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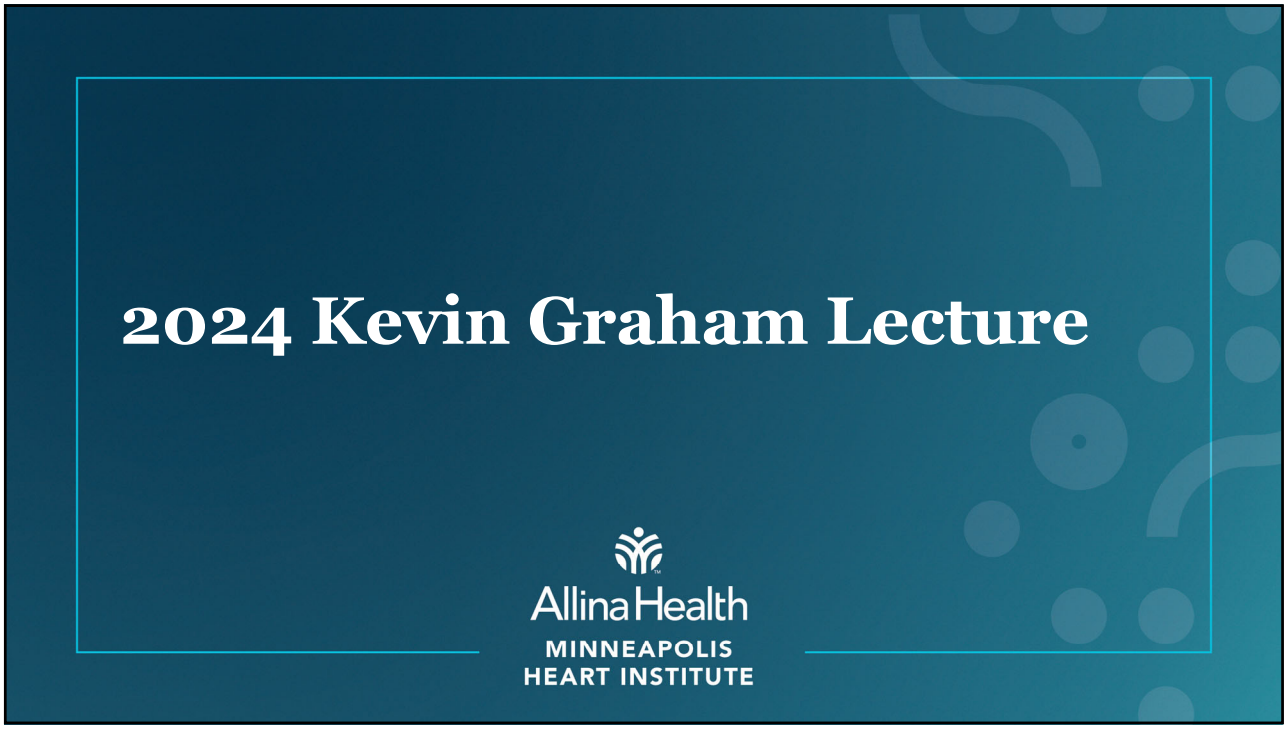
2024 Kevin Graham Lecture
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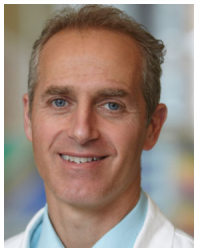

Dariush Mozaffarian

Martha Gulati

Roger Blumenthal

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Dr. Amit Khera

- Training:
  - Medical School – Baylor College of Medicine
  - Internal Medicine Residency – Brigham and Women's Hospital
  - Cardiovascular Fellowship – UT-Southwestern
- Faculty
  - Director of Preventive Cardiology – UT Southwestern
  - Associate Chief of Cardiology for Faculty Development
- Research and Leadership
  - Past President - American Society of Preventive Cardiology
  - Associate Editor - Circulation
  - Chair – 2024 AHA Scientific Sessions

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2024 Kevin Graham Lecture

Dr. Amit Khera

Familial Hypercholesterolemia: New Era in Diagnosis and Treatment

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Familial Hypercholesterolemia: New Era in Diagnosis and Treatment

Kevin Graham Prevention Lecture

Amit Khera, MD, MSc, FACC, FAHA, MASPC
Professor of Medicine
Director, Preventive Cardiology
Co-Director, UTSW Familial Hypercholesterolemia Clinic
Associate Chief of Cardiology, Faculty Development
Dallas Heart Ball Chair in Hypertension and Heart Disease
UT Southwestern Medical Center

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Case

46yo male presents for his annual PCP visit. He has a history of dyslipidemia and has been on a statin for about 10 years.

Social History: Married, 2 children ages 14 and 18, no tobacco
Family History: Mother with CABG age 62, maternal grandfather with MI in 50's.
2 younger siblings, unknown medical history

Meds: Atorvastatin 20mg daily

Exam: P-68, BP-128/76mm/Hg, BMI- 28kg/m^2; otherwise normal,
no xanthomas or xanthelasma

Lipids: Tot Chol- 165, LDL-C- 107, HDL-C-42, Trig-80 mg/dL

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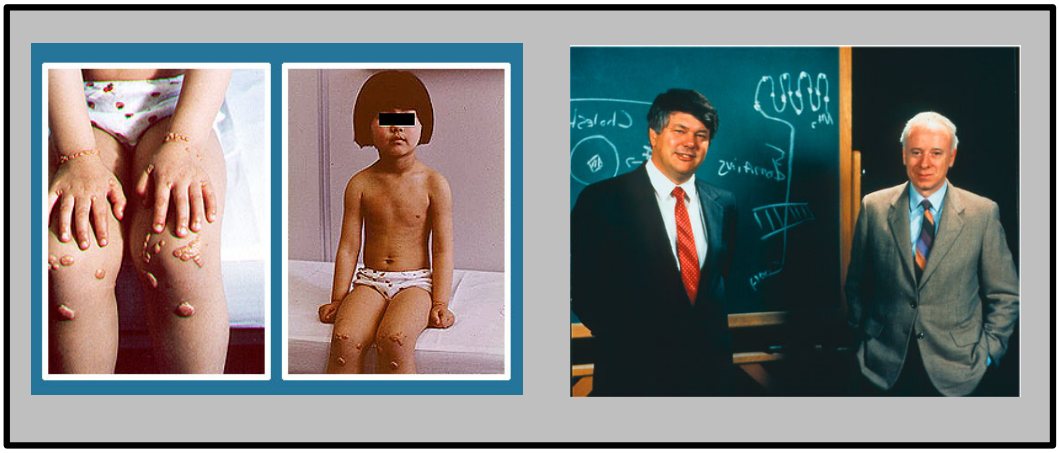
Brown and Goldstein
Nobel Prize in Physiology or Medicine 1985



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Brown and Goldstein
Nobel Prize in Physiology or Medicine 1985

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Familial Hypercholesterolemia(s)

Definition: Severe hypercholesterolemia with autosomal dominant inheritance pattern

Primary Autosomal Dominant forms:

- *LDLR (classic FH) ~85-90% cases*
- *APOB (Agr3500Gln) ~5-10% cases*
- *PCSK9 (gain-of-function) ~5% cases*

Homozygous (~1:500,000); LDL-C >400mg/dl

Heterozygous (~1:250); LDL-C 200-400mg/dl

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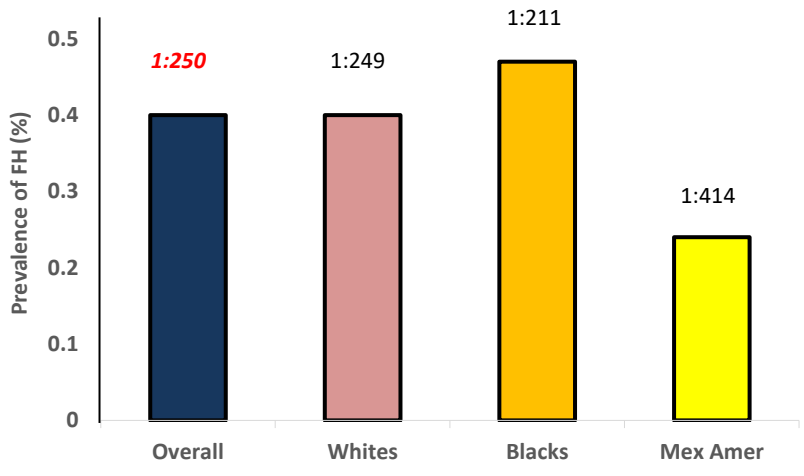
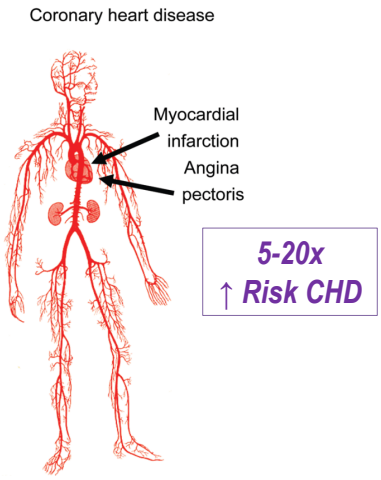
FH is Common and Associated with Increased CVD

~1.2 Million People with FH in the US





DLCN definite/probable FH (≥6 points)

de Ferranti et al Circulation 2016;133:1067-1072.

