Artificial Intelligence & Predictive Analytics

- **Kelly Myers**, Chief Technology Officer, Familial Hypercholesterolemia Foundation

NATIONAL HEALTH COUNCIL

213

213

FH Foundation

The FH Foundation is a patient-centered nonprofit organization, dedicated to **research, advocacy, and education** for Familial Hypercholesterolemia (FH).

Our mission is to raise awareness of FH and save lives by increasing the rate of early diagnosis and encouraging proactive treatment.

FH FOUNDATION
Raising Awareness. Saving Lives.

NATIONAL HEALTH COUNCIL

214

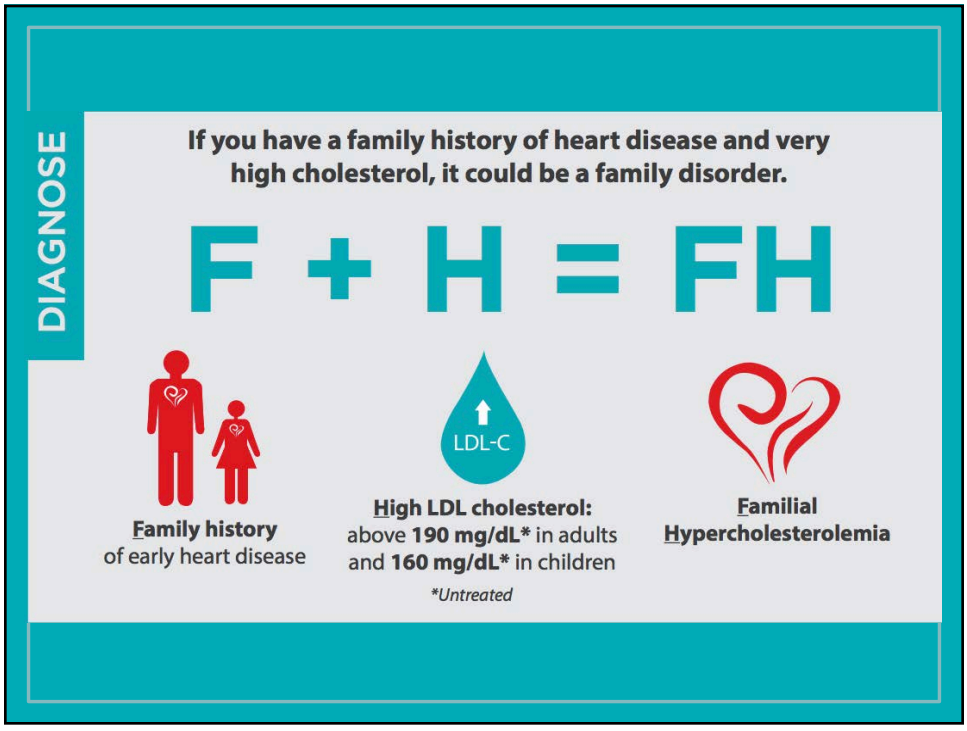
214

Artificial Intelligence and Predictive Analytics to FIND FH®

- What is Familial Hypercholesterolemia and why is predictive analytics needed?
- Validation of FIND FH model
- Implementation of FIND FH model
- Barriers to address

