FACULTY/PRESENTER DISCLOSURE

- **Faculty:** Rob Hegele

- **Relationships with commercial interests:**
  - **Grants/Research Support:** Amgen, Ionis, Sanofi, Pfizer, Lilly, Aegerion, Gemphire
  - **Speakers Bureau/Honoraria:** Valeant, Amgen, Aegerion
  - **Consulting Fees:** Amgen, Gemphire, Boston Heart Diagnostics, Sanofi, Valeant, Aegerion, Lilly
  - **Other:** N/A

Case report 1

- 34 year-old truck driver, 2^{o} CHD prevention
- father & 2 uncles: fatal MIs <50 years
- age 29: TC and LDL-C = 10.6 and 8.5 mmol/L
- age 33: - AMI
  - diffuse CAD
  - three stents placed
- Rx: atorvastatin 80 mg, ezetimibe 10 mg,
  ramipril 5 mg, clopidogrel 75 mg,
  metoprolol 25 mg, ASA 81 mg

Yuan *et al. CMAJ* 2006; 174:1124-9.

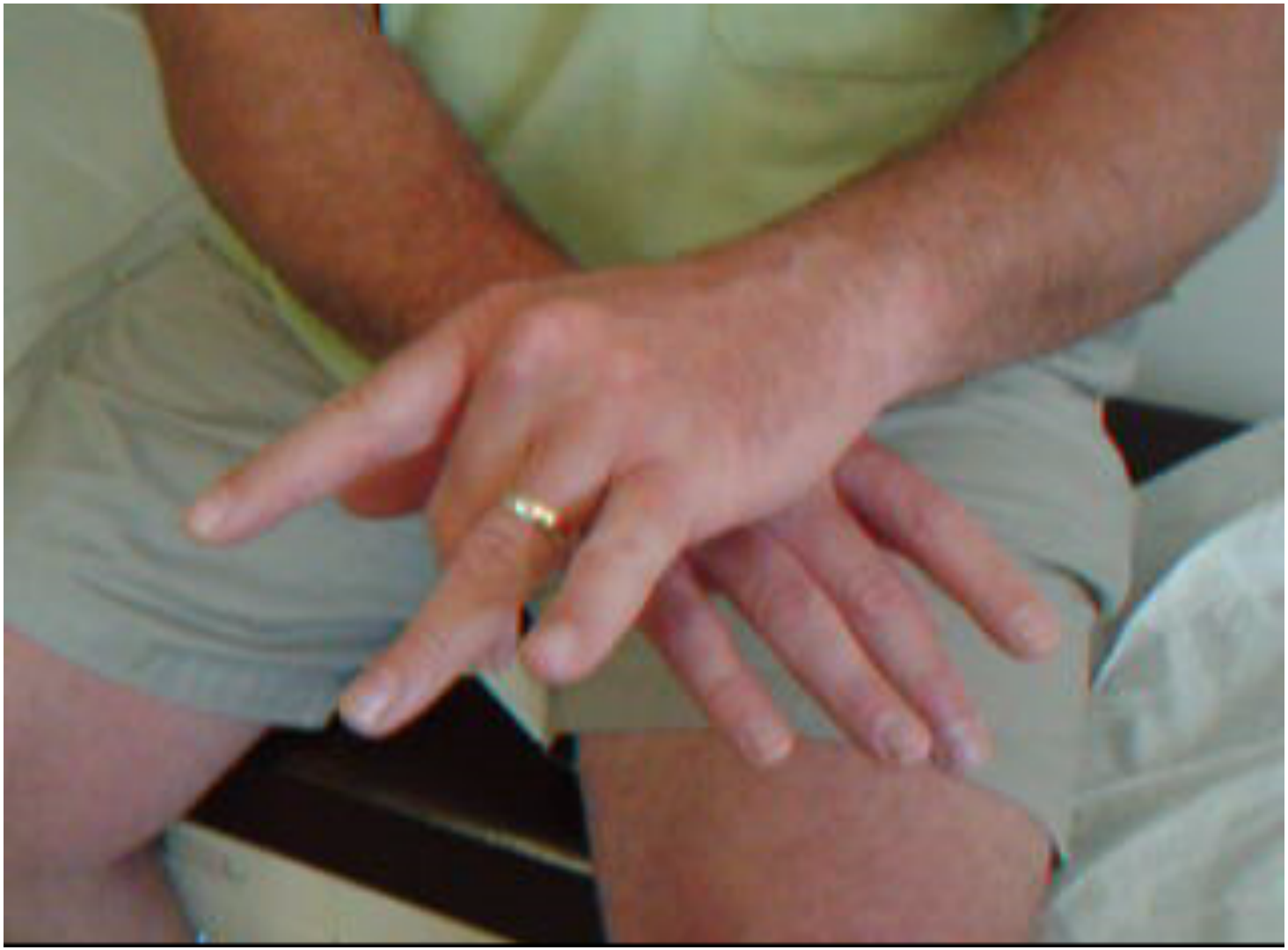
Case report 1

LipidSeq analysis

1. monogenic ↑LDL: simple heterozygote *LDLR* IVS14 +1G>A
2. 2^{o} ↑LDL: none
3. polygenic ↑LDL: 16/20 (99th percentile)