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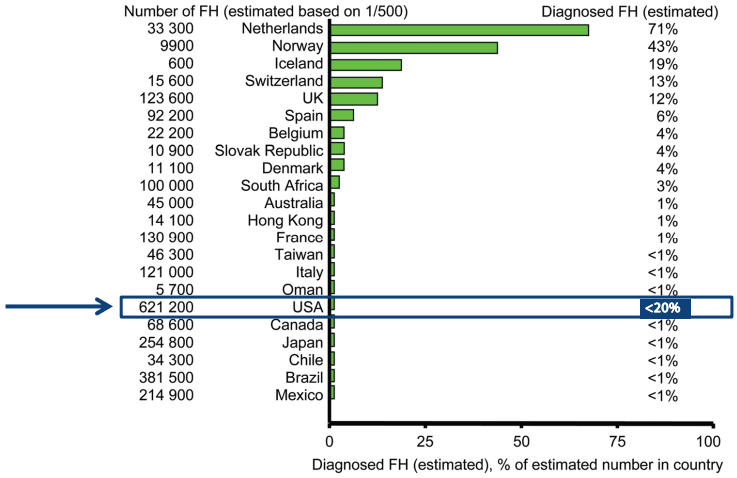
FH Is Underdiagnosed Worldwide



15.2-30.4 million with FH worldwide

Nordestgaard B et al. EHJ 2013

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Diagnosing FH: Clinical Criteria

1. ***Simon-Broome Register***
2. ***Dutch Lipid Clinic Network***
3. ***US MedPed***

Simon-Broome

Total cholesterol >290 or LDL >190 mg/dl in adult,
or total cholesterol >260 or LDL>160mg/dl in child
AND
Definite: Tendon xanthoma in patient or relative
or DNA mutation
Possible: Family history of premature heart attack, OR
Hypercholesterolemia in 1st or 2nd degree relative

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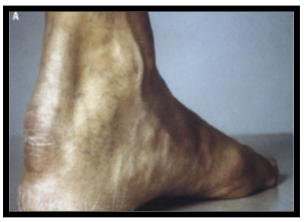
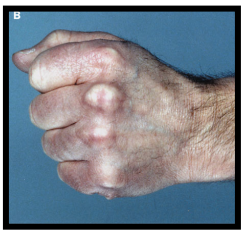
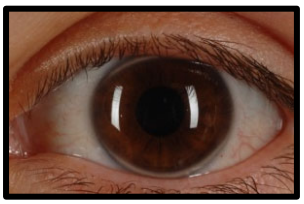
Physical Exam Findings In FH

Probability of xanthoma:
age minus 10%
<50% have them

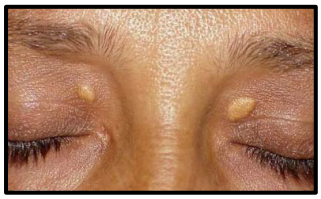




Tendinous Xanthomas (any age)



Corneal Acus (<45yo)



Xanthelasma (<25yo)

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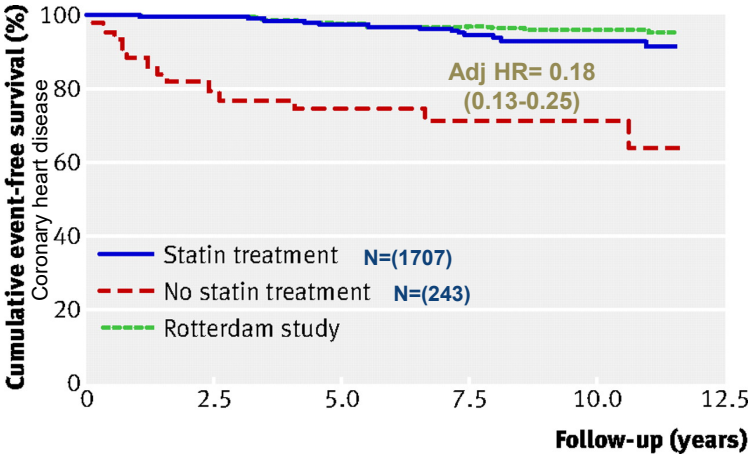
Improved CHD Outcomes In FH Patients Using Statins

Dutch Registry of 1950 FH patients pre/post initiation of statins in 1990



Versmissen J et al. BMJ 2008;337:2423

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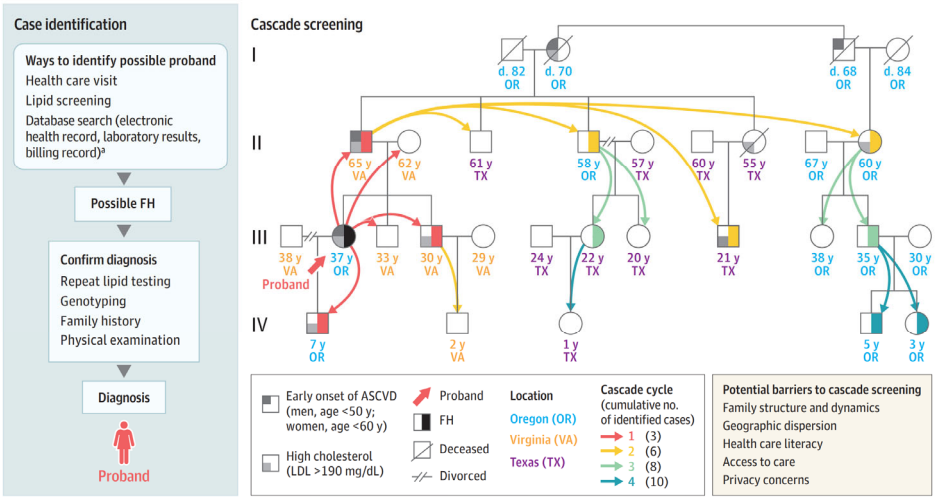
Cascade Screening For FH



1 Proband
~8 Relatives

Knowles J. et al JAMA 2017;318:381-382.

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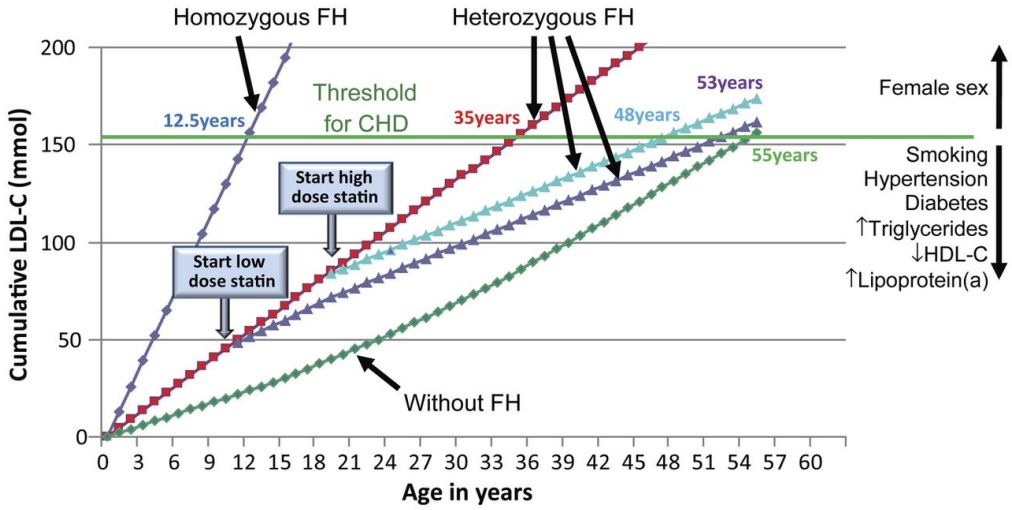
Early Intervention For FH: LDL-C Gram-years Concept



Nordestgaard B G et al. Eur Heart J 2013;3478-3490.

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2018 AHA/ACC Cholesterol Guidelines Top 10 Take Home Messages

4. **In patients with severe primary hypercholesterolemia (LDL-C level ≥ 190 mg/dL[≥4.9 mmol/L]), begin high-intensity statin therapy <u>without calculating 10-year ASCVD risk</u>. *(COR I, LOE B-R)***

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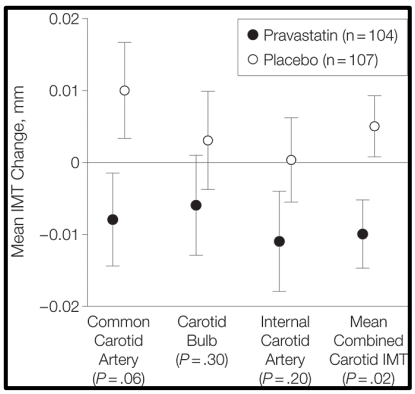
RCT of Statin Use In Children With FH

2yr placebo-controlled study, children ages 8-18

n=214



<u>LDL-C</u>

237 mg/dl (+0.3%)

239 mg/dl (-24.1%)

<u>No Difference</u>
Weight
Height
BMI
LFT's
Sex hormones
Tanner stage
Testicular volume
Onset menses

*pravastatin 20-40mg daily

Wiegman, A. et al. JAMA 2004;292:331-337

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RCT of Statin Use In Children With FH: Long-Term Follow up

Statin Use in Children with FH: 20-year Follow-up

Subclinical Disease

children ages 8-18

LDL-C

237 mg/dl

FH

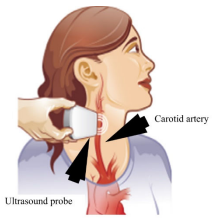
Statin

20 years

99 mg/dl

No FH Sibling

No Difference



Clinical Disease

FH Parents to Age 39

26% Heart Attack

vs.

Statin

1%

n=214

Liurink I. et al. NEJM 2019; 381:1547-56

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2018 AHA Cholesterol Guidelines: LDL-C Testing In Children

IIa	B-R	3. In children and adolescents 10 years of age or older with an LDL-C level persistently 190 mg/dL (≥4.9 mmol/L) or higher or 160 mg/dL (4.1 mmol/L) or higher with a clinical presentation consistent with FH (see Section 4.2.) and who do not respond adequately with 3 to 6 months of lifestyle therapy, it is reasonable to initiate statin therapy (S4.4.4.3-13–S4.4.4.3-16).
IIa	B-NR	4. In children and adolescents with a family history of either early CVD* or significant hypercholesterolemia,† it is reasonable to measure a fasting or nonfasting lipoprotein profile as early as age 2 years to detect FH or rare forms of hypercholesterolemia (S4.4.4.3-17–S4.4.4.3-21).