215

215



216

Familial Hypercholesterolemia

as many as 1/250 PEOPLE are estimated to have FH

FH is common

up to a 20 x higher risk of heart disease*

FH is life threatening

Therapies

Life Style

FH is manageable

90% UNDIAGNOSED

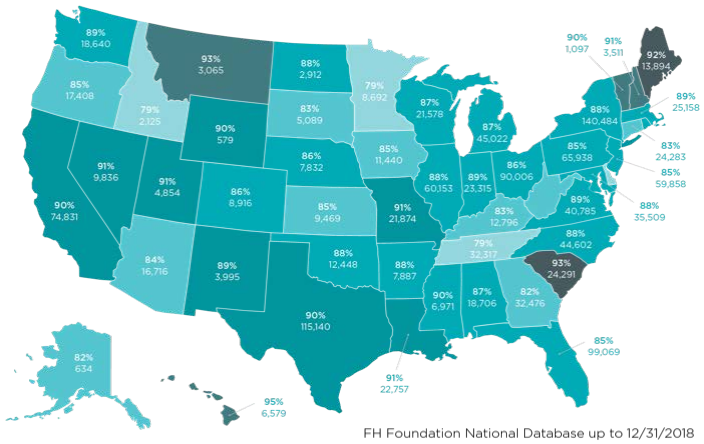
FH is undiagnosed

*if left untreated

217

217

How do we find 90% undiagnosed FH?



FH Foundation National Database up to 12/31/2018

218

218

THE LANCET
Digital Health

Precision screening for familial hypercholesterolaemia: a machine learning study applied to electronic health encounter data

Kelly D Myers, Joshua W Knowles, David Staszak, Michael D Shapiro, William Howard, Mrinal Yadava, David Zuzick, Latoya Williamson, Nigam H Shah, Juan M Banda, Joe Leader, William C Cromwell, Ed Trautman, Michael F Murray, Seth J Baum, Seth Myers, Samuel S Gidding, Katherine Wilemon, Daniel J Rader

Summary

Background Cardiovascular outcomes for people with familial hypercholesterolaemia can be improved with diagnosis and medical management. However, 90% of individuals with familial hypercholesterolaemia remain undiagnosed in the USA. We aimed to accelerate early diagnosis and timely intervention for more than 1·3 million undiagnosed individuals with familial hypercholesterolaemia at high risk for early heart attacks and strokes by applying machine learning to large health-care encounter datasets.

Methods We trained the FIND FH machine learning model using deidentified health-care encounter data, including procedure and diagnostic codes, prescriptions, and laboratory findings, from 939 clinically diagnosed individuals with familial hypercholesterolaemia (395 of whom had a molecular diagnosis) and 83 136 individuals presumed free of familial hypercholesterolaemia, sampled from four US institutions. The model was then applied to a national

Lancet Digital Health 2019
Published Online
October 21, 2019
https://doi.org/10.1016/S2589-7500(19)30150-5
See Online/Comment
https://doi.org/10.1016/S2589-7500(19)30161-X

The Familial Hypercholesterolemia Foundation, Pasadena, CA, USA

219

FIND FH validation at Stanford & Geisinger

Positive Predictive Value
85%

www.nature.com/npjdigitalmed

npj | Digital Medicine

www.nature.com/npjdigitalmed

ARTICLE OPEN

Finding missed cases of familial hypercholesterolemia in health systems using machine learning

Juan M. Banda[1,2], Ashish Sarraju[3], Fahim Abbasi[3], Justin Parizo[3], Mitchel Pariani[3], Hannah Ison[3], Elinor Briskin[3], Hannah Wand[3], Sebastien Dubois[3], Kenneth Jung[3], Seth A. Myers[4], Daniel J. Rader[5,6], Joseph B. Leader[7], Michael F. Murray[8], Kelly D. Myers[4,6], Katherine Wilemon[6], Nigam H. Shah[1] and Joshua W. Knowles[3,6,9]

Familial hypercholesterolemia (FH) is an underdiagnosed dominant genetic condition affecting approximately 0.4% of the population and has up to a 20-fold increased risk of coronary artery disease if untreated. Simple screening strategies have false positive rates greater than 95%. As part of the FH Foundation's FIND FH initiative, we developed a classifier to identify potential FH patients using electronic health record (EHR) data at Stanford Health Care. We trained a random forest classifier using data from known patients ($n = 197$) and matched non-cases ($n = 6590$). Our classifier obtained a positive predictive value (PPV) of 0.88 and sensitivity of 0.75 on a held-out test-set. We evaluated the accuracy of the classifier's predictions by chart review of 100 patients at risk of FH not included in the original dataset. The classifier correctly flagged 84% of patients at the highest probability threshold, with decreasing performance as the threshold lowers. In external validation on 466 FH patients (236 with genetically proven FH) and 5000 matched non-cases from the Geisinger Healthcare System our FH classifier achieved a PPV of 0.85. Our EHR-derived FH classifier is effective in finding candidate patients for further FH screening. Such machine learning guided strategies can lead to effective identification of the highest risk patients for enhanced management strategies.

