

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

## **FINAL PROGRESS REPORT**

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## Abstract

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

**Purpose:** The overall goal of the project was to increase awareness of familial hypercholesterolemia (FH) among health care professionals (HCP), their patients and family members. **Scope:** We wanted 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 HCP. In brief, to simplify FH diagnosis and improve healthcare in FH patients, we have created educational resources and web-based applications. **Methods:** The project combined 1)- the creation of educational resources for 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. The Canadian FH Registry ([www.FHCanada.net](http://www.FHCanada.net)) was leveraged to achieve these goals. **Results:** We successfully created the listed diagnosis tools 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. These interventions were clearly in line with the mission of the FH Canada registry initiative and, now implemented, directly improve the care of Canadian FH patients, a population at high risk of cardiovascular events.

**Key Words:** Familial hypercholesterolemia, diagnosis of FH, awareness of FH, lipid-lowering therapy.

## Purpose

The overall goal of the project was 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. The Canadian FH Registry and its website ([www.FHCanada.net](http://www.FHCanada.net)) were leveraged to achieve this goal.

The **3 principal objectives** of the proposal were 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 expected 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.

## Scope

### Background:

Familial hypercholesterolemia (FH) is a genetic lipoprotein disorder characterized by elevations in low-density lipoprotein cholesterol (LDL-C) >95<sup>th</sup> 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<sup>1</sup>. When identified and treated early, life expectancy is normal.

There are at least three accepted definitions for FH, based on absolute LDL-C levels: the MedPed criteria<sup>2</sup>, the Simon-Broome criteria, including fixed cut-point for LDL-C, the presence of DNA mutations and xanthomas<sup>3</sup>, and the Dutch Lipid Clinics Network Criteria<sup>4</sup>. 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.

### Context and settings:

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 to improve health and healthcare delivery. FH Canada is characterized by a well-developed and extensive network of 19 lipid clinics specializing in FH in Canada ([www.FHCanada.net](http://www.FHCanada.net)). Over 65 experts in lipidology, endocrinology, cardiology, pediatrics, public health and epidemiology participate in this project. They are recognized at the national level for their expertise in lipoprotein disorders and with advanced laboratory facilities. Moreover, we have linked more than 150 investigators, clinicians, basic researchers and industry participants across Canada so far. These partners are our link to the family physicians across Canada since all new information on FH is radiating from these academic centers to the regional clinics that treat patients with FH.

### Participants:

The targeted audience for the proposed project were HCP and family doctors across Canada. We used the “hub and spoke” model of medical care established in the FH Canada registry so that the specialized clinics (hubs) translated the knowledge to the community clinics (spokes). We estimated that over 20,000 family physicians could be reached to help increase awareness of FH in patients, improve the diagnosis of FH and provide better healthcare, including access to newly available therapies such as PCSK9 inhibitors. The network was really the key in the present project: with an easier diagnosis and implementation of cascade screening, all participants, including HCP and patients, were and still are transmitting new knowledge on FH and help disseminate new tools across the country.

## Incidence and Prevalence:

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 in 500 individuals in the general population<sup>1</sup>. A recent meta-analysis from FH Canada colleagues now estimates the prevalence of FH to be 1 in 250 individuals<sup>5</sup>. The number of patients with FH in Canada is then estimated to be more than 140,000 individuals, with less than 10% diagnosed so far. There is a considerable need for HCP as well as patient education so we can 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%<sup>1</sup>.

## Methods

### Study design:

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 wanted to specifically:

**Objective 1)** create educational resources for 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.

### Data Sources/Collection and Interventions:

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

- Created an accredited teaching material on FH and other lipoprotein disorders, bilingual and freely available online, and including the latest knowledge on FH, its revised Canadian definition and diagnostic criteria, the available treatments in Canada, including PCSK9 inhibitors. The new resources also include the most recent publications on FH in Canada such as the Canadian Cardiovascular Society (CCS) position statement on FH<sup>6</sup> and the unique LipidSeq and MLPA techniques for genetic diagnosis of FH<sup>7</sup>. This educational material is available at [www.fhcanada.net](http://www.fhcanada.net) for dissemination to the general public and to HCP (clinicians, dieticians, pharmacists, genetics counsellors, psychologists and physical exercise specialists).
- Compiled data from main Canadian Lipid Clinics for their integration into the FH Canada Registry and we wrote the Canadian experience with FH and new definition, prevalence and treatment recommendations (peer-review papers).
- Organized 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 was included in this meeting.

