP who wish to take the *Certified Lipid Specialist (CLS)* exams. The new resources will also include a summary of the Canadian Cardiovascular Society (CCS) position statement on FH [Genest 14] as well as a section on understanding the genetic basis of FH in Canada including the unique LipidSeq and MLPA techniques [Johansen 14]. This

educational material will be assessed and updated yearly, and will be downloadable for tablets, iPods and iPhones. It will be possible to customize the downloads according to specific needs, with applications to support family screening for FH and dissemination to the general public; first line interventions and clinicians, dieticians, pharmacists, genetics counsellors, psychologists and physical exercise specialists; clinical training and education; and understanding and documenting the genetic and specialized tests used or available in lipidology (management of intolerance to lipid-lowering drugs; patient education and science popularization including animations, drawings and funny skirts).

- To compile data from main Canadian Lipid Clinics for their integration into the FH Canada Registry and to write the Canadian experience with FH and new definition, prevalence and treatment recommendations (peer-review paper).
- To organize the FH Canada Reunion (Oct 2016) to present updates on the FH Canada registry and the new educational resources for HCP, and to invite guest speakers to describe their country-specific experience on FH diagnosis and treatment. A patient forum is included in this meeting.

Objective 2. The design of apps for Canadian FH diagnosis criteria and treatment will include:

- The creation of an app for a simplified FH diagnosis. It will be based on the Simon-Broome criteria but adapted for Canada, and it will be bilingual. This new and simple tool will increase the number of FH patients diagnosed in Canada and help provide them with better access to care, and family cascade screening.
- The validation, in the Canadian population, of the Dutch FH algorithm aimed at predicting the presence of a genetic defect and better identifying definite FH patients (i.e. high-risk FH patients), and provide them with appropriate treatment.
- The creation of an app to impute baseline LDL-C from values obtained while on lipid-lowering therapy. This tool will be useful for assessing the degree of severity of FH for new patients.

Objective 3. In line with the FH Canada mission, the project is aimed at increasing awareness of FH in patients and their family members. We plan on generating educational resources on FH for patients including:

- A patient brochure on FH and on the FH Canada registry
- A presentation on how to easily draw a family tree (pedigree) and assess a pattern in high LDL-C and FH among family members.
- Photographs and educational videos on the genetic basis of FH and its clinical diagnosis, in lay language.
- Moreover, the revision of the core curriculum in lipoproteins will also be essential in increasing awareness of FH among patients since the web and electronic versions will have an interface promoting networking with patient organizations (Canadian Organization for Rare Disorders (CORD) and Regroupement Québécois des Maladies Orphelines (RQMO), with the FH Canada registry and its partners; between patients and with HCP, will support multicenter clinical trials, and will provide updated information on genetic or advanced lipidology testing.

4.b) Established needs and results. The creation of these educational resources will definitely increase awareness among HCP and patients. Data compiled by the FH Canada registry will be

essential to make sure that the proposed activities generate the desired results. For example, we will be able to measure the dissemination of new knowledge on FH by measuring specific outcomes (see **Section 5. Evaluation Design**).

4.c) Determining engagement. To determine the engagement of the HCP and their patients in disseminating new knowledge on FH, we will be following up on the measures of outcomes described. The discussions that will be generated among all participants of FH Canada, including the patients and specific organizations will also be a good assessment of their involvement, as well as their presence in presentations, workshops or conferences on FH, organized or not by the FH Canada registry.

4.d) Originality of project. The FH Canada registry is aimed to be a “projet rassembleur” (unifying project), where clinicians and scientists work to optimize the care of patients with FH. The FH Canada initiative is unique and will allow a maximum of patients to receive a precise diagnosis and personalized medicine, as well as access to new therapeutic modalities and initiation of cascade screening of affected relatives. As stated previously, no “gold standard” for a diagnosis of FH exists and there is a need to develop one in Canada. Most of the proposed educational resources are new, only 2 resources already exist but need to be either updated to current knowledge on FH (re-edition of the book “Dyslipoproteinemias: The Clinical Approach”) or included in the newly developed tools (CCS position statement on FH; [Genest 14]) (see **Section 4.e**) below).

