The EAS FH Studies Collaboration

The Global Registry of FH

Dr Antonio J. Vallejo-Vaz, MD, PhD

EAS FHSC Chief Scientist

- Department of Medicine, University of Seville, Spain
- Clinical Epidemiology and Vascular Risk, Institute of Biomedicine of Seville, Spain
- Imperial Centre for CVD Prevention, School of Public Health, Imperial College London, UK

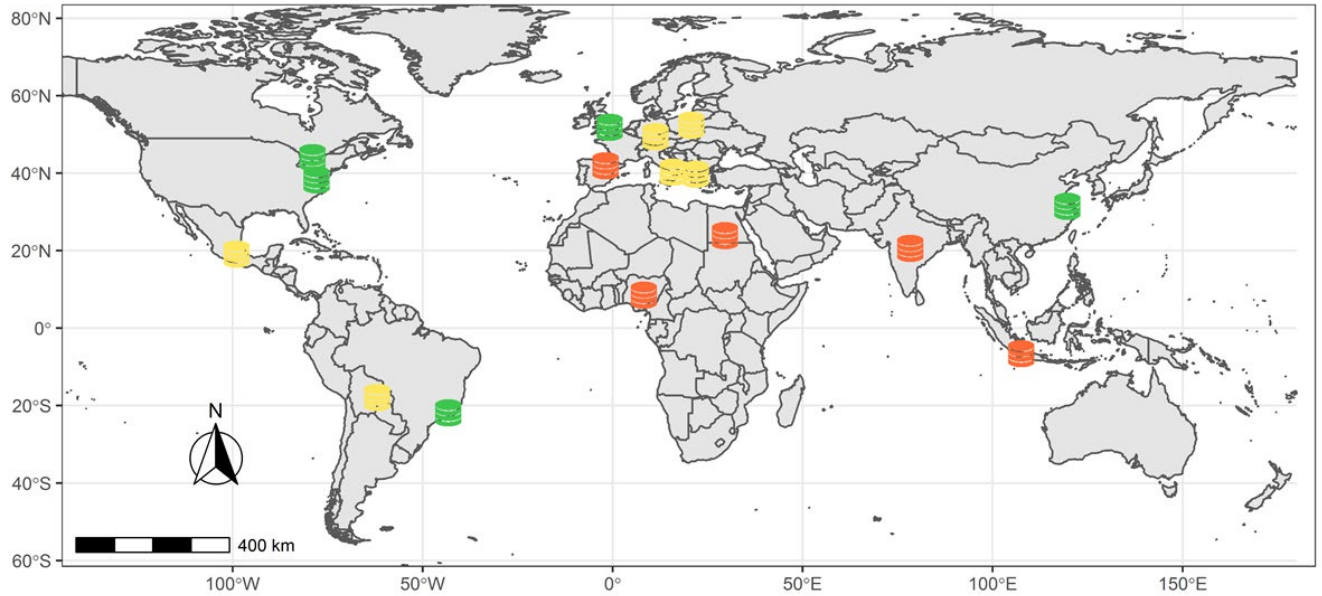
The EAS FH Studies Collaboration – The Global Registry of FH