**Objective 2.** The design of apps for Canadian FH diagnosis criteria and treatment. We specifically:

- Validated a simplified FH diagnosis based on the Simon-Broome criteria but adapted for Canada. The 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.
- Created an app for this new Canadian definition of FH, freely downloadable and bilingual.
- Validated, in the Canadian population, an algorithm to impute baseline LDL-C from values obtained while on lipid-lowering therapy. This tool is useful for assessing the degree of severity of FH for new patients. The imputation of baseline LDL-C was also incorporated in an app.

**Objective 3.** In line with the FH Canada mission, the project was aimed at increasing awareness of FH in patients and their family members. We wanted to generate 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.
- Update both versions of the FH Canada website i.e. patient and HCP, with new resources.

#### Measures:

The major tool for dissemination of the new educational resources is the FH Canada website ([www.fhcanada.net](http://www.fhcanada.net)), which presents sections for both patients and HCP. The new material is freely available and updated regularly. All documents created were also made available to all academic centers participating in FH Canada. We can measure the dissemination of new knowledge on FH by measuring specific outcomes such as the number of new patients and their family members entered in the FH Canada database in time or the number of new users of the website or how many downloads of the FH Calculator app. Our interaction with FH Canada colleagues and the FH Canada annual meetings also helped us get feedback from HCP as well as from patients. We are in constant communication with all members of FH Canada, including the patients and specific organizations, and we meet a lot of users in presentations, workshops or conferences on FH, organized or not by the FH Canada registry.

#### Limitations:

The FH Canada Network is composed of HCP such as family doctors and specialists (cardiologists, endocrinologists, pediatricians, etc), nurses and clinical coordinators, all with very busy schedule. To help us increase awareness of FH with an improve diagnosis, teaching, attending meetings or perform cascade screening on family members might be quite time-consuming for them so time was our main barrier. For instance, we were supposed to work on 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. We are currently working on it but need an extra year before being able to present the new edition to

the public. Meanwhile, users still have access to the third edition. Fortunately, we have had new initiatives recently in Canada (listed below), which represented an additional opportunity for us to promote FH across the country and helped us progress significantly:

- 2016 update of the CCS Guidelines on the Prevention of Cardiovascular Diseases<sup>8</sup>;
- New developments in research in the field of familial hypercholesterolemia (FH), including new therapies available and new technologies for DNA diagnosis<sup>7,9</sup>;
- Novel lipid-lowering therapeutic approaches such as PCSK9 inhibitors.

The newly developed diagnosis tools and the 3 manuscripts on FH to be published this year, including new guidelines and definition of FH for the Canadian population, will rapidly help to reduce the explained delay.

## Results

### Principal findings:

Our project deliverables were aligned with the objectives, and were achieved according to the planned timeline. Here's the list of the resources created as part of the present proposal:

- Creation of a slide kit on FH ([www.fhcanada.net](http://www.fhcanada.net), in FR and EN; attached);
- Creation of FH Canada-based information such as brochures, family tree drawing, educational videos for patients (all on [www.FHcanada.net](http://www.FHcanada.net); attached file "YouTube FH Video FR and EN");
- Validation of a new definition of FH to ease diagnosis: manuscript entitled "Pragmatic, simplified Canadian definition for FH" submitted to *the Canadian Medical Association Journal* ("Canadian definition of FH algorithm 16JAN2018");
- Creation of an app to impute baseline LDL-C and for FH diagnosis: publication in *Clinical Chemistry* ("Clin Chem Imputed Baseline LDL-C OCT2017") and creation of the FH Calculator app on android or iPhone/iOS platforms ("FH Calculator layout pdf 16JAN2018");
- Organization of the FH Canada Reunion 2016 ("Report Réseau HF Canada du 21OCT2016") and subsequent meetings (Vancouver 2017 "FH Canada Agenda flyer Meeting Vancouver 20OCT2017", Toronto 2018);
- Publication on the Canadian experience with FH: "FH in Canada: Initial Results from the FH Canada National Registry", submitted to *Atherosclerosis* 21MAR2018;
- Publication of the new guidelines on FH: "2018 update of the CCS position statement on FH" to be published in the *Canadian Journal of Cardiology* in Oct 2018.
- Update of the website with new material.

