Health Disparities among Adult Patients with Familial Hypercholesterolemia in the CASCADE FH™ Patient Registry

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Background

- Patients with familial hypercholesterolemia (FH) have severe elevations in low density lipoprotein-cholesterol (LDL-C) from birth, leading to increased risk for atherosclerotic cardiovascular disease (ASCVD).
- FH is a common inherited disorder affecting 1 in every 250 individuals.
- FH affects all races/ethnicities and both sexes.
- ASCVD risk can be mitigated by reducing LDL-C.
- First-line therapy is statins and non-statins are often required to reduce LDL-C to goal levels (i.e., <100 mg/dL).
- Only 25% of US FH patients achieve LDL-C <100 mg/dL.
- We hypothesized that health disparities contribute to the undertreatment of FH patients in the US.
- We analyzed data from a nationwide database of FH patients to assess for health disparities

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.

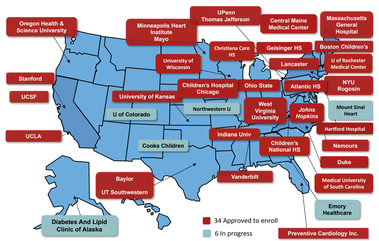


Figure 1: Active clinical sites and number of patients enrolled per site

Methods

Study Population

- All patients had ≥1 visit at a participating lipid clinic within the past 5 years with either heterozygous or homozygous FH diagnosed based on existing clinical or genetic diagnostic methods.
- Exclusion criteria included any secondary cause of hypercholesterolemia (e.g. hypothyroidism, nephrotic syndrome, and cholestasis).
- From September 2013 to September 2016, 3537 individuals were enrolled at 26 sites throughout the US.
- Individuals were excluded if they were <18 years old (n = 352) or if data on sex was missing (n = 18).
- Clinical and laboratory data were abstracted in a systematic fashion by trained research staff.

Outcomes and Variables

- Outcomes included:
  1. Achieved LDL-C of <100 mg/dL,
  2. Treatment with any statin, and
  3. Among those on statins, treatment with a high-intensity statin (i.e., atorvastatin 40 or 80 mg daily, or rosuvastatin 20 or 40 mg daily)
- Race/ethnicity was categorized in a hierarchical fashion. First, those of Hispanic ethnicity were identified and considered as a single entity. Those not of Hispanic ethnicity were then identified on the basis of self-reported race: white, black, Asian, or being of another race.

Statistical Analysis

- Multivariable logistic regression was used to evaluate differences in statin therapy and LDL-C goal achievement by sex or race/ethnicity.
- Regression models used generalized estimating equations with clustered standard errors which were employed to account for intersite variability.
- Missing data were accounted for by the creation of five multiple imputed datasets by Markov Chain Monte Carlo methods, and combined using standard rules.

Results

- Patient characteristics are shown in **Table 1**.
- Men and women had similar pretreatment LDL-C (women, median 236 interquartile range [IQR] 209-286 mg/dL vs. men, median 231 IQR 206-289 mg/dL; p = 0.17) (Figure 2).
- Women were diagnosed with FH at older ages than men (median 54, IQR 38-64 vs. men, median 47, IQR 34-59 years; p < 0.0001).
- Different racial/ethnic groups also had similar pretreatment LDL-C, though racial/ethnic differences were noted in the age of FH diagnosis.
- Results from regression models are shown in **Table 2**.

Table 1. Baseline sample characteristics (N=3167).*

Characteristic	
Age–yrs	54.6 ± 15.7
Age of FH diagnosis–yrs	48.0 ± 18.4
History of smoking–no. (%)	1090 (34.4%)
Hypertension–no. (%)	1461 (46.13)
Diabetes–no. (%)	448 (14.2%)
ASCVD–no. (%)	916 (28.9%)
Family history of FH–no. (%)	647 (20.4%)
Family history of premature ASCVD	1532 (48.4%)
Race/ethnicity–no. (%)	
Hispanic	155 (4.9%)
White	2505 (79.1%)
Black	260 (8.2%)
Asian	93 (2.9%)
Other	154 (4.9%)
Pre-Treatment Lipids	
Total cholesterol–mg/dL	344.5 ± 92.7
LDL-C–mg/dL	255.9 ± 78.9
Triglycerides–mg/dL	204.5 ± 127.3
HDL–mg/dL	48.9 ± 26.3
On Treatment Lipids	
Total cholesterol–mg/dL	235.1 ± 78.9
LDL-C–mg/dL	155.0 ± 72.6
Triglycerides–mg/dL	140.7 ± 85.6
HDL–mg/dL	53.7 ± 17.5
Lipid Lowering Therapy–no. (%)	
Any statin	2211 (69.8%)
Ezetimibe	1026 (32.4%)
Niacin	291 (9.2%)
Bile acid sequestrants	301 (9.5%)
Fibrate	118 (3.7%)
Fish oils/Omega 3 fatty acids	869 (27.4%)
PCSK9 inhibitors	127 (4.0%)
LDL apheresis	134 (4.2%)
Statin intolerance	478 (15.1%)

* Listed values correspond to means ± standard deviations or, when noted, numbers and percentages.