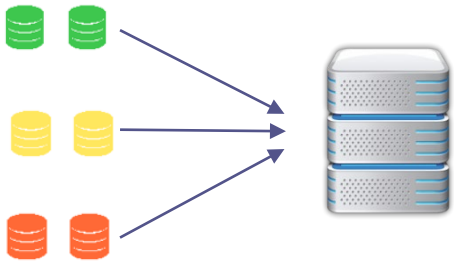
Disclosures

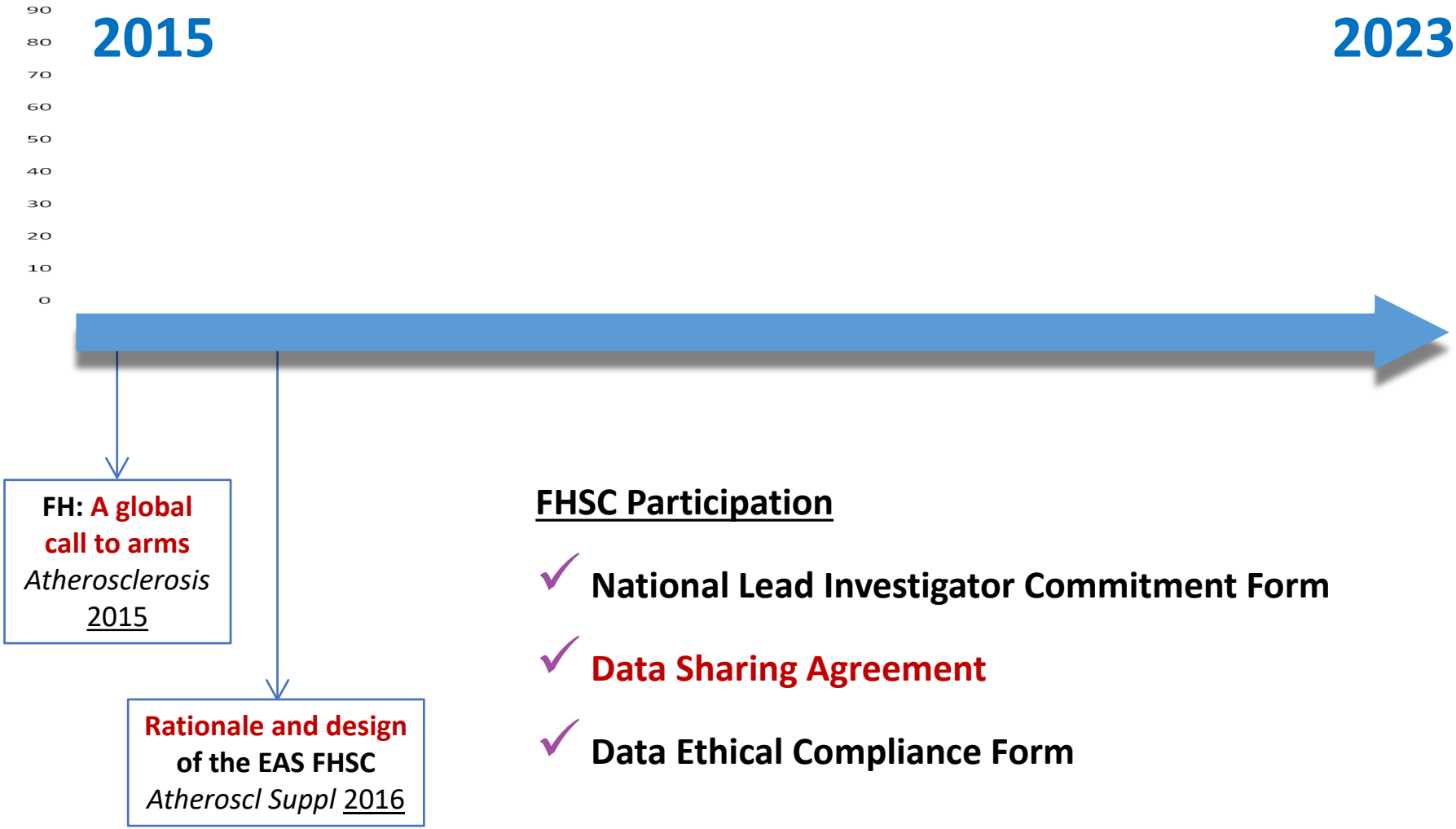
- Participation in Research Grants to Imperial College London from Amgen, Regeneron and Daiichi-Sankyo.
- Consulting fees from Bayer and Regeneron.

The EAS FHSC is an academic initiative that has received funding from a Pfizer Independent Grant for Learning & Change 2014 and from investigator-initiated research grants to Imperial College London from Amgen, Merck Sharp & Dohme, Sanofi-Aventis, Daiichi-Sankyo, and Regeneron.