Diagnosis: heterozygous familial hypercholesterolemia (HeFH) + strong polygenic risk

On exam



Case report 1

date	meds	TC	TG	LDL-C	HDL-C
1997	none	10.6	1.52	8.52	1.02
2003	atorvastatin 80 mg	7.40	1.30	5.04	1.05
2004	rosuvastatin 40 mg + ezetimibe 10 mg	6.22	1.25	3.82	1.05
2007	above 2 + niacin ER 2000 mg	5.65	1.02	3.36	1.19
2011	above 3	5.50	1.08	3.18	1.14
2016	rosuvastatin 40 mg + ezetimibe 10 mg + evolocumab 140 mg q2wk	3.36	0.79	1.34	1.08

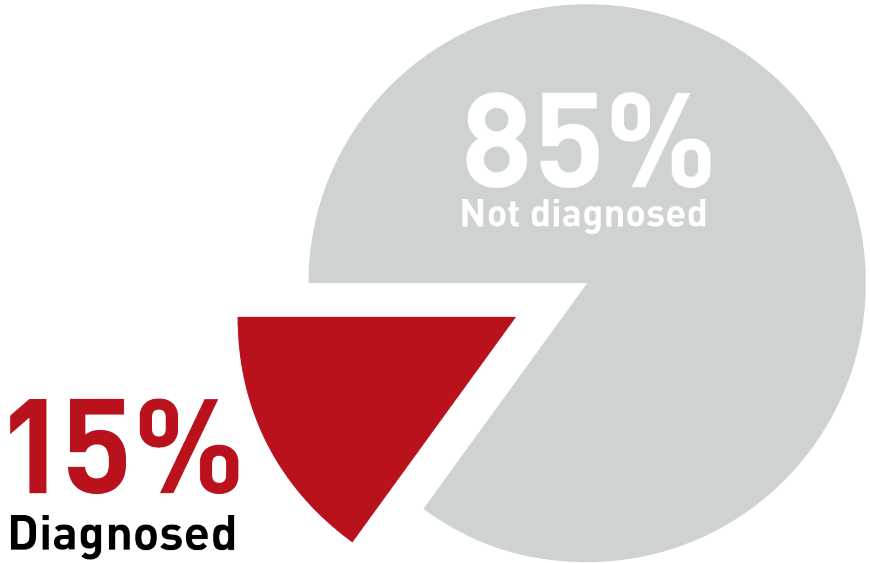
What is FH?

- inheritable, autosomal co-dominant disorder[1]
- usually due to mutations in *LDLR* gene[2,3]
  - >1700 mutations
  - *LDLR* mutation 1: 300; higher in Quebec, Lebanon, Afrikaners
  - <5% due to other mutations in the *APOB, PCSK9* and *ARH* genes
- two forms: HoFH and HeFH
- decreased clearance of LDL particles from plasma[1].
- severe hypercholesterolemia and lifelong accumulation of plasma LDL leading to atherosclerosis
- despite current therapies, premature death from CVD, with cardiac event rate > 6% annually[4]

1. Marais AD. *Clin Biochem Rev.* 2004;25:49-68.
2. Mahley RW, et al. In: *Kronenberg: Williams Textbook of Endocrinology.* 2008.
3. Rader DJ, et al. *J Clin Invest.* 2003;111:1795-1803.
4. Scandinavian Simvastatin Survival Study Group, 1995, Lancet

What is the burden of disease?

