

Canadian Familial Hypercholesterolemia Registry YEAR 2018 Annual Progress Report

Annual report for year 2018, 4 FEB 2019

Dear Colleagues,

We are pleased to present the 2018 FH Canada progress report. We would like to thank you for your commitment, your support and your many contributions. We have made tremendous progress at the National and International levels. Looking forward to 2019, we hope to continue to provide guidance to patients with FH and other lipoprotein disorders and advocate to access to proper diagnosis and treatments.

1. 2018 PUBLICATIONS

Here's a list of publications from FH Canada in 2018. Please do not hesitate to contact us if you would like a pdf copy of these articles.

- **Algorithm for imputed baseline LDL-C: paper published in Clinical Chemistry**

This article is on the imputation of baseline LDL-C from values obtained while on lipid-lowering therapy. With this paper, we provide a validated estimation of baseline LDL-C for patients with FH that will help clinicians in making a diagnosis.

The full reference is:

Imputation of Baseline LDL Cholesterol Concentration in Patients with Familial Hypercholesterolemia on Statins or Ezetimibe.

Ruel I, Aljenedil S, Sadri I, de Varennes É, Hegele RA, Couture P, Bergeron J, Wanneh E, Baass A, Dufour R, Gaudet D, Brisson D, Brunham LR, Francis GA, Cermakova L, Brophy JM, Ryomoto A, Mancini GBJ, Genest J. *Clinical Chemistry* 2018. 64(2):355-362.

PMID: 29038147

<https://www.ncbi.nlm.nih.gov/pubmed/29038147>

- **Snapshot of the FH Canada registry: paper published in Atherosclerosis**

As of June 2018, 3195 patients were included in the database, including 63 patients with other lipoprotein disorders (*ABCA1*, *SMPD1*, *APOAI*, *CPT2*, *LCAT* mutations). Preliminary results from the FH Canada registry were published in *Atherosclerosis*.

The full reference is:

Familial Hypercholesterolemia in Canada: Initial Results from the FH Canada National Registry.

Brunham LR, Ruel I, Khoury E, Hegele RA, Couture P, Bergeron J, Baass A, Dufour R, Francis GA, Cermakova L, Mancini GBJ, Brophy JM, Brisson D, Gaudet D, Genest J. *Atherosclerosis* 2018. 277:419-424.

PMID: 30270080

<https://www.ncbi.nlm.nih.gov/pubmed/30270080>

• **New Canadian definition of FH: paper published in the Canadian Journal of Cardiology**

We are pleased to report that the paper on the Canadian definition of FH was published in the Canadian Journal of Cardiology. In this manuscript, we show that the simplified and practical Canadian FH definition has diagnostic performance comparable to existing algorithms but adapted to the Canadian population. The Canadian FH definition is available on the FH Calculator web-based and downloadable application (<http://www.circl.ubc.ca/cardiorisk-calculator.html>).

The full reference is:

Simplified Canadian Definition for Familial Hypercholesterolemia.

Ruel I, Brisson D, Aljenedil S, Awan Z, Baass A, Bélanger A, Bergeron J, Bewick D, Brophy JM, Brunham LR, Couture P, Dufour R, Francis GA, Frohlich J, Gagné C, Gaudet D, Grégoire JC, Gupta M, Hegele RA, Mancini GBJ, McCrindle BW, Pang J, Raggi P, Tu JV, Watts GF, Genest J. *Can J Cardiol.* 2018. 34(9):1210-1214.

PMID: 30093300

<https://www.ncbi.nlm.nih.gov/pubmed/30093300>

• **CCS position statement on FH: update 2018: paper published in the Canadian Journal of Cardiology**

Specific changes took place since the first CCS position statement on FH published in 2014 and both a primary and secondary panel have worked together to review this important document. The update includes, for instance, new data on the prevalence of FH worldwide, suggesting that the frequency is greater than previously thought, the new information on the risk estimates for atherosclerotic cardiovascular disease in the presence of a mutation causing FH, the new Canadian definition of FH, and the availability in Canada of new drugs available to treat FH. The revised position statement guidelines were published in the *Canadian Journal of Cardiology* last Fall.

The full reference is:

Canadian Cardiovascular Society Position Statement on Familial Hypercholesterolemia: Update 2018.