### Outcomes:

With the help of the implemented network of the FH Canada Registry, we succeeded in increasing awareness among a maximum of HCP and patients with FH across Canada. As part of the present proposal, we increased the network of participating HCP from 60 to over 150 members with 19 academic sites and 7 new peripheral sites now involved in FH across the country, and went from 1400 to more than 3000 patients with FH entered in the registry. With the addition of our new

diagnosis tools, material on FH, one published paper, and the annual CME accredited meetings on FH that were held in the past years, there is no doubt that our initiatives have helped to disseminate new knowledge of FH across the country. Three additional manuscripts will be published in 2018 in journals reaching a maximum of HCP. Please refer to uploaded material for the details of the achievements for the present project.

### Discussion:

There is a considerable need for HCP as well as patient education on FH, and a need for the implementation of proper diagnostic tools, and we wanted to help fill this gap. 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 allows 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. For instance, there is no “gold standard” for a diagnosis of FH and there was a need to develop one in Canada.

HCP and community physicians across Canada were the targeted audience for the proposed project. We used the “hub and spoke” model of medical care established in the FH Canada registry so that the specialized clinics (hubs) could translate the knowledge to the community clinics (spokes). We estimated at the beginning of the project that over 20,000 family physicians could 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. From the participation to the annual meetings, the increase of FH Canada members, the number of downloads and the number of users of the FH Calculator app, and from the feedback from our colleagues and industrial partners, we estimate that we reached at least 75% of HCP estimated to be reached originally. However, with the 3 manuscripts to be published in 2018, including a new position statement on FH for Canada (*Canadian Journal of Cardiology*) and a new definition of FH (*Canadian Medical Association Journal*; submitted), we expect to easily reach more than the 20,000 HCP originally planned. There is no doubt that the implemented network of FH Canada succeeded in increasing awareness among a maximum of HCP across Canada. The network was really the key in the present project: with an easier diagnosis and implementation of cascade screening, all participants, including patients, were and still are transmitting new knowledge on FH. The type of HCP targeted in the present proposal was mainly family physicians, and we created new diagnosis tools for them. However, from the FH Canada registry and from the feedback we received from these tools, we were also able to reach a significant proportion of specialists – cardiologists, endocrinologists and medical biochemists mainly. Nurses and clinical coordinators were also reached during the present project.

As of Jan 2018, 3122 patients with FH were registered in the FH Canada registry. It must be stressed out that a great proportion of Canadians with FH were discovered during the present project but are simply not registered yet because of a delay in the opening of some registry sites (delays in ethics approval, which differs considerably from site to site). Cascade screening was also initiated but the number of family members newly diagnosed and treated is hard to estimate



since these are not necessary registered in FH Canada yet. There is no doubt that a lot more patients directly benefited from the project outcomes. Some of the patients never had a lipid profile done before so FH was new to them. They are now being followed by lipid specialists. A few patients with other rare lipid disorders were also enrolled in the registry (n=85) under a “Systems and Molecular Approaches in Severe Hyperlipidemias – SMASH” component (a registry of orphan lipoprotein diseases) linked to FH Canada.

### Conclusions:

Since the beginning of the present project, we created tools to ease the diagnosis of FH, we therefore had more patients diagnosed with FH, we started cascade screening among the family members of the newly diagnosed patients, and we offered specialized healthcare, including access to new medication such as PCSK9 inhibitors, which will lead to a better management of cholesterol levels and prevention of heart disease.