	Acceptable, mg/dL	Borderline, mg/dL	Abnormal, mg/dL
TC	<170 (<4.3 mmol)	170-199 (4.3-5.1 mmol)	≥200 (≥5.1 mmol)
Triglycerides (0-9 y)	<75 (<0.8 mmol)	75-99 (0.8-1.1 mmol)	≥100 (≥1.1 mmol)
Triglycerides (10-19 y)	<90 (<1.0 mmol)	90-129 (1.0-1.5 mmol)	≥130 (≥1.4 mmol)
HDL-C	>45 (>1.2 mmol)	40-45 (1.0-1.2 mmol)	<40 (<1.0 mmol)
LDL-C	<110 (<2.8 mmol)	110-129 (2.8-3.3 mmol)	≥130 (≥3.4 mmol)
Non–HDL-C	<120 (<3.1 mmol)	120-144 (3.1-3.7 mmol)	≥145 (≥3.7 mmol)

FH?

Statin option ≥ 10yrs

LDL-C testing ≥ 2yrs

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Improving Detection And Diagnosis Of FH

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Strategies To Improve FH Diagnosis

- Genetic Testing
- EHR Strategies
- Other Innovations

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Why Genetic Testing In FH?

- **Enhance identification of affected individuals**
  - **Improve efficiency of cascade screening**
  - **Clarify ambiguous cases**
- **Risk stratification**
- **Improved phenotyping/precision medicine**

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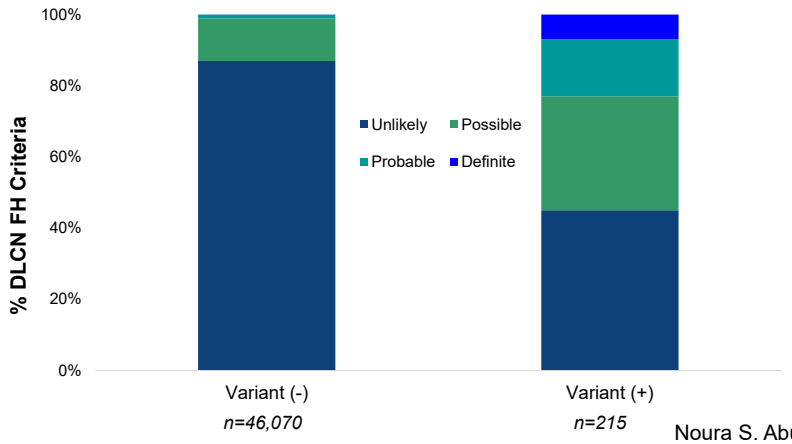
Genetic Screening For FH: Geisinger Health System

50,726 Individuals w/whole exome sequencing (*LDLR, APOB, PCSK9*)



1:256 Variant (+)

56% on statin
46% LDL-C<100
15% "FH" diagnosis

Noura S. Abul-Husn et al. Science 2016;354:aaf7000

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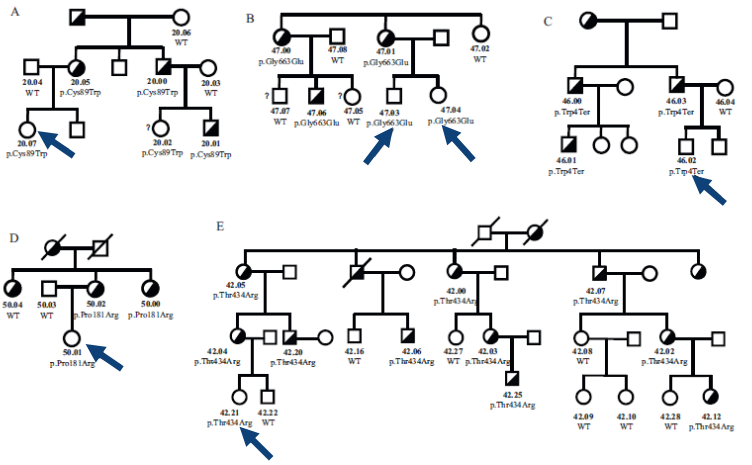
Pedigree Study: "Normal" Cholesterol In Genotype Positive Family Members

20 families with ADH



6/20 families= 30%with normocholesterolemic carrier

Garcia-Garcia A et al. Atherosclerosis 2011;218:423-430.

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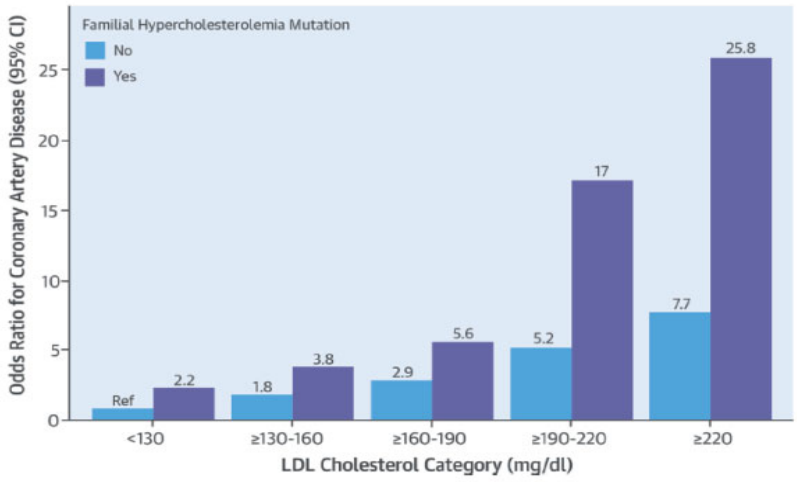
FH Variants And LDL-C Cholesterol: Implications For CAD Risk

20,485 Subjects, Sequenced for LDLR, APOB, PCSK9 Variants



Khera A.V. et al. JACC 2016;67:2758-2789.

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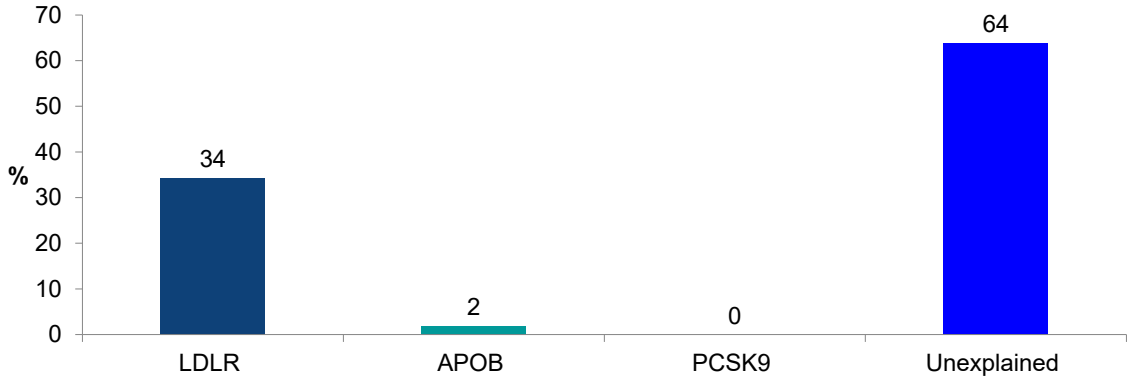
Most Individuals With FH Do Not Have Mutation In FH Causing Gene: Dallas FH Cohort

n = 399 FH patients (Simon Broome) ascertained from Dallas-area lipid specialty clinics



Ahmad Z et al. Circ Cardiovasc Genet. (2012)

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Genetic Evaluation Of FH: Potential Phenocopies

Test	Proportion of Cases
LDLR, APOB, PCSK9, LDLRAP1	**5-50%**
ABCG5*, *ABCG8*, *APOE*, *LIPA*, and *STAP1	**0.1-1.0%**
***LDLR* copy number variation**	**5-15%**
Polygenic LDL score	**20-30%**
Lp(a) measurement	**5-20%**

Berberich A and Hegele R Nat Rev Card 2019

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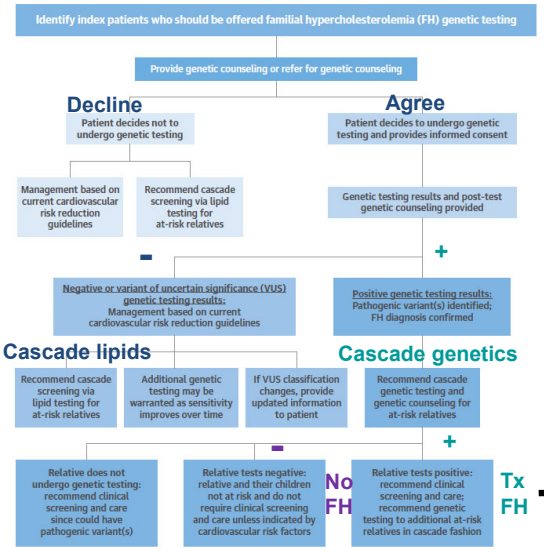
FH Foundation Algorithm: Genetic Testing In FH



Offer to every patient w/strong suspicion of FH

Strum A. et al JACC 2018;72:662-80.