Primary panel: Brunham LR, Ruel I, Aljenedil S, Rivière JB, Baass A, Tu JV, Mancini GBJ, Raggi P, Gupta M, Couture P, Pearson GJ, Bergeron J, Francis GA, McCrindle BW, Morrison K, St-Pierre J, Henderson M, Hegele RA (Co-chair), Genest J (Co-chair). Secondary panel: Goguen J, Gaudet D, Paré G, Romney J, Ransom T, Bernard S, Katz P, Joy TR, Bewick D, Brophy J. *Can J Cardiol.* 2018. 34(12):1553-1563.

PMID: 30527143

<https://www.ncbi.nlm.nih.gov/pubmed/30527143>

• **FH Canada registry: collaboration with the EAS-FHSC: paper published in Atherosclerosis**

The EAS-FH Studies Collaboration (FHSC) is a global initiative led by Prof Kausik Ray (Imperial College London, UK) and an international steering committee (http://www.eas-society.org/?page=fhsc_registry). The mission of the EAS-FHSC is to empower the medical and global community to seek change in their respective countries or

organizations regarding how FH is detected and managed, with a view to promoting early diagnosis and more effective treatment of this condition. Through international collaboration of stakeholders, the EAS-FHSC aim to generate large scale robust data on how FH is detected, managed and the clinical consequences of current practice on outcomes. The FH Canada network participates in this initiative for which a manuscript was published in *Atherosclerosis* in 2018.

The full reference is:

Overview of the current status of familial hypercholesterolaemia care in over 60 countries - The EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC).

EAS Familial Hypercholesterolaemia Studies Collaboration; EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC) Investigators. *Atherosclerosis* 2018. 277:234-255.

PMID: 30270054

<https://www.ncbi.nlm.nih.gov/pubmed/30270054>

2. FH Canada registry - update

Over 120 clinicians and scientists in 19 academic centers across Canada (the “hubs”) and 7 peripheral sites (the “spokes”) composed the FH Canada network (Clinicaltrials.gov: NCT02009345). Including clinical coordinators and members of the biopharma industry, it is more than 200 individuals working together to increase awareness of FH in Canada. Sites ready to submit the project to their institutional REB need to contact us for updated versions of the project proposal, consent form and patient questionnaire, and to get help in answering REB letters. Contact info: www.fhcanada.net.

As mentioned in the previous reports, the James Hogg Research Centre at St-Paul’s Hospital, UBC, Vancouver is providing the iCAPTURE platform used to capture the data from the FH Canada Registry. Individual secure access to the database is given once the project is approved locally. Data captured include familial history of elevated cholesterol levels and CVD, the patient’s medical and surgical history, the physical signs of FH, and the patient’s medication profile. It has built-in algorithms to generate a FH diagnosis score using the Canadian definition, Simon-Broome, and Dutch Lipid Clinic Network criteria, as well as one to impute a baseline LDL-C value for patients on lipid-lowering medication for which the untreated LDL-C is unknown.

Bulk upload of already existing databases is possible: the iCAPTURE IT team can re-format and upload the data onto the database and grant access to users. Funds granted by the industry for the initialization of the registry are available for site data entry stipend if needed.

3. The FH Calculator: an “app” for a diagnosis of FH

Make sure you are using the most recent version of the FH Calculator has it is constantly being updated. Current version is 1.4.0. For current iPhone and Android users, your device(s) should have automatically updated the software to this new version but for PC/Windows users, you have to manually download the new version from this link: <http://www.circl.ubc.ca/cardiorisk-calculator.html>

The app provides the imputed baseline LDL-C but also leads to a clinical diagnosis of FH based on the Canadian definition as well as the known FH criteria (DLCN and Simon-

Broome). The tool is freely available to all health care professionals; it generates a report to be saved and added to patient's file.

4. Impact of a genetic diagnosis of FH: systematic review

We have been working closely with the late Dr. Jack V. Tu from ICES and his student, Leo Akiyamen to determine the impact of genetic testing on the: 1) diagnosis of "definite FH", 2) initiation and adherence of lipid-lowering therapy, and 3) risk of atherosclerotic cardiovascular disease (ASCVD) by performing a systematic review and meta-analysis. Our manuscript: "Genetic Testing for Familial Hypercholesterolemia: Impact on Diagnosis, Treatment and Cardiovascular Risk" was accepted for publication in the *European Journal of Preventive Cardiology* and should be available soon in PubMed.