### Significance:

In addition to the creation of slide kits, brochures and videos, we have been able to create specific tools from which we received significant positive feedback from all users:

- Update of the app for the clinical diagnosis of FH: the “FH Calculator”, an app available for HCP to easily diagnose FH, freely downloadable on android or iPhone/iOS platforms, in French or in English. It allows for an accurate diagnosis of FH even in patients on lipid-lowering treatment and include the clinical diagnosis of FH from the new Canadian definition of FH but also from the known FH criteria (DLCN and Simon-Broome). Users were pleased to be able to save and print a final report on FH diagnosis and add it to patient’s chart. Physicians are now using it to submit request for PCSK9 inhibitors.
- Validation and publication of the algorithm for imputed baseline LDL-C: the algorithm developed to impute baseline LDL-C from values obtained while on lipid-lowering therapy has been validated and was published in the *Clinical Chemistry* journal (see attachment). With this paper, we provide a validated estimation of baseline LDL-C for patients with FH that really helps clinicians in making a diagnosis when the untreated or baseline LDL-C value is unknown.
- Validation and preparation of a manuscript on the new Canadian definition of FH: we validated a new Canadian definition of FH, based on the Simon-Broome criteria. In a manuscript submitted to the *Canadian Medical Association Journal* in Dec 2017, we show that the simplified and practical Canadian FH definition has diagnostic performance comparable to existing algorithms. We are now disseminating the new definition and are pleased to hear that nurses and physicians are using it since it is much simpler than the previous definitions.
- We held the 2016 FH Canada Network in Montreal (see previous sections) and in 2017, the meeting was held on October 20<sup>th</sup>, 2017, at St-Paul’s Hospital, in Vancouver, BC, prior

to CCC 2017. These events were accredited by the RCPSC and the College of Family Physicians of Canada, and was intended primarily for GPs and physicians involved in prevention with the primary goal of increasing awareness of FH in Canada. Presentations on diagnosis of FH, genetics of FH and treatments of FH were given and followed by a public forum. We received incredible positive feedback from the participants across the country.

### Implications:

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.

## List of Publications and Products

***All files were attached to the final report online***

“1-Slide Kit on FH English”: Slide kit comprising 5 separated presentations on FH: History of FH, What is the FH Canada Registry, FH explained to patients, Other lipid-lipoprotein disorders (SMASH and How to draw a genetic family pedigree).

“2-Slide Kit on FH French”: Same slide kit but with presentations translated in French.

“3-YouTube FH Video FR and EN”: Overview of the 2 videos that were created and added to the FH Canada website ([www.fhcanada.net](http://www.fhcanada.net)). They explain what is FH to patients.

“4-Canadian definition of FH algorithm 16JAN2018.pdf”: Canadian definition of FH, validated, to be used to diagnose FH in Canada. This definition is simple and adapted to the Canadian population and the manuscript was submitted recently for publication in the *Canadian Medical Association Journal*, which is the journal of choice to reach a maximum of HCP in Canada.

“5-Clin Chem Imputed Baseline LDL-C OCT2017.pdf”: Paper on the algorithm to be used to impute the baseline LDL-C when a patient is seen for the first time while on lipid-lowering medication, to appear in *Clinical Chemistry* in February or March 2018. This paper will be useful to clinicians to diagnose FH.

### *Published reference:*

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URL: <http://clinchem.aaccjnls.org/content/64/2/355.long>

PMID: 29038147

“6-FH Calculator layout pdf 16JAN2018”: Layout of the freely available app for the diagnosis of FH, which includes the calculations for imputing baseline LDL-C from LDL-C on treatment, and the clinical diagnosis of FH using the Canadian definition of FH, the Simon Broome criteria and the DLCN criteria.

“7-Report Réseau HF Canada du 21OCT2016”: FH Canada Network meeting we entirely organized. It was held in Montreal, on Oct 21st, 2016.

“8-FH Canada Agenda Flyer Meeting Vancouver 20OCT2017.pdf”: FH Canada Network meeting held in Vancouver on the 20OCT2017, including presentations by 3 specialists in FH and one general practitioner.

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