Estimate of Diagnosis in Canada



Heterozygous FH is not rare:

- Canadians - 1: ≥500
- French-Canadians - 1: 270

>85,000 Cases in Canada

Homozygous FH is rare:

- Globally - 1: 1 million
- Typically Diagnosed in Childhood

<100 Cases in Canada

Adapted from Nordestgaard BG et al. *Eur Heart J* 2013;34:3478-90a

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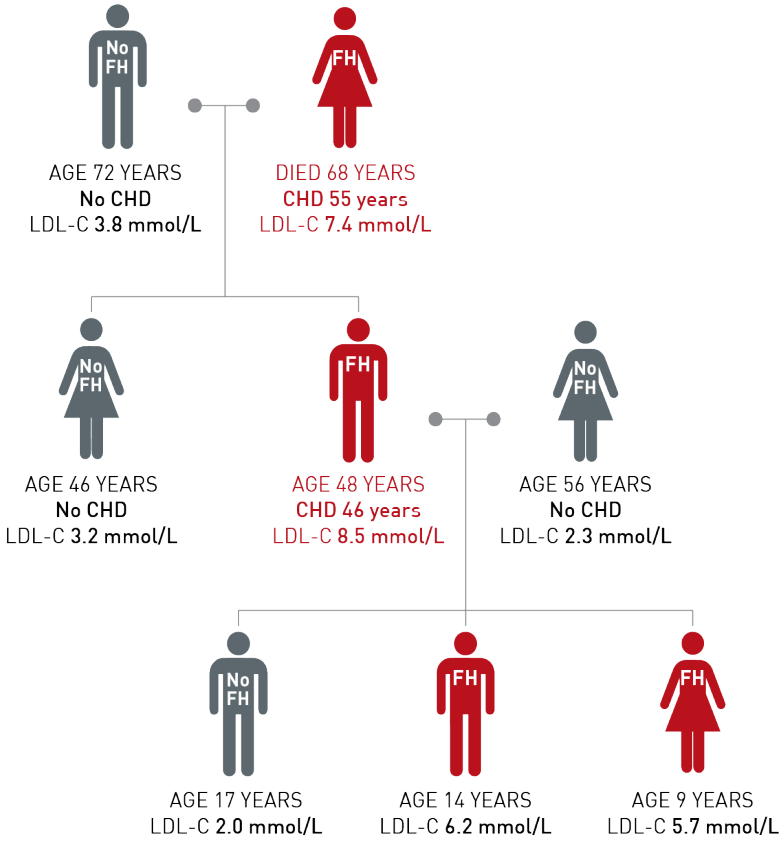

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TOC

Cascade Screening for HeFH

- ✓ Notifying relatives needs consent of the index case.
- ✓ Protocols concerning disclosure of medical information without consent.
- ✓ Proactive respect for privacy, justice, and autonomy.
- ✓ Material communicated should be comprehensible and not cause alarm.
- ✓ Pre-testing counselling should be offered to at risk family members.
- ✓ If DNA testing detects a causative mutation, a definitive diagnosis of FH can be made particularly when the phenotype also suggests FH.
- ✓ If DNA testing does not detect a causative mutation, diagnosis of FH can be excluded, except when clinical phenotype is highly suggestive.
- ✓ If DNA testing detects a causative mutation but the phenotype does not suggest FH, then a definitive diagnosis of FH should not be made; monitor.
- ✓ DNA test results may have implications for insurance.

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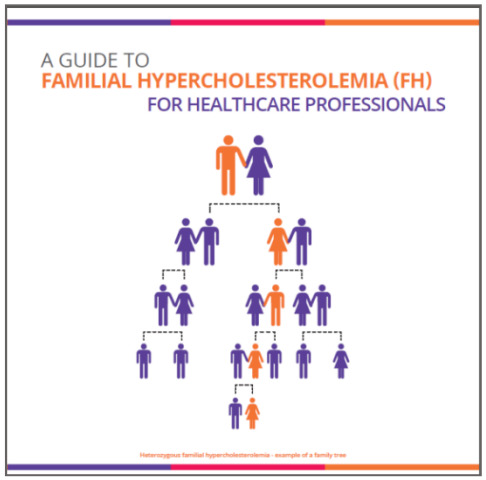
FH Resources

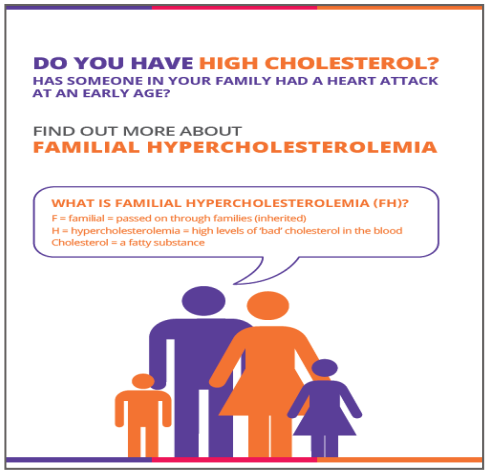
The Canadian FH Registry

www.FHCanada.net



Physicians' Guide available on www.FHCanada.net

www.fhpatientcanada.org



Patient Information Guide available on www.FHCanada.net