4.e) Previous work. Some of the resources will include knowledge on FH that is already being shared among HCP across Canada. The aim is to gather all information from specialists in the field of FH and generate resources that will be complete and up to date. For example, we will start from the fourth edition of the book “Dyslipoproteinemias: The Clinical Approach” and update it with current knowledge, while creating different versions for different users (patients vs. primary care clinicians vs. lipidologists vs. residents). We will use some data already published like the CCS position statement on FH and summarize them in all new resources to help disseminating the information. The FH Canada registry website is already in place and it will be easy to update it with new information on FH, including new applications and other resources.

4.f) Cost of new tools. All tools to be developed as part of the present project will be made available to HCP and patients at no cost, using publically available documents and websites.

5. Evaluation Design

5.a) Addressing the practice gap.

Data compiled using the FH Canada registry (Canadian iCAPTURE database) will be essential to determine how the newly created educational resources had an impact on FH patient care. The de-identified data on Canadian patients with FH (demographics, familial history of elevated cholesterol levels and CVD, patient’s medical and surgical history, physical signs of FH, lifestyle, biochemistry lab results and patient’s medication profile) will be useful to determine the prevalence of FH cases and their regional distribution, to determine health outcomes, resource utilization and health economics. More specifically for this project, we will be able to measure the dissemination of new knowledge on FH by measuring **specific outcomes** such as:

- 1) The number of new patients and their family members entered into FH Canada in time;
- 2) The baseline and on-treatment LDL-C levels of patients entered into the registry. When baseline LDL-C levels are not available, a computer-generated imputed value is entered according to the patient's current therapy. This feature is built-in the Canadian FH registry.
- 3) The number of patients on lipid-lowering therapy during the mandated 1-year follow-up and the proportion not at LDL-C target, who might benefit from alternative treatments such as PCSK9 inhibitors.
- 4) The annual FH Canada Reunion will help us get feedback from HCP as well as from patients.

5.b) Quantify change. The metrics used will consist of the number of physicians trained and getting NLA certification, attendance at the yearly FH Canada Reunion. We will also track the number of sites "hubs" opening on a yearly basis on the www.FHCanada.net website and the number of physicians forming the "spokes" of FH Canada.

5.c) Dissemination. The major tool for dissemination of the new educational resources will be the already existing FH Canada website (www.fhcanada.net), which presents sections for both patients and HCP. The new material will be freely available and updated regularly. All documents will also be made available on the FH Canada social media and in all academic centers participating in FH Canada. They will also be presented during the FH Canada Reunion 2016, which, with the help of the Canadian Organization for Rare Disorders (CORD) and Regroupement Québécois des Maladies Orphelines (RQMO) organizations, will include discussion with patients.

6. Detailed Work Plan and Deliverables Schedule

We anticipate that with the help of the already set-up FH Canada network, all educational resources will be implemented within 12 months (May 2017) and a robust evaluation of the dissemination of the resources using the FH Canada database will be possible by October 2017. Table 1 presents the timeline for the proposed deliverables. It also includes in parentheses the main leaders for each proposed activity and the estimated associated cost.

Figure 1 shows the commitment of the FH Canada registry to knowledge translation. Our training program can easily be evaluated by measuring:

- The number of fellows who receive NLA certification
- The exchanges between Canadian centers of excellence in lipidology by our trainees
- The number of International fellows participating in our program
- Attendance at the FH Canada Reunion (Fall every year)
- Number of patients with FH who agree to and participate in, cascade screening

As an example of our training program, Dr. Khalid Alrasadi, Dr. Khalid Alwaili (both from Oman), Dr. Zuhier Awan (Saudi Arabia) are graduates of the McGill University advances fellowship in lipidology. They have all established solid programs on FH in their countries. We currently have two fellows enrolled in the McGill University Postdoctoral Fellowship in Lipidology.