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FH Identification Strategies in Healthcare Systems

Population genetics
- >50% without FH mutation
- Requires infrastructure

AI/M-L Algorithms
- Not reliant on lipids
- Those on treatment identified

Elevated LDL-C (>190mg/dL)
- Easier to implement
- Miss those on treatment

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EHR Strategies for Identification of FH: MHI Experience

FH Prevalence 1:470

34% adequately treated

4.3% with FH diagnosis

Characteristic	80% likely FH classification: Yes (n = 841)	80% likely FH classification: No (n = 391,166)	*P* value
Age (y), mean (SD)	53.3 ± 15.9	54.1 ± 16.2	.027
Male (%)	328 (39)	177,012 (45)	<.001
Race			
White (%)	745 (91)	350,520 (93)	.059
Non-white	72	25,250	
History of CAD (%)	148 (17.6)	36,527 (9.3)	<.001
History of PAD (%)	58 (6.9)	12,931 (3.3)	<.001
Diabetes (%)	158 (18.8)	53,627 (13.7)	<.001
Currently on statin (%)	545 (64.8)	118,407 (30.2)	<.001

Knickelbine et al. J Clin Lip 2016;10;1182-1187.

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UTSW FH Quality Improvement Initiative: Baseline Data

27,988 patients with lipid values from Nov 2015- June 2016

	LDL-C≥190 (n=227)	LDL-C≥220 (n=53)
Statin		
Current	**19%**	**23%**
Prior	**41%**	**47%**
Follow up appointment	**>90%**	**>90%**
No Δ in therapy	**45%**	**34%**
Specialist referral	**18%**	**23%**

Jackson C. et al Am J Prev Cardio 2020

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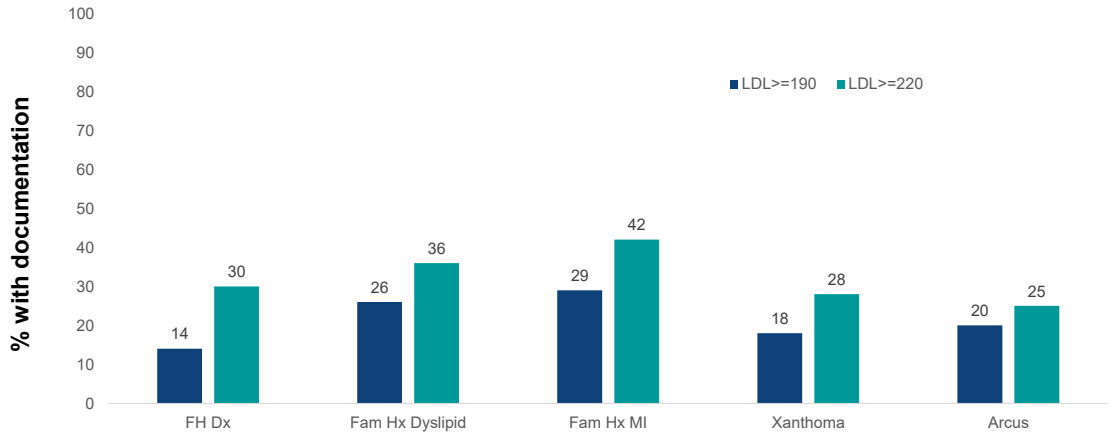
UTSW FH Quality Improvement Initiative: Documentation of FH Characteristics



Jackson C. et al Am J Prev Cardio 2020

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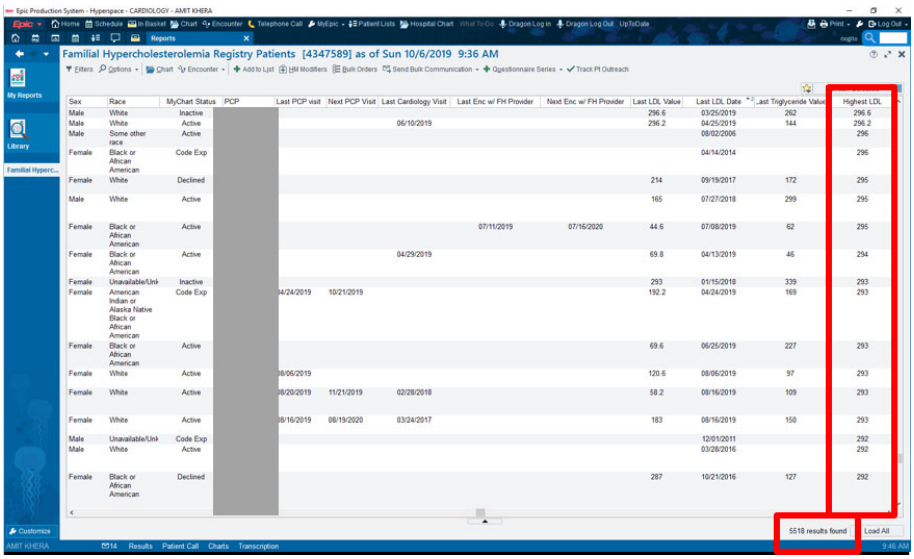
EPIC Registry Of Patients With LDL-C ≥190 mg/dL



>9000 patients

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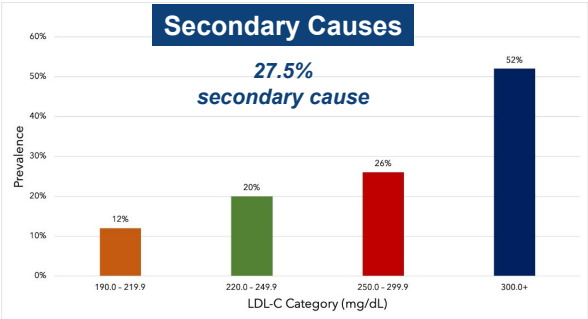
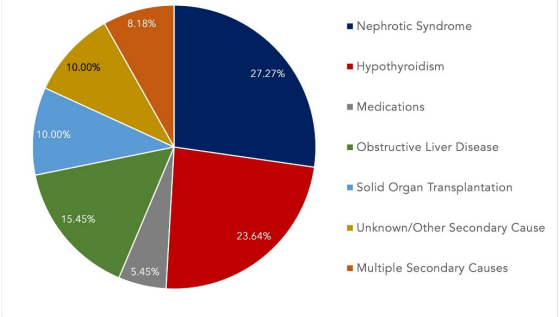
Applying An LDL-C Threshold-based Approach To Identify FH: Lessons Learned

Review of 400 patients, 100 each LDL-C category





LDL-C Categories
190.0 – 219.9 mg/dL
220.0 – 249.9 mg/dL
250.0 – 299.9 mg/dL
≥ 300.0 mg/dL

Jasani R et al J Clin Lipid 2022

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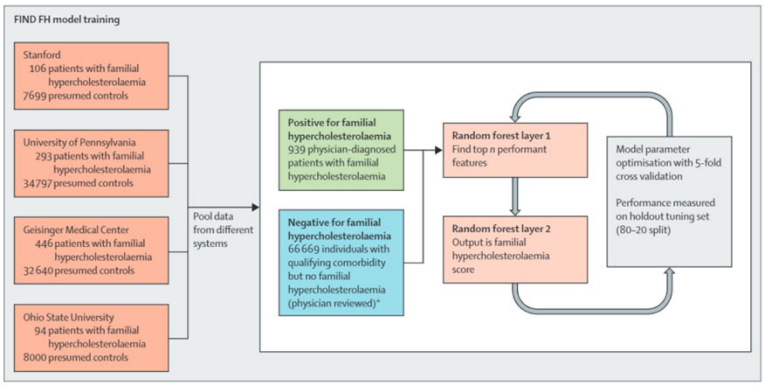
FIND FH machine learning model trained to identify patients with FH

- Model trained using ~1K patients with FH and ~67K patients without FH

- Accuracy for FH Dx
  - –87% (95% CI 73–100) in the national database
  - –77% (68–86) in the health-care delivery system dataset



Myers K, et al. Lancet Digital Med, 2019;1:393-402.

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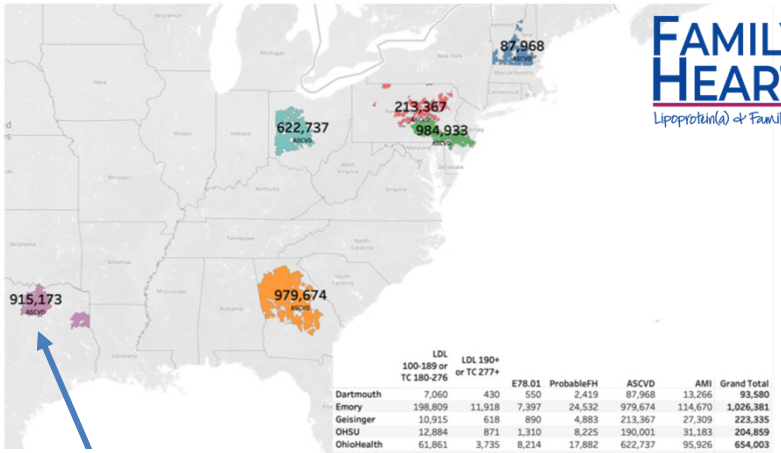
FIND FH Collaborative Learning Network



	LDL 100-189 or TC 180-276	LDL 190+ or TC 277+	E78.01	ProbableFH	ASCVD	AMI	Grand Total
Dartmouth	7,060	430	550	2,419	87,968	13,266	93,580
Emory	198,809	11,918	7,397	24,532	979,674	114,670	1,026,381
Geisinger	10,915	618	890	4,883	213,367	27,309	223,335
OHSU	12,884	871	1,310	8,225	190,001	31,183	204,859
OhioHealth	61,861	3,735	8,214	17,882	622,737	95,926	654,003
Penn Medicine	169,062	8,884	9,405	33,177	984,933	127,834	1,037,792
UTSW	157,705	9,046	6,470	32,705	915,173	122,232	972,023
Rest of US	5,106,633	284,276	284,878	1,066,461	35,161,777	4,435,622	37,057,687
Grand Total	5,864,640	328,383	322,831	1,214,104	39,769,923	5,054,558	41,926,047