npj Digital Medicine (2019)2:23 ; https://doi.org/10.1038/s41746-019-0101-5

220

FIND FH (Flag, Identify, Network, Deliver) validation process

Step 1
Secure longitudinal encounter data to train the model

939 clinically diagnosed FH individuals

66,669 presumed FH negative individuals

Step 2
Apply the model to national and health system datasets

Validation on national healthcare encounter data

FIND FH applied to database

N=170,000,000 individuals

1.3 M Probable FH individuals nationally

Validation on healthcare system encounter data

FIND FH applied to integrated healthcare delivery system database

N=174,000 individuals

866 probable FH individuals identified

Step 3
Charts reviewed by FH Expert

Charts reviewed by FH Expert

DLCN, MEDPED, Simon Broome and expert clinical judgment

Results

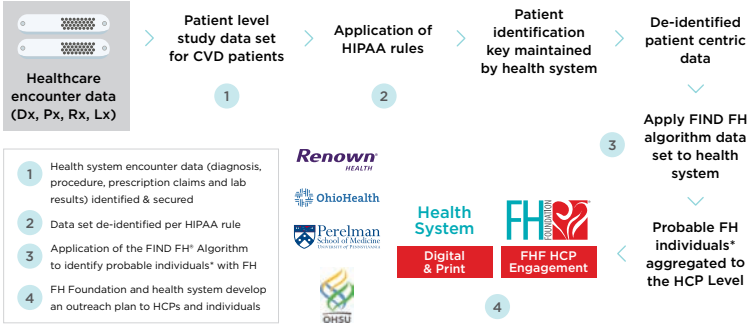
National dataset **87%** confirmed FH

OHSU dataset **77%** confirmed FH

221

221

Implementing FIND FH in health systems



*Patient that has a profile consistent with other individuals with FH

222

222

Quality Improvement Workflow at Penn Medicine

FHF → Penn Medicine Data Transfer	HCP Outreach	Patient Outreach	Medical Consultation	Patient Education Consultation
Return "Probable FH" Patients with brief history from FIND FH® to study team	Contact HCP to engage Patient	If permission granted, patient contacted and invited to clinic	Evaluation for FH, advanced cardiac risk assessment, interventions to reduce risk, genetic testing	Diagnosed FH patient encouraged to join CASCADE FH® Registry and patient portal
	HCP responds yes/no and/or provide details of previous clinical strategies	Patient visits Center for Preventive Cardiology		Patient provided print/digital FHF resources

Penn Medicine

FH FOUNDATION Raising Awareness. Saving Lives.

NATIONAL HEALTH COUNCIL

223

223

FIND FH: Penn Medicine progress through May 2019

- 442 providers treating ~3,000 patients contacted
- 233 providers responded (53% response rate), who managed a total of 2,174 patients
- Received permission to contact 1,755 patients (81%)
- 300 patients reached as of May 2019
  - 47 patients seen in clinic
  - 22/47 received a positive FH clinical diagnosis during visit
  - 40/47 had a change in clinical management (85%)

FH FOUNDATION Raising Awareness. Saving Lives.