5. A strategy for a molecular diagnosis of FH is being discussed

Initiatives are ongoing across Canada to offer a new genetic assay for the molecular diagnosis of FH, mainly in BC, Ontario and Quebec. For instance, the Core Molecular Diagnostic Laboratory at the MUHC, in Montreal offers the genetic testing for FH from a clinically-certified laboratory (CLIA #99D1042152). In brief, the algorithm includes 1) testing of the familial variant when known; 2) when no known family variant: NGS sequencing of the *LDLR*, *APOB* and *PCSK9* genes (MiSeq); 3) proceed with deletion/duplication analysis of the *LDLR* gene by MLPA. Please contact the CMDL lab director Dr Jean-Baptiste Rivière for more details: jean-baptiste.riviere@mcgill.ca.

6. FH Canada Network MEETING 2018

The annual FH Canada Network meeting was held on October 20th, 2018, at the Li Ka Shing Knowledge Institute in Toronto, ON, prior to CCC 2018. Like for the previous meetings, the event was accredited by the Royal College of Physicians & Surgeons of Canada 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.

SAVE THE DATE: the next annual meeting will be held in Montreal, at the Research Institute of the McGill University Health Centre, possibly on October 23, prior to the CCC 2019 in Montreal. More details to come.

ON-GOING INITIATIVES

7. Montreal Cholesterol Summit, May 30, 2019

The Montreal Cholesterol summit will honor Dr. Nabil Seidah, for his contributions to cardiovascular disease research. Dr. Seidah received the Lucian Award at McGill University for his discovery of PCSK9. An International panel of Speakers will discuss clinical trials of PCSK9, the new 2019 Canadian Cholesterol Guidelines, the genetics of lipoprotein disorders and the public policies of genetic diagnosis. The symposium is open to residents and staff of McGill University and physicians within our CIUSSS, and will be followed by a public forum. This is accredited by the Royal College of Physicians and Surgeons of Canada.

The Montreal Cholesterol Summit will be held on May 30, 2019, at the Drs. Sylvia and Richard Cruess Amphitheatre at the Research Institute of the McGill University Health Centre in Montreal, Qc. Please contact us for more information.

12:00 – 12:45	Registration and Lunch
12:45 – 13:00	Opening remarks Dr Sophie Bernard, IRCM, University of Montreal
13:00 – 13:45	PCSK9 from Discovery to Therapeutic Dr Nabil G. Seidah, IRCM, University of Montreal
13:45 – 14:30	Clinical Trials of PCSK9 inhibitors for the Prevention of ASCVD Dr Shaun Goodman, St. Michael's Hospital, University of Toronto
14:30 – 15:15	Canadian Guidelines for the Treatment of Dyslipidemias Dr George Thanassoulis, RI-MUHC, McGill University
15:15 – 15:30	Break
15:30 – 16:15	Genetic Lipoprotein Disorders, Diagnosis and Management Dr Robert A. Hegele, Robarts Research Institute, Western University
16:15 – 17:00	The implications of Genetic Diagnosis Dr Yann Joly, Centre of Genomics and Policy, McGill University
17:00 – 17:30	Discussion and Public Forum Dr Jacques Genest, RI-MUHC, McGill University

8. Ongoing studies on use of a PCSK9 inhibitor during pregnancy

Data on the use of a PCSK9 inhibitor during pregnancy are lacking so if one of your patients was on a PCSK9 inhibitor just before or while being pregnant (any number of days, at any dose, and at any time from the first day of the the last menstrual period up to and including the end of pregnancy), they can register to specific on-going clinical trials (registries). The registries are also looking for non-PCSK9i exposed FH or ASCVD pregnant women (disease control group) and non-PCSK9i exposed non-FH, non-ASCVD pregnant women (non-disease control group).

The experts from MotherToBaby, a non-profit organization, are in charge of collecting the data so please use the following link to get more information:

<https://mothertobaby.org/ongoing-study/high-cholesterol/>

9. www.FHCanada.net website

The FH Canada registry website is www.fhcanada.net. Please contact us if you would like to be listed on our list of lipid specialists so patients with FH or other lipoprotein disorders can be referred to your clinic. Contact us if you would like to have specific Powerpoint slides (only pdfs files were uploaded). Do not hesitate to send us reference papers and new accomplishments in the field of FH: we will be happy to add them on the website.

10. Homozygous FH patient registry

There is a global effort to raise awareness on FH and our colleagues in Europe have initiated an important international registry on FH (Familial Hypercholesterolemia Studies Collaboration (FHSC)). We have agreed to capture data on all Canadians with homozygous FH (HoFH). We can help format the patient data for physicians with HoFH patients willing to participate.