Family Heart Foundation — Lipoprotein(a) & Familial Hypercholesterolemia

FIND FH — Flag · Identify · Network · Deliver — Familial Hypercholesterolemia

Dartmouth Health

Geisinger

OhioHealth

Penn Medicine

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EMORY HEALTHCARE

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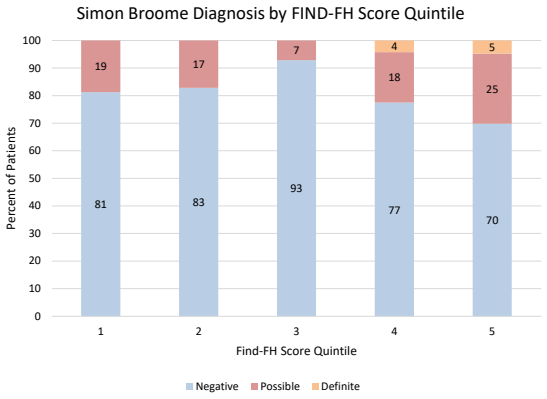
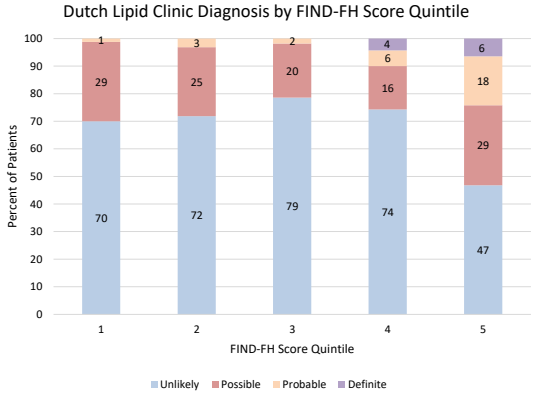
Accuracy of FH Diagnosis by FIND FH: UTSW Data



20.3% Possible/Definite

N=340



32.3% Possible/Prob/Definite

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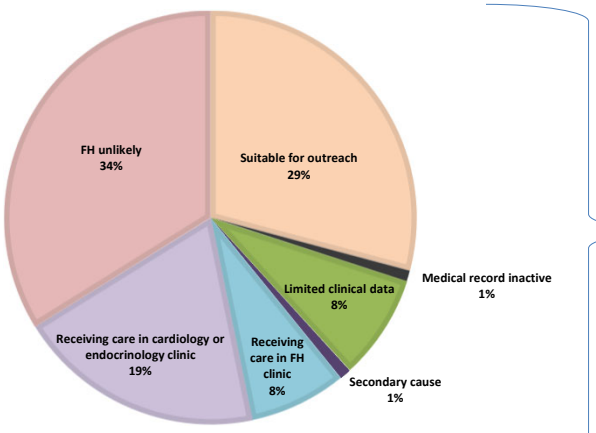
Accuracy vs. Clinically Actionable Results: FIND FH



191 patients suitable for outreach

53% highest LDL-C <190mg/dL

56% enough clinical suspicion for FH outreach

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FIND FH Penn Experience: Implementation Gap

5006 Patients identified

153 (3%) Visits scheduled

5006 patients with healthcare providers eligible for contact (Includes **452** patients who visited Preventive Cardiology in the past)

2366 (47% [2366/5006]) patients with no response from providers
473 (9% [473/5006] patients with negative provider response

2167 (43% [2167/5006]) patients with positive response from providers

1607 (32% [1607/5006]) patients successfully reached by phone, email, or mypennmedicine for phase I outreach

1353 (27% [1353/5006]) patients with no response
67 (1% [67/5006]) patients with negative response

187 (4% [187/5006] patients expressing interest in scheduling a visit to Preventive Cardiology

153 (3% [153/5006]) patients scheduled for visit and clinical evaluation

Sheth S et al Circ QO 2021;14

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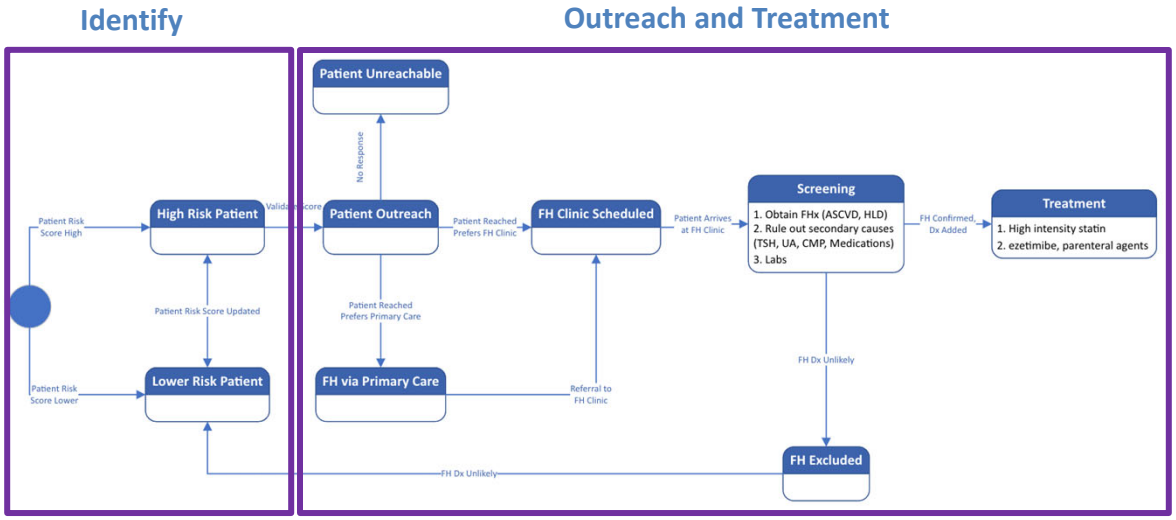
UTSW Find FH Process Overview State Diagram



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Improving FH Care: UT Southwestern Experience

Patients with LDL-C ≥190mg/dL

108 contacted (My Chart, call, letter) → 35% (n=38) Subsequent visit → 22% (n=24) Change in care

Only 50% on statin
Highest LDL-C 267
Recent LDL-C 237

- *Change in LLT*
- *FH Dx*
- *Family screening*

→ *Factors Assoc: PCP contact More contacts (2.2 v 1.5)*

Lee H et al *in Review*

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Blood Donation System And Public Health

Large number of individuals and blood samples

Generally younger and healthy

Not being seen in a traditional medical encounter

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JAMA Cardiology | Brief Report

Identifying Familial Hypercholesterolemia Using a Blood Donor Screening Program With More Than 1 Million Volunteer Donors

Candace L. Jackson, MD, MPH; James Z. Keeton, MD; Stephen J. Eason, MBA; Zahid A. Ahmad, MD; Colby R. Ayers, MS; M. Odette Gore, MD, MSCS; Darren K. McGuire, MD, MHSc; Merlyn H. Sayers, MBBCh, PhD; Amit Khera, MD, MSc

	Overall (n=1,178,102)
Meets MEDPED Criteria (with at least one TC value)	***3,473 (1:339)***
Total Cholesterol (mg/dL)	**332 (297,377)**
Does Not Meet MEDPED Criteria	**1,174,629**
Total Cholesterol (mg/dL)	**183 (157,212)**

*median age, 32 [IQR, 19-47] years

Jackson CL et al JAMA Cardio 2019; 1;4:685-689

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Implementing a Multicomponent Intervention to Treat Blood Donors with Familial Hypercholesterolemia

R61 Phase- 1 year
Development

Interviews

Carter Staff	N=8
PCP's	N=7
Donors w/FH	N=25
Family Of Donors	N=4

Implementation Scientists

Barriers

Facilitators

Implementation Bundle

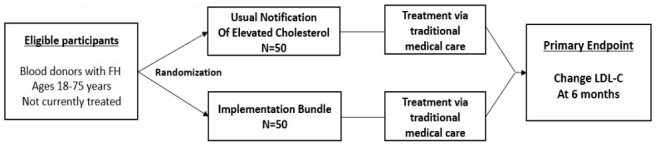
(package of resources, actions, and tools to enhance high intensity statin initiation)

3/1/22-2/28/23

R33 Phase- 4 years
Clinical Trial

DONATE-FH Study

Blood DONor Awareness and TrEatment of Familial Hypercholesterolemia Study



ClinicalTrials.gov: NCT05693701

3/1/23-2/28/27

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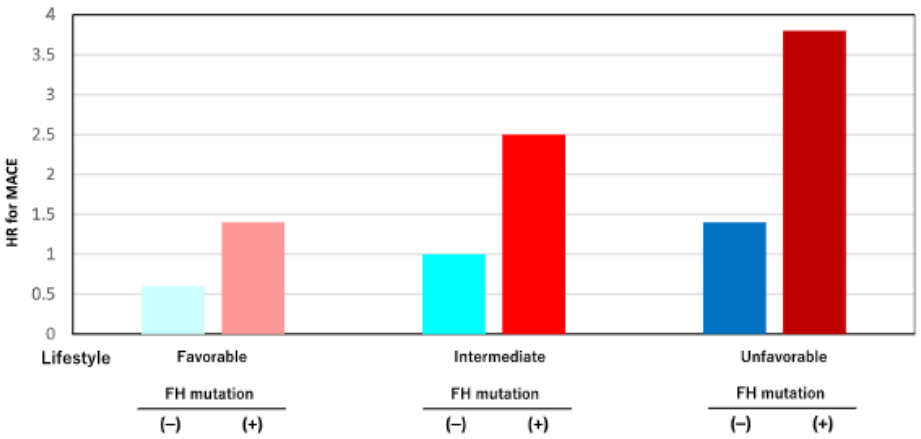
Treatment Of FH: Considerations Beyond Statins

48

Lifestyle Factors And ASCVD Risk In FH

N=961 (699 with mutation)



Lifestyle: healthy dietary pattern, regular exercise, not smoking, and absence of obesity

Tada H. et al JACC Asia 2023;3:152-160.