Different registries initiated, but tackling the global burden of FH limited by lack of integrated approaches

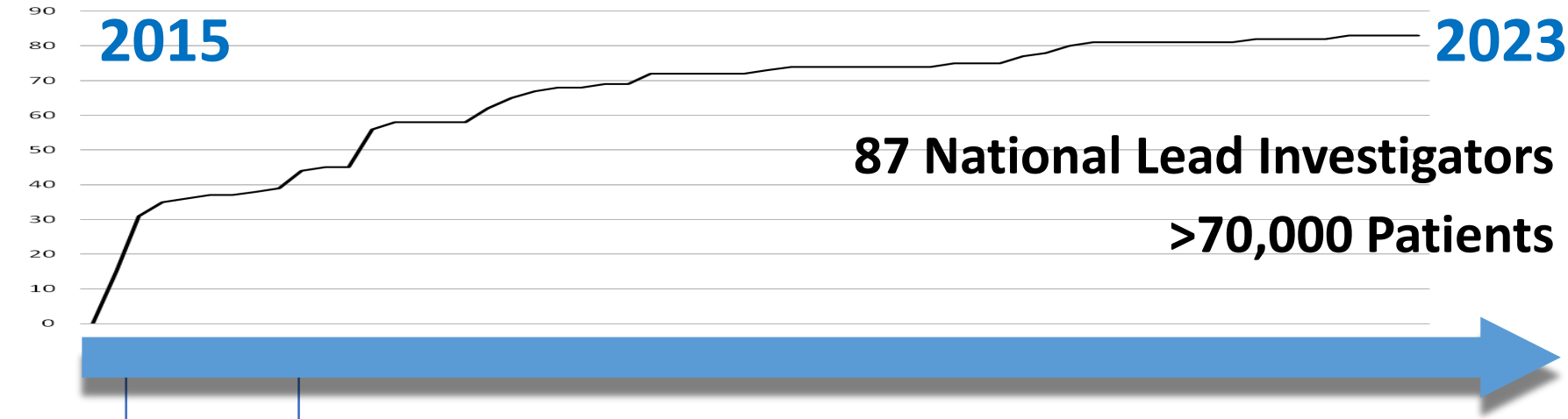






FHSC Participation

- ✓ National Lead Investigator Commitment Form
- ✓ Data Sharing Agreement
- ✓ Data Ethical Compliance Form



FH: A global call to arms
Atherosclerosis 2015

Rationale and design of the EAS FHSC
Atheroscl Suppl 2016

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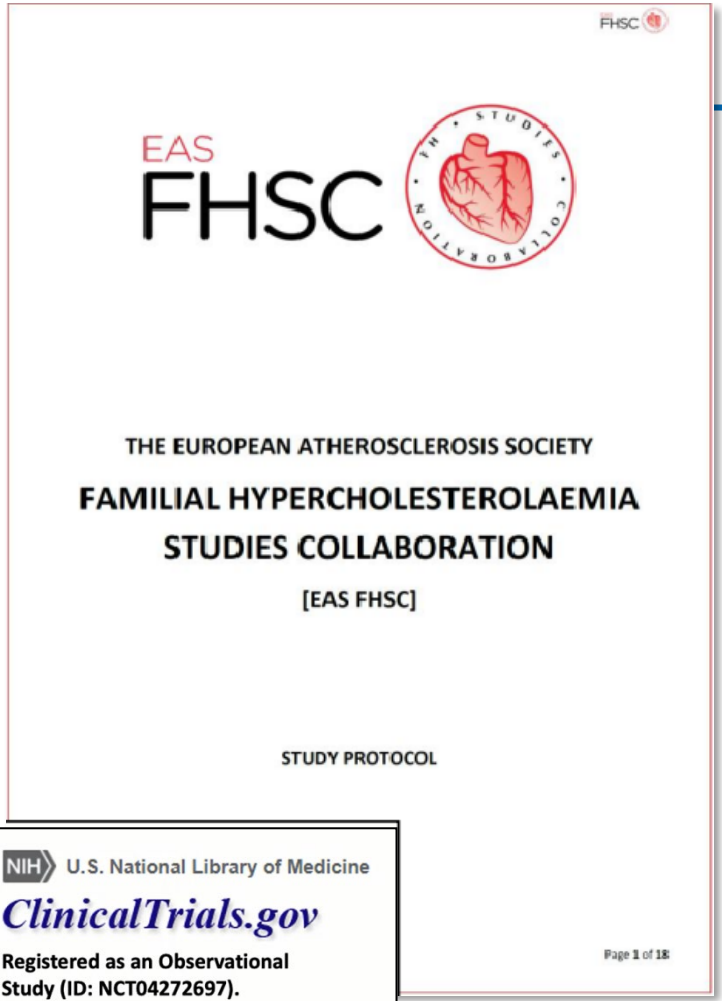
Global FH Studies Collaboration (FHSC) Network & Registry

Investigators from

74 countries

@ Apr 2023

https://www.eas-society.org/fhsc



NIH U.S. National Library of Medicine
ClinicalTrials.gov
Registered as an Observational Study (ID: NCT04272697).