Penn Medicine

NATIONAL HEALTH COUNCIL

224

224

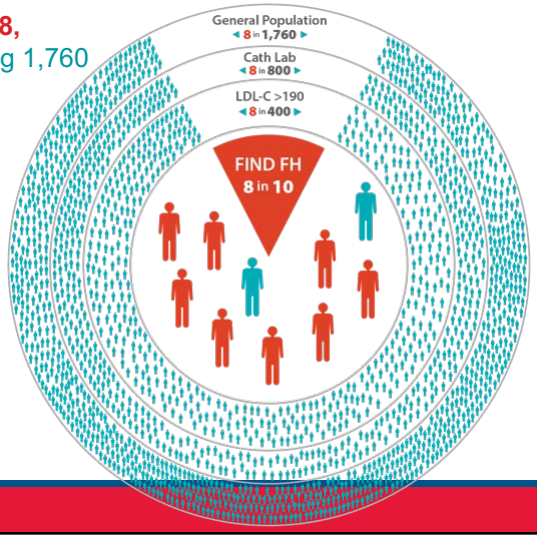
Implementing FIND FH: Barriers to Address

- FH awareness and education among PCPs is low
- Evidence-based guidelines (ACC/AHA) to consider FH & LDL-C > 190 mg/dL high risk conditions are not institutionalized
- Policy or quality metrics to incentivize guideline recommended treatments are lacking
- Cascade screening currently not easily performed in the US

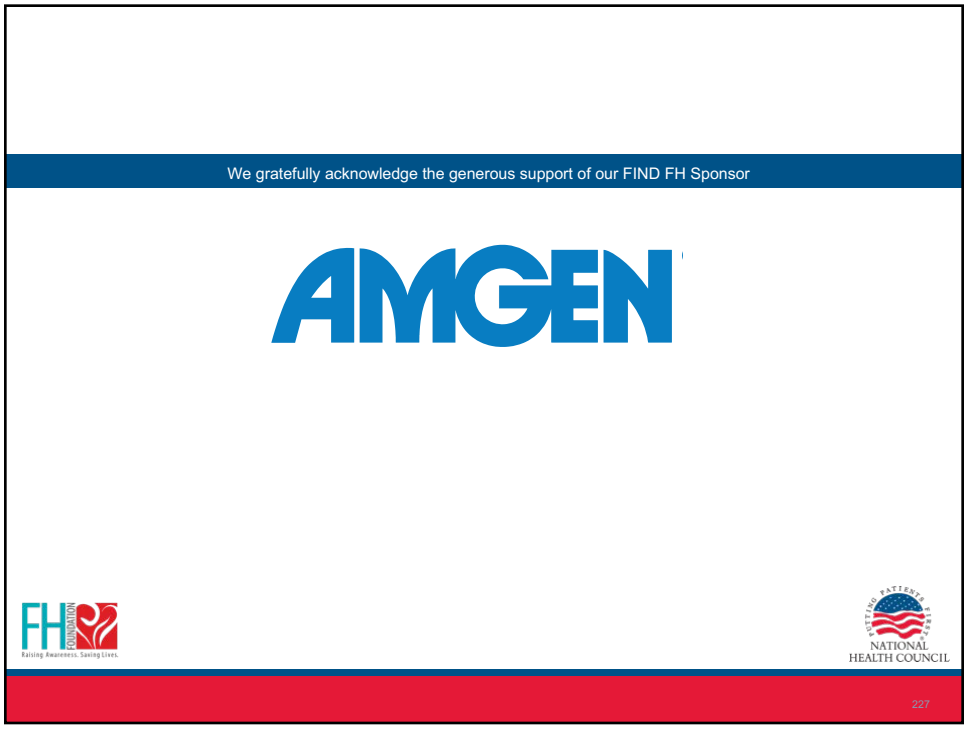
225

Precision screening is now a reality

Screen 10 to find 8,
instead of screening 1,760



226


We gratefully acknowledge the generous support of our FIND FH Sponsor
AMGEN
FH FOUNDATION
Raising Awareness. Saving Lives.
NATIONAL HEALTH COUNCIL
227

227