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FH Treatment Recommendations For Adults

Organization	CHD/ASCVD	No CHD/ASCVD
NICE Guidelines 2008	50% LDL-C reduction	50% LDL-C reduction
NLA 2013	50% LDL-C reduction and LDL-C <100mg/dL*	50% LDL-C reduction and LDL-C <160 mg/dL
International FH Foundation 2014	50% LDL-C reduction and LDL-C <70 mg/dL	50% LDL-C reduction and LDL-C <100 mg/dL
AHA FH 2015	50% LDL-C reduction and LDL-C <70 mg/dL	50% LDL-C reduction and LDL-C <100 mg/dL
AHA/ACC Cholesterol Guidelines 2018		50% LDL-C reduction and LDL-C <100 mg/dL (add EZE; ± PCSK9i IIb)
ESC Cholesterol Guidelines 2019	50% reduction and LDL-C <55mg/dL	50% reduction and LDL-C <70mg/dL (or 55 if any RF)

*any ASCVD, DM, family history early CVD, smoking, ≥2 risk factors, high Lpa
** CHD or DM
** LDL-C >190, not specifically FH

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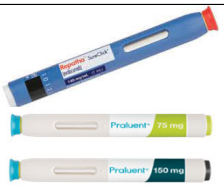
Non-Statin Add On LDL-C Lowering Options in 2024

Ezetimibe

FDA Approved 10/2002
Cholesterol absorption inhibitor
Oral pill, daily
15-20% LDL-C lowering
Improves ASCVD outcomes



Evolocumab
Alirocumab

FDA Approved 2015
PCSK9 mAb
SQ injection Q2 weeks (or monthly)
50-60% LDL-C lowering
Improves ASCVD outcomes

Bempedoic Acid

FDA Approved 2/2020
ACL inhibitor (no myalgia)
Oral pill, daily
~20% LDL-C lowering (EZE combo ~40%)
Improves ASCVD outcomes

Inclisiran

FDA Approved 12/21
PCSK9 siRNA
SQ injection baseline, 3mo, then Q6mo
~50% LDL-C lowering
Ongoing outcomes trial

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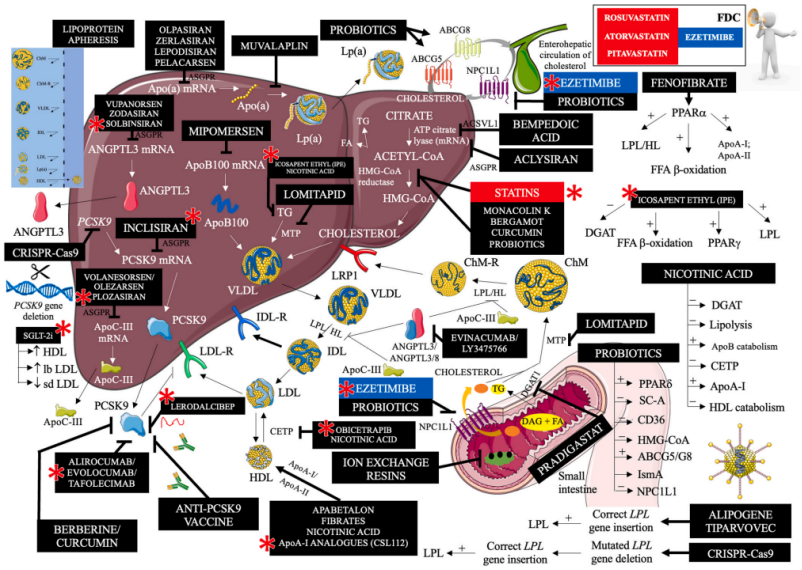
Lipid Modifying Therapies Available and In Development



Surma S et al. Pharm Res 2024;205:107246

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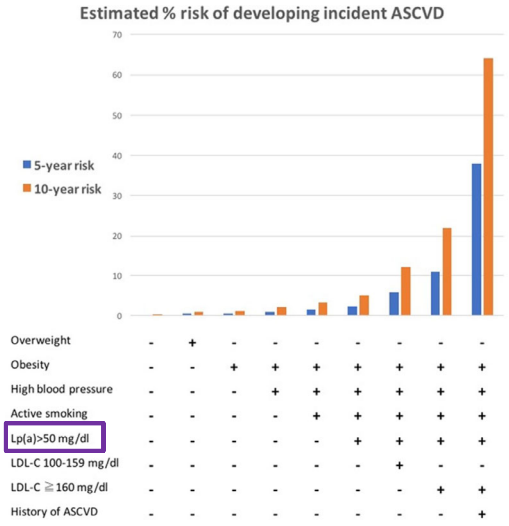
SAFEHEART Study: FH Specific ASCVD Risk Score

66-year-old men with FH and LDL-C <100 mg/dL.



n=2404
HeFH

C-stat= 0.85

Leopoldo Pérez de Isla et al. Circulation. 2017;135:2133-2144

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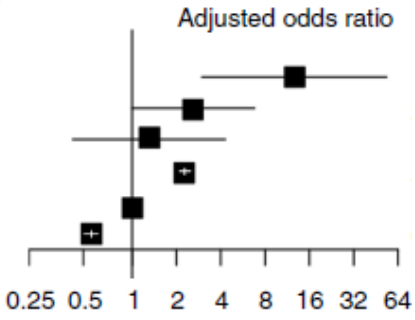
Modifiers Of FH Genetics: CAD Polygenic Risk Scores

a

FH variant	Polygenic score	*N* of 6432 Cases	*N* of 6420 Controls
Carrier	High	23	2
Carrier	Intermediate	14	6
Carrier	Low	6	5
Noncarrier	High	2348	1173
Noncarrier	Intermediate	3400	3868
Noncarrier	Low	641	1366



Fahed AC et al Nature Comm 2020;11:1-9

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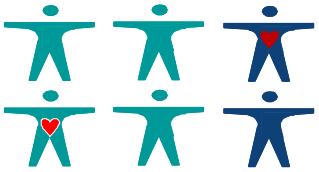
Potential Applications Of Atherosclerosis Imaging In Patients With FH and No Clinical ASCVD



Statin
± Ezetimibe

?

Intensify Therapy
LDL-C
GLP1-RA
ASA
(Lp(a), other?)

Monitoring Response

Serial Imaging

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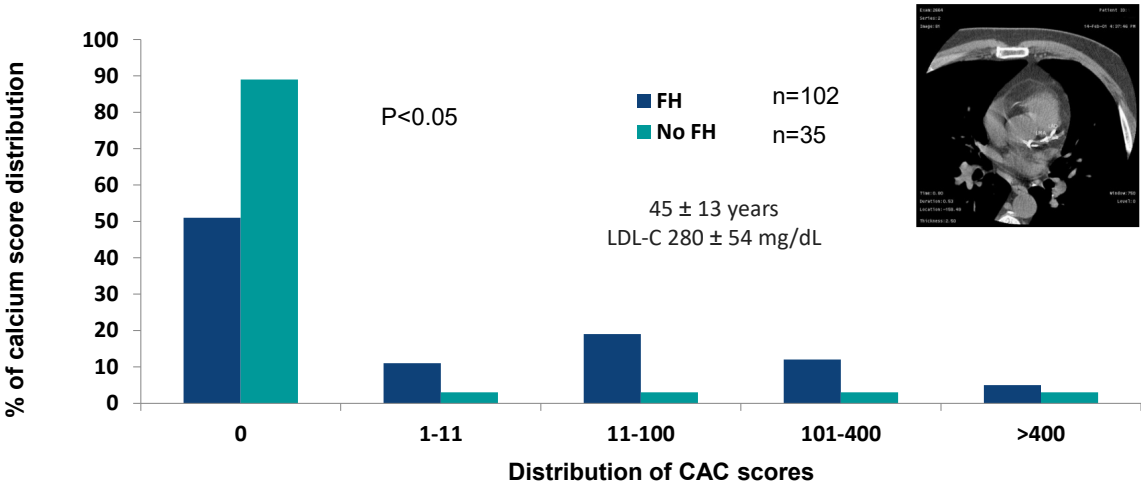
Coronary CT Angiography Findings In FH



Miname M. et al Atherosclerosis 2010;213:486-491.

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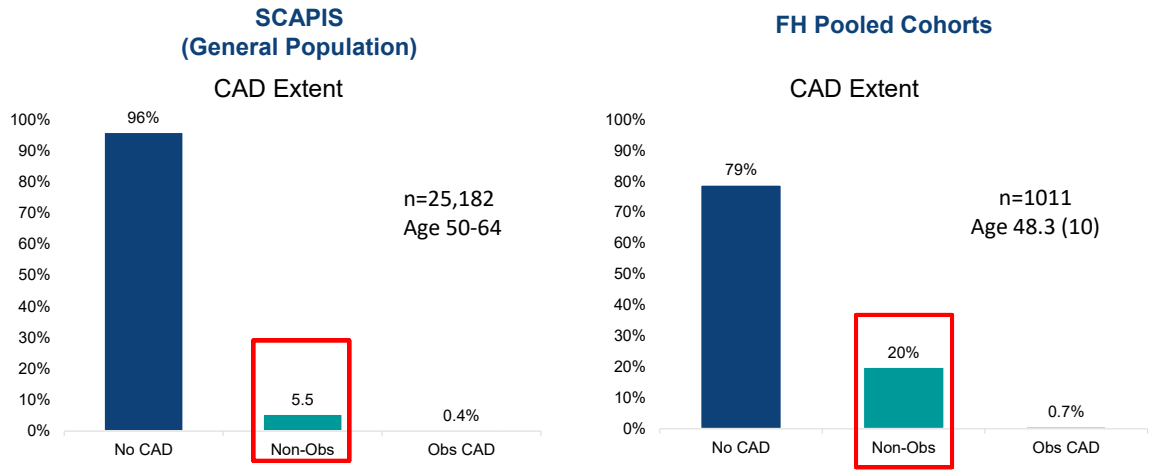
CAC=0 Does Not Rule Out Atherosclerosis in FH



Nasir K et al AJPC 2024;17:100611.
Bergstrom G et al Circulation 2021;144:916-929.