EAS FHSC

FHSC Study Protocol

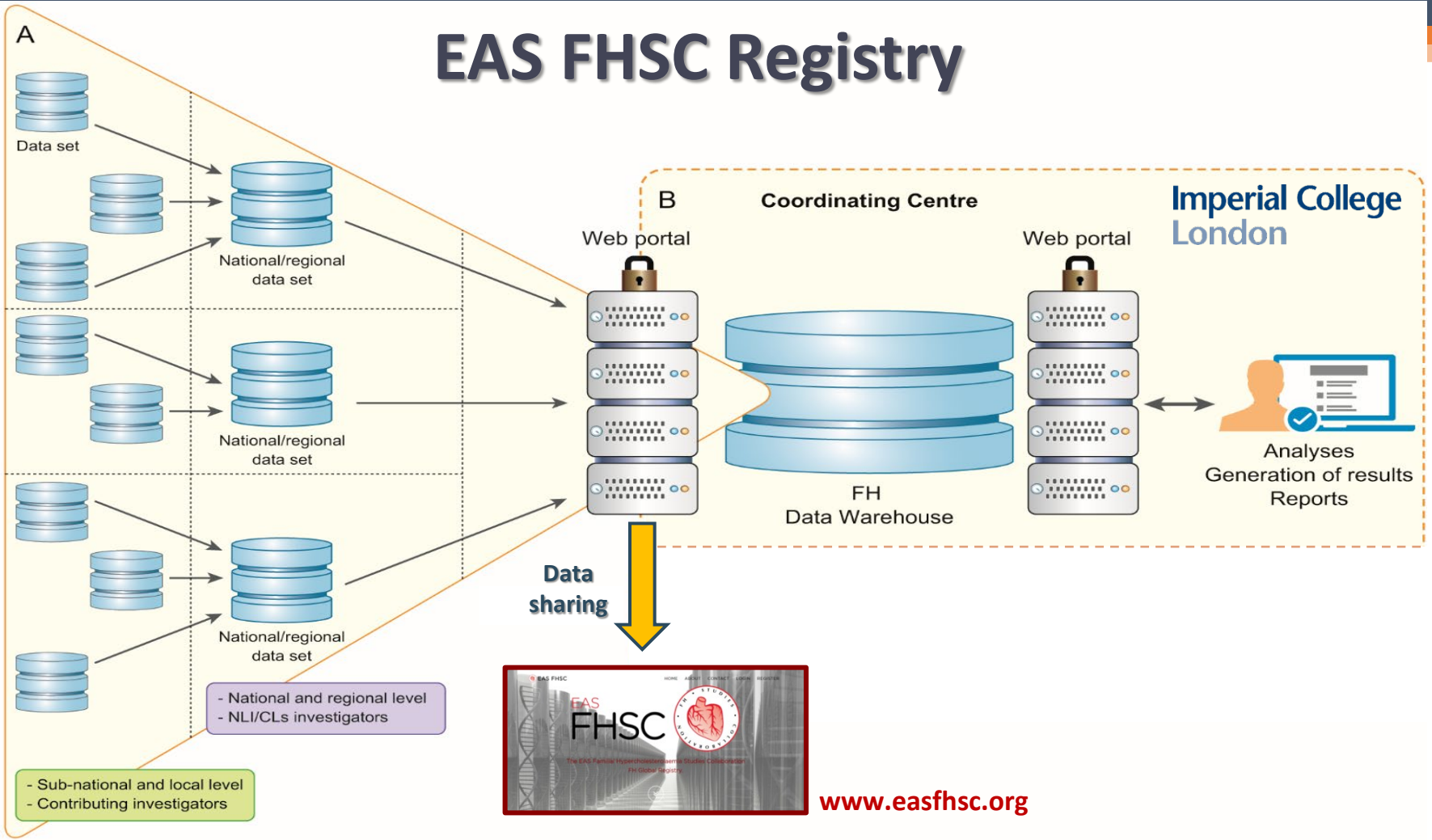
Individuals with a diagnosis of
Heterozygous or homozygous FH