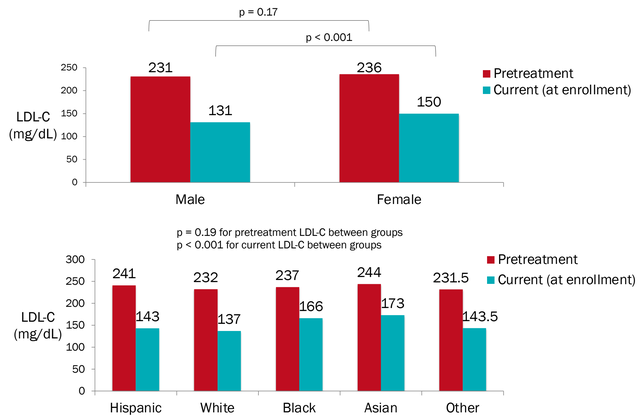
Results (continued)

Table 2. Odds ratios for achievement of LDL-C < 100 mg/dL and statin utilization, by sex and race/ethnicity*.

	LDL-C < 100mg/dL		Any Statin		High-intensity Statin	
Sex	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Women	0.69 (0.57-0.82)	<.0001	0.60 (0.50-0.73)	<.0001	0.60 (0.49-0.72)	<.0001
Men	Ref.		Ref.		Ref.	
Race/Ethnicity						
Asian	0.48 (0.24-0.94)	0.003	1.25 (0.74-2.11)	0.024	0.50 (0.30-0.83)	0.004
Black	0.49 (0.32-0.74)		0.81 (0.60-1.11)		1.66 (1.14-2.43)	
Hispanic	1.02 (0.67-1.56)		1.81 (1.16-2.82)		1.12 (0.74-1.70)	
Other	0.84 (0.55-1.28)		1.20 (0.78-1.85)		1.07 (0.71-1.61)	
White	Ref.		Ref.	—	Ref.	—

* Multivariate model additionally adjusts for age, race/ethnicity, age at diagnosis with FH, ASCVD, diabetes mellitus, hypertension, region, tendon xanthomas, xanthelasmas, corneal arcus, and, in the case of the regression analyzing LDL-C goal achieved, statin intolerance, ASCVD was defined as any prior diagnosis of coronary heart disease, stroke, transient ischemic attack, or peripheral artery disease.

Figure 2. Median pretreatment and current LDL-C levels, stratified by sex and race/ethnicity



Summary

- Compared with men, women were less likely to be on any statin therapy, less likely to be on a high-intensity statin, and less likely to achieve LDL-C < 100 mg/dL.
- Asians and blacks were also less likely than whites to achieve an LDL-C < 100 mg/dL.
- Notably, Asians were more likely to be on any statin but less likely to be prescribed high-intensity statins. Prior research suggests that Asians may have reduced metabolism of statins (especially rosuvastatin). Concerns for inducing myopathy at higher statin doses might have inadvertently led to the undertreatment of Asian FH patients.
- While blacks were undertreated compared to whites, blacks with FH that did receive treatment were more likely to be on a high-intensity statin. Healthcare providers who prescribe to blacks might be influenced by their known rates of worse cardiovascular outcomes.
- Our results mirror prior findings from non-FH populations in the US: women and minorities receive less guideline-based cardioprotective therapies.
- Few prior studies have evaluated health disparities in FH patients, and none have included multiethnic cohorts. In the Spanish Familial Hypercholesterolemia Cohort Study (SAFEHEART) study, women were found to be less likely than men to receive a high-intensity statin and less likely to achieve LDL-C goals.

Limitations

- Data are cross-sectional and observational in nature, limiting our ability to detect causal relationships.
- We are unable to detect which patient, social, or healthcare systems factors might have led to the associations we report.

Conclusions

We utilized data from a multicenter US registry of individuals with recognized FH to examine differences in statin therapy and LDL-C lowering. Our findings suggest that health disparities contribute to undertreatment of FH patients in the US. Increased efforts are warranted to raise awareness.

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