Homozygous Familial Hypercholesterolemia in the United States: Data from the CASCADE FH® Registry

M. Cuchel[1], J.W. Knowles[2], I. Kindt[3], P. Shrader [4], L.C. Hudgins[5], P.B. Duell[6], M.D. Shapiro[6], D.J. Rader[1], S.D. de Ferranti[7], J.A. Larry[8], L.C. Hemphill[9], I. Benuck[10], R.L. Andersen[11], S. Baum[12], K. Wilemon[3], M.T. Roe[13], J. Guyton[13], J. Kane[14], C.M. Ballantyne[15], M.F. Linton[16], P.M. Moriarty[17], S.S. Gidding[3]

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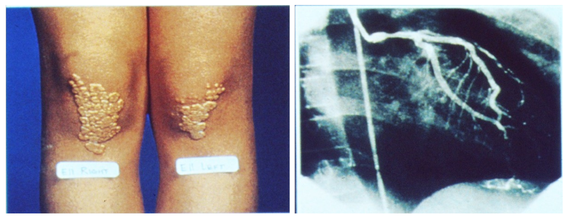
BACKGROUND

- Familial Hypercholesterolemia (FH) is under-diagnosed and under-treated in the U.S.
- **The cardiovascular disease (CVD) burden and treatment intensity among homozygous familial hypercholesterolemia (HoFH) patients in the U.S. is poorly characterized.**
- Data from the CASCADE FH Registry were used to describe patients with HoFH in the U.S.

Figure 1: Representative case of an untreated HoFH patient. *Click to enlarge*

12 Y.O. female LDL-C=780 mg/dL, xanthomas since age 3, CHD, CABG.



HoFH Prevalence: 1:250,000

Homozygous FH: Optimizing Management

- Patients must be diagnosed in childhood.
- CVD burden must be repeatedly assessed at diagnosis and longitudinally
- Intensive multiple lipid lowering treatment (LLT) regimen must be started at diagnosis:
  - Lipid lowering drugs
  - LDL apheresis
  - Liver transplant
- Care should be provided by an experienced lipid specialist

The CASCADE FH Patient Registry

In 2013, the FH Foundation (a patient-led nonprofit organization) created the CAscade SCreening for Awareness and DEtection (CASCADE) FH Registry, a national initiative to increase FH awareness, characterize trends in treatment, and monitor clinical and patient-reported outcomes over time. Children were included in the registry.

Figure 2: Clinical registry sites *Click to enlarge*

METHODS

CASCADE FH Registry

- 4549 FH patients present in the registry
  - Full cohort reviewed for those meeting criteria for definite HoFH
  - 40 meet criteria for unambiguous diagnosis of HoFH defined by:
    - Positive genetic diagnosis (n=29, 72.5%)
    - Untreated LDL-C>500 mg/dL and a positive family history

RESULTS

Figure 3: Demographics and medical history *Click to enlarge*

	Overall (n=40)	Age ≥ 18 (n=26)	Age <18 (n=14)
Age* at enrollment at diagnosis	24 (10, 42) 4 (2, 12)	36 (24, 50) 7 (3, 21)	9 (5, 10) 2 (1, 4)
Gender, F	55.0%	61.5%	42.9%
Race: Caucasian Hispanic	47.5% 35.0%	53.8% 30.8%	35.7% 42.9%
Xanthomas	65.0%	73.1%	50.0%
Corneal arcus	17.5%	26.9%	0.0%
CAD PCI,CABG Aortic valve repl.	62.5% 40.0% 12.5%	73.1% 53.8% 19.2%	42.9% 14.5% 0%
FH family history	82.5%	76.9%	92.9%

* Median (Q1,Q3)

Figure 4a, b: Lipid lowering treatment *Click to enlarge*

a.

	Overall (n=40)	Age ≥ 18 (n=26)	Age <18 (n=14)
Age* at start	6 (3, 15)	8 (6, 22)	3 (2, 5)
LL drugs	85%	85%	86%
Apheresis	43%	50%	29%
Liver transpl	10%	3.9%	21%

* Median (Q1,Q3)

b.

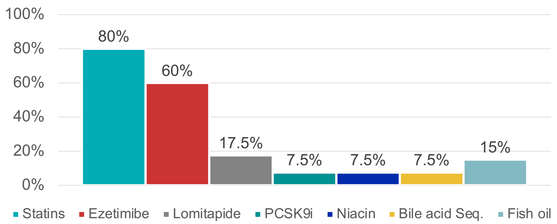
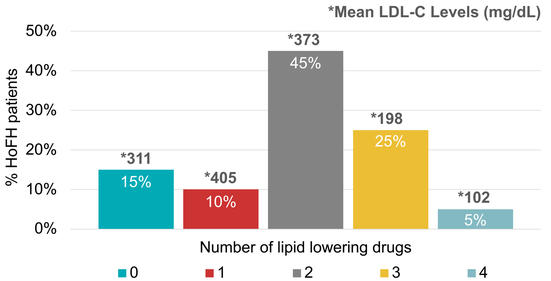


Figure 5: Impact of lipid lowering treatment *Click to enlarge*

	Untreated	Treated
Total Cholesterol	744 ± 174	381 ± 228
LDL-C	694 ± 167	310 ± 224
HDL-C	36 ± 12	39 ± 14
Triglycerides	153 ± 85	105 ± 72

mg/dl (mean±SD)

Figure 6: HoFH patients are sub-optimally treated *Click to enlarge*



CONCLUSION

- In the CASCADE HoFH cohort, despite relatively early HoFH diagnosis:
  - CAD and aortic valvular disease are highly prevalent
  - LDL-C levels remain suboptimal despite early initiation of LLT
- HoFH remains difficult to treat:
  - Novel treatment approaches are needed

A MORE AGGRESSIVE APPROACH TO LLT MUST BE IMPLEMENTED

Next Steps

- Careful review of patients in the registry with possible HoFH for inclusion in the cohort
  - LDL-C>400 mg/dL and meet other criteria
  - LDL-C>150 mg/dL and on 3 medications
- Characterize the genotype of as many possible/definite cases as possible
- Obtain additional clinical information beyond current information available in the registry

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