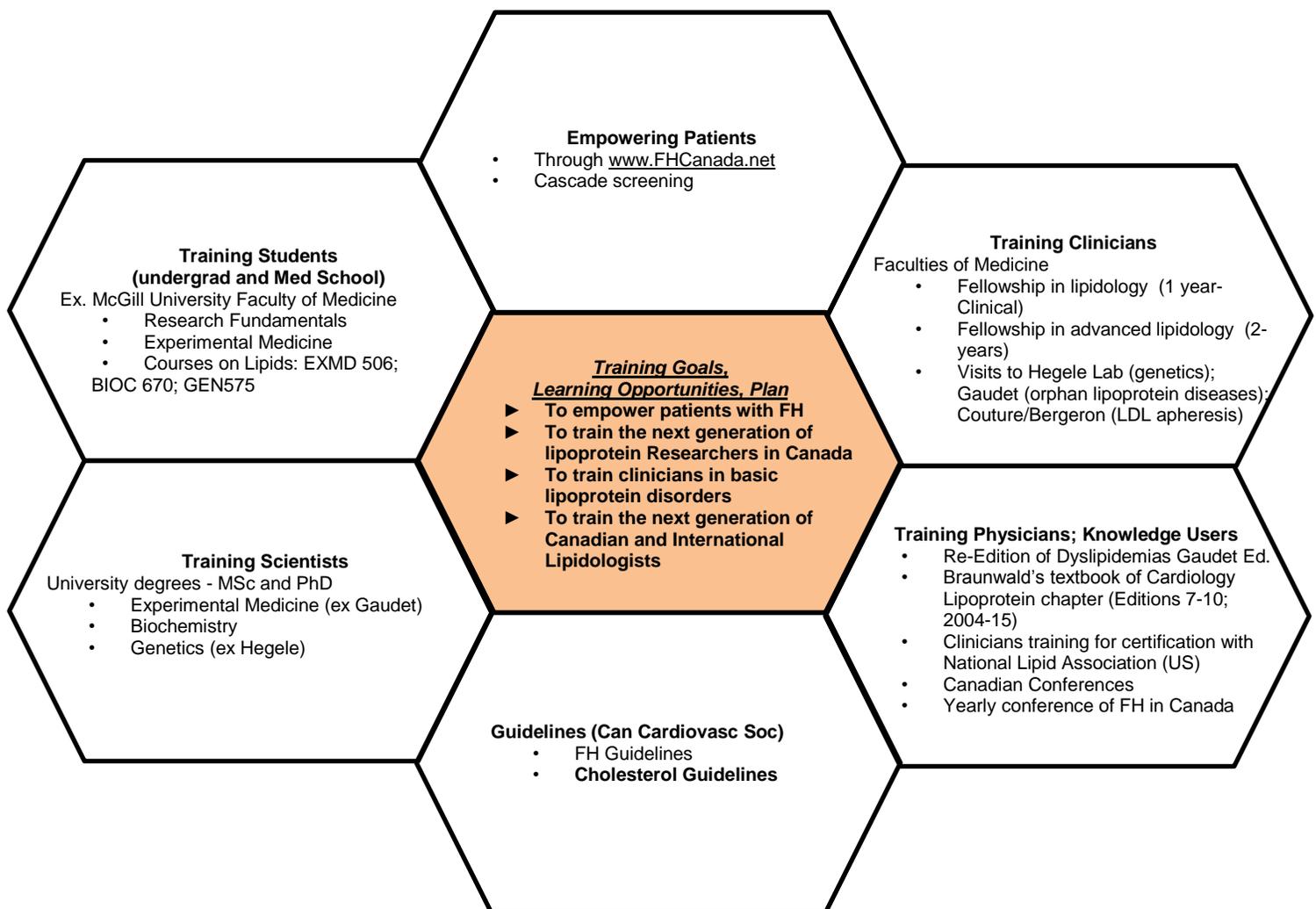


Figure 1. FH Canada registry commitment to knowledge translation

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