Clinical and/or genetic diagnosis.
Criteria: DLCN, Simon Broome, Medped, etc.
Not self-reported FH

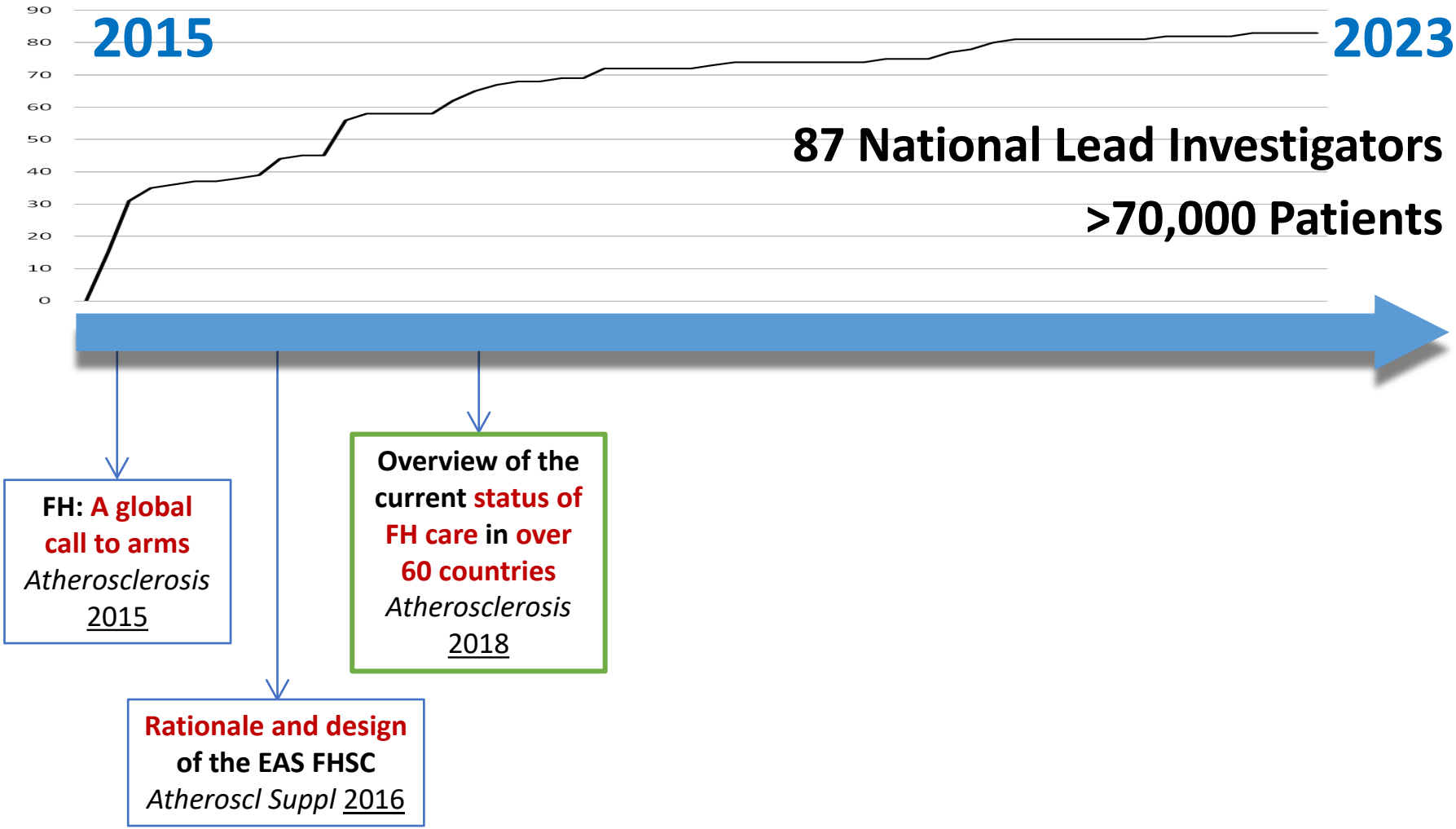
Unaffected relatives of FH individuals
without a diagnosis of FH where screening is carried out.