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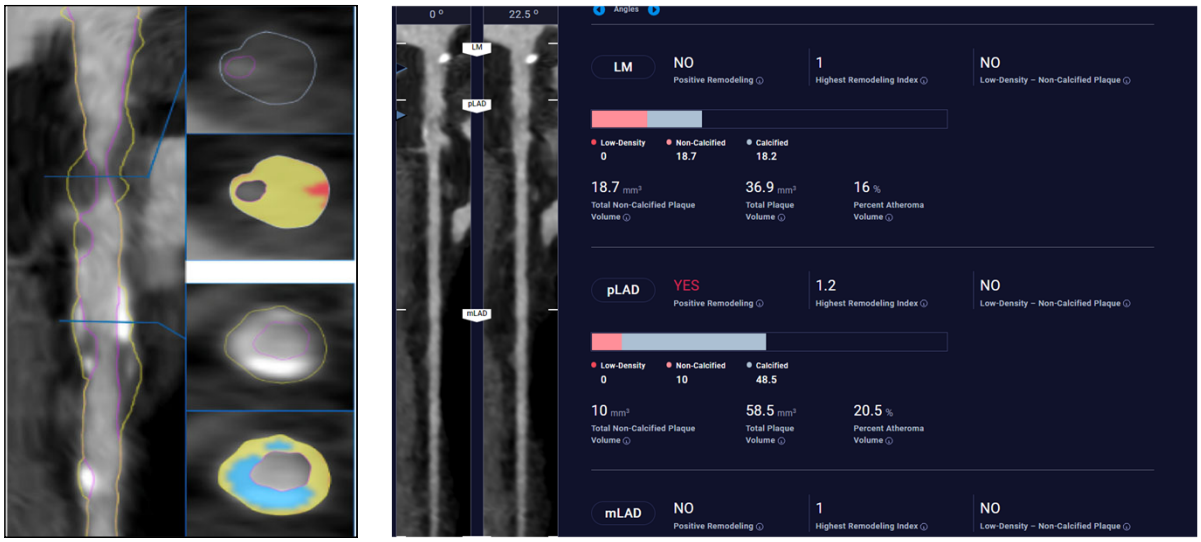
AI Based Quantitative CT Plaque Burden Assessment



Willams MC et al JCCT 2021;16:124-137

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IAS Guidelines for FH 2023

Although CACS is useful in the initial risk assessment in asymptomatic patients before starting cholesterol-lowering medication, CACS should not be used to monitor the effectiveness of cholesterol-lowering treatment (Class I- strong; LOE B- moderate)

In asymptomatic patients, imaging of ASCVD (for example, carotid ultrasonography and CT coronary angiography for the detection of plaques and stenoses) may be considered for monitoring the effectiveness of cholesterol-lowering treatment (Class 3- weak; LOE B- moderate)

Watts GF et al. Nat Rev Card 2023;20:845-869.

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Case 1 (Cont)

46yo male with dyslipidemia and family history of CVD, on atorvastatin 20mg daily with LDL-C 107 mg/dL

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Case 1 (Cont)

46yo male with dyslipidemia and family history of CVD, on atorvastatin 20mg daily with LDL-C 107 mg/dL

PCP received an alert about possible FH
Old LDL-C values as high as 208 mg/dL

Diagnosed with probable FH, offered genetic testing and recommended screening of two children and siblings

CAC scan with score of 68 (92nd percentile); Lpa 267 nmol/L

PCKS9i mAb was added→ LDL-C 53mg/dL

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Conclusions

- *FH is a common AD disorder (1:250) that significantly increases the risk of ASCVD*
  - *It is underdiagnosed and undertreated*
- *High intensity statin therapy and cascade screening are cornerstones of management*
- *Genetic test and novel EHR screening algorithms may help in identification*
- *There is heterogeneity of risk in those with FH*
  - *Possible implications for subsequent therapies*

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Prevalence Of FH In Blood Donors By Age

	< 20 years (n=321,718)	20-29 years (n=224,901)	30-39 years (n=194,528)	> 40 years (n=436,955)	p-value
Meets MEDPED Criteria	1,001 (1:321)	1,126 (1:200)	432 (1:450)	914 (1:478)	<0.001
Total Cholesterol (mg/dL)	286 (277,307)	309 (298,330)	367 (351,402)	384 (371,414)	<0.001

*median age, 32 [IQR, 19-47] years

Jackson CL et al JAMA Cardio 2019; 1;4:685-689

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Prevalence And Prognosis Of FH After Acute Coronary Syndrome

4534 patients with ACS, multicenter, prospective cohort in Switzerland

	No FH	Simon Broome	Dutch Lipid
n	3589	250	73
Percentage	79%	5.5%	1.6%
Age, y	66	52	50
Pre-existing CVD (%)	27%	13%	11%
Family history (%)	18%	47%	78%
LDL cholesterol mg/dL	124	224	255
Statin use admit (%)	29%	31%	38%
High dose statin at discharge (%)	67%	81%	74%
LDL <100mg/dl 1 yr	75%	47%	36%

Nanchen D. et al. Circulation 2016;134:698-709

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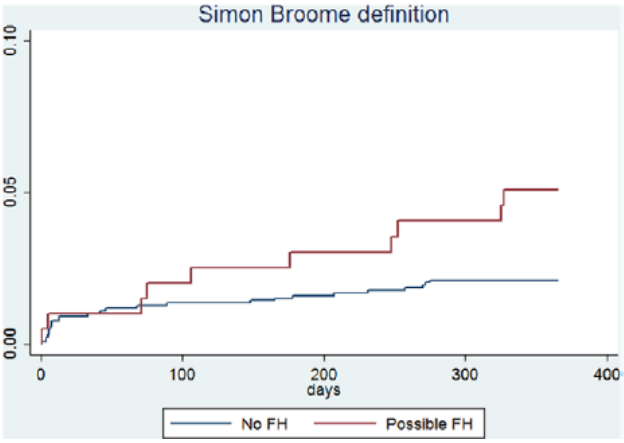
Prevalence And Prognosis Of FH After Acute Coronary Syndrome

1369 men <55 years and women <60 years



Adjust HR 2.2-2.6

Nanchen D. et al. Circulation 2016;134:698-709

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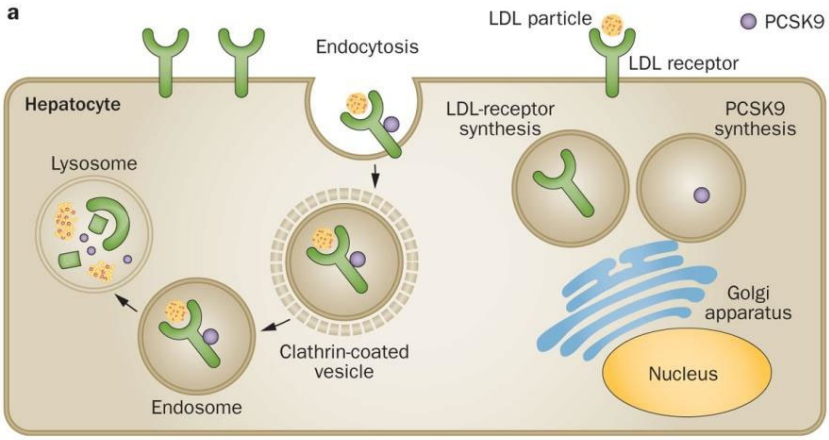
PCSK9 Inhibitors: Mechanism of Action



↑ PCSK9
(↓LDL receptors)
↑ LDL-C

↓ PCSK9
(↑LDL receptors)
↓ LDL-C

Ballantyne. *Nat. Rev. Cardiol.* 2014.84

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PSCK9i: mAB vs Inclisiran

Evolocumab
Alirocumab

Inclisiran

Mechanism	mAb	siRNA
Delivery	SQ inj Q2 wks (4 wks)	SQ inj Q 6mo (3mo 2nd dose)
Administration	Home/Individual	Infusion Center/Clinic
Insurance Component	Pharmacy benefit	Medical benefit (Part B)
Cost	~$5800/year	~$6500/year
LDL-C lowering	~50-60%	~40-50%
Lpa lowering	~20-30%	~20-30%
CV Outcomes trial	*Yes*	*No*

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LDL Apheresis- Overview

- Veno-venous filtration system (PIV or port)
- Generally every other week for Heterozygous FH (2-3 hours)
  - –Acute LDL-C reduction ~60-80% (and Lpa)
- FDA Approved Indications:
  - –FH Homozygotes with LDL-C >500 mg/dL
  - –FH Heterozygotes with LDL-C ≥300 mg/dL
  - –FH Heterozygotes with LDL-C ≥100 mg/dL and CAD or PAD
  - –FH Heterozygotes with LDL-C ≥100 and Lp(a) ≥60 mg/dL, and CAD or PAD