Published at: **FHSC Investigators, *Atheroscl Suppl* 2016;22:1-32.**

EAS FHSC Registry



www.easfhsc.org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2015
2023
87 National Lead Investigators
>70,000 Patients
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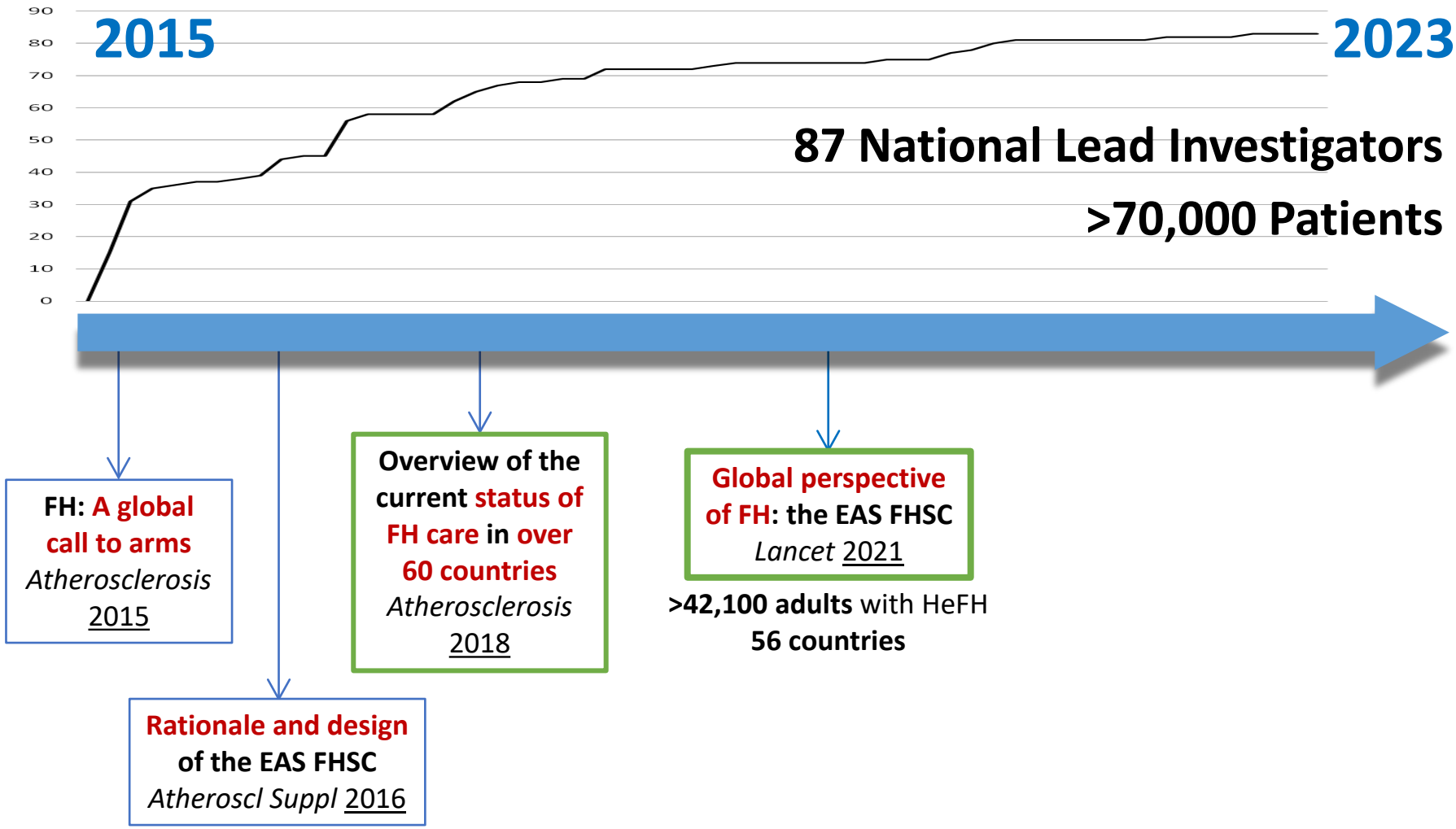
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