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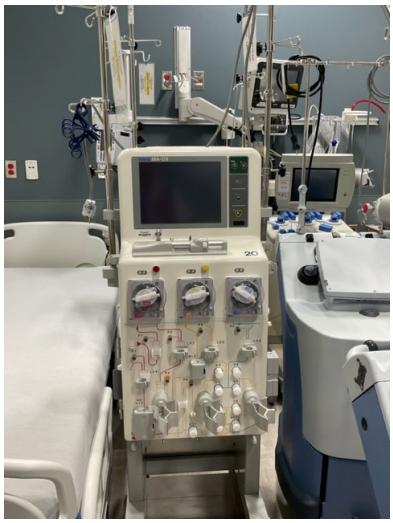
LDL Apheresis at UT Southwestern

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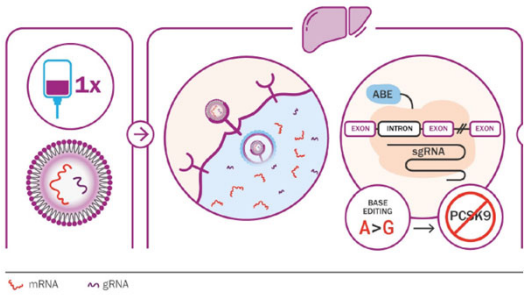
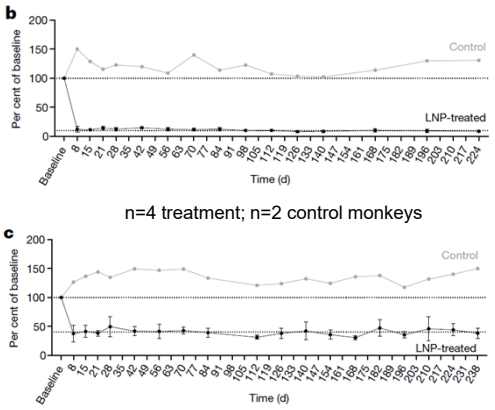
CRISPR *PCSK9* Gene Editing for FH/Dyslipidemia



Effects of Adenine Base Editing of *PCSK9* in Cynomolgus Monkeys



Musunuru K et al Nature 2021; 593:429-434.

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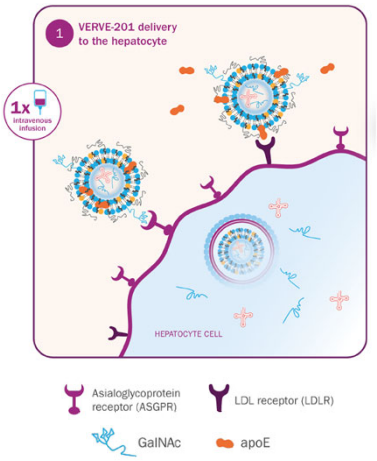
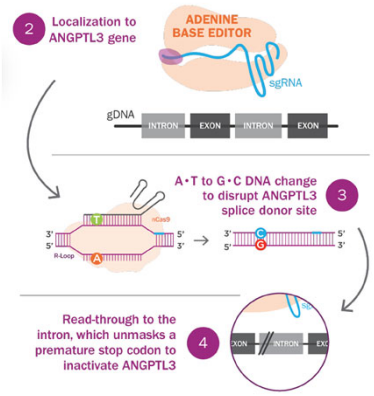
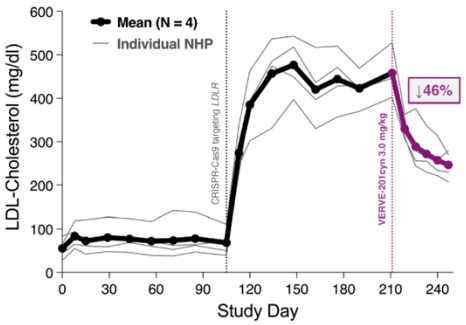
CRISPR *ANGPTL3* Gene Editing for LDL-C/TG Lowering





LDLR-deficient NHPs treated with VERVE-201cyn



Khera AV et al ACC 2023

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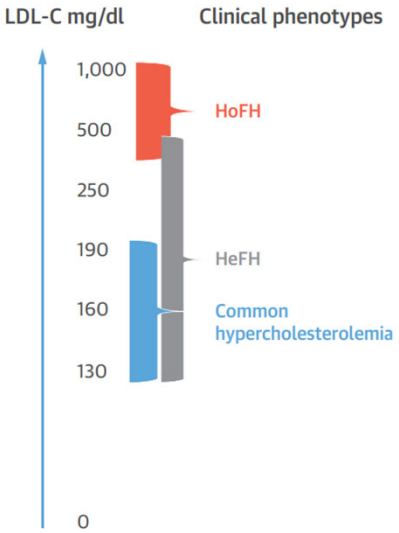
Defining Homozygous FH: Molecular and Clinical Criteria



Molecular etiology

- Homozygous *LDLR* null
- Homozygous *LDLR* defective
- Compound heterozygous

- Heterozygous pathogenic variant
  - *LDLR* null
  - *LDLR* defective
  - *PCSK9*
  - *APOB*

- Polygenic (multiple LDL-C raising SNPs
- High Lp(a)

Clinical Trial Definition

Genetic testing consistent with HoFH or untreated total cholesterol > 500 mg/dL with either the presence of cutaneous or tendinous xanthomas before the age of 10 years or documentation of an untreated total cholesterol >250 mg/dL in both parents.

Sturm A et al JACC 2018;6:662-80.

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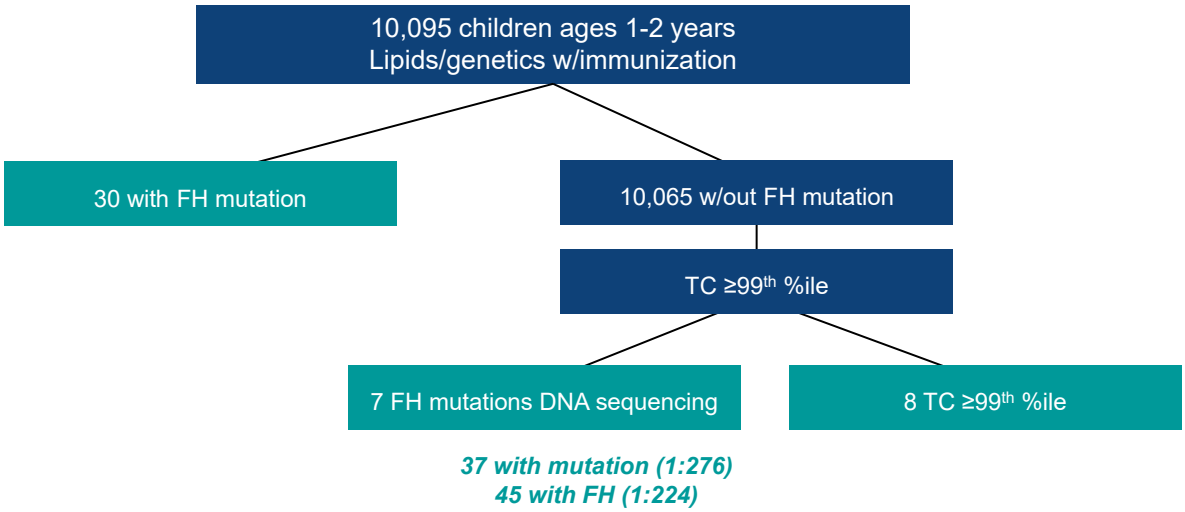
Childhood FH Screening Program In The UK



37 with mutation (1:276)
45 with FH (1:224)

*FH48 mutation panel

Wald D et al. NEJM 2016;375:1628-1637.

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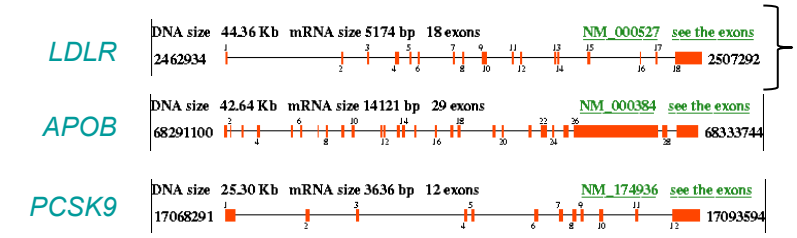
Commercial Genetic Testing For FH



Exome Sequencing

Minimal Intronic

Deletions Insertions

Not CNV

LDLRAP1 *(Autosomal Recessive Hypercholesterolemia)*

Select Other Genes *ABCG5 ABCG8 APOE LIPA*

Targeted pathogenic mutation testing in family members

"Free" 90 days

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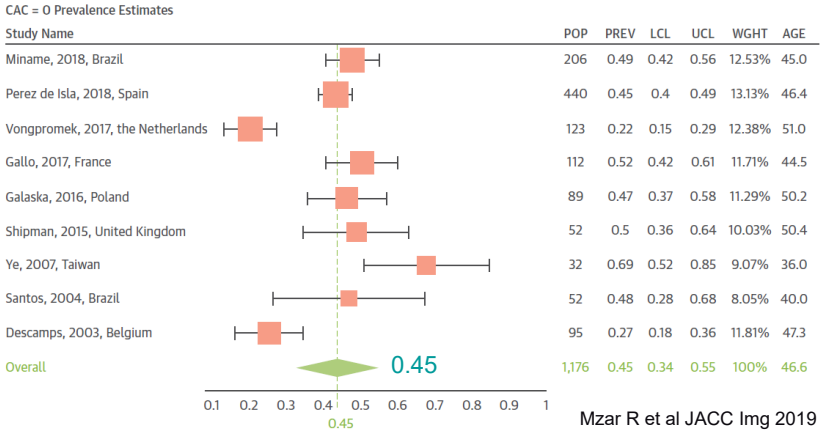
Coronary CT Angiography

FIGURE 1 Forest Plot of Overall Pooled Prevalence of CAC = 0 in HeFH



Mzar R et al JACC Img 2019

Distribution of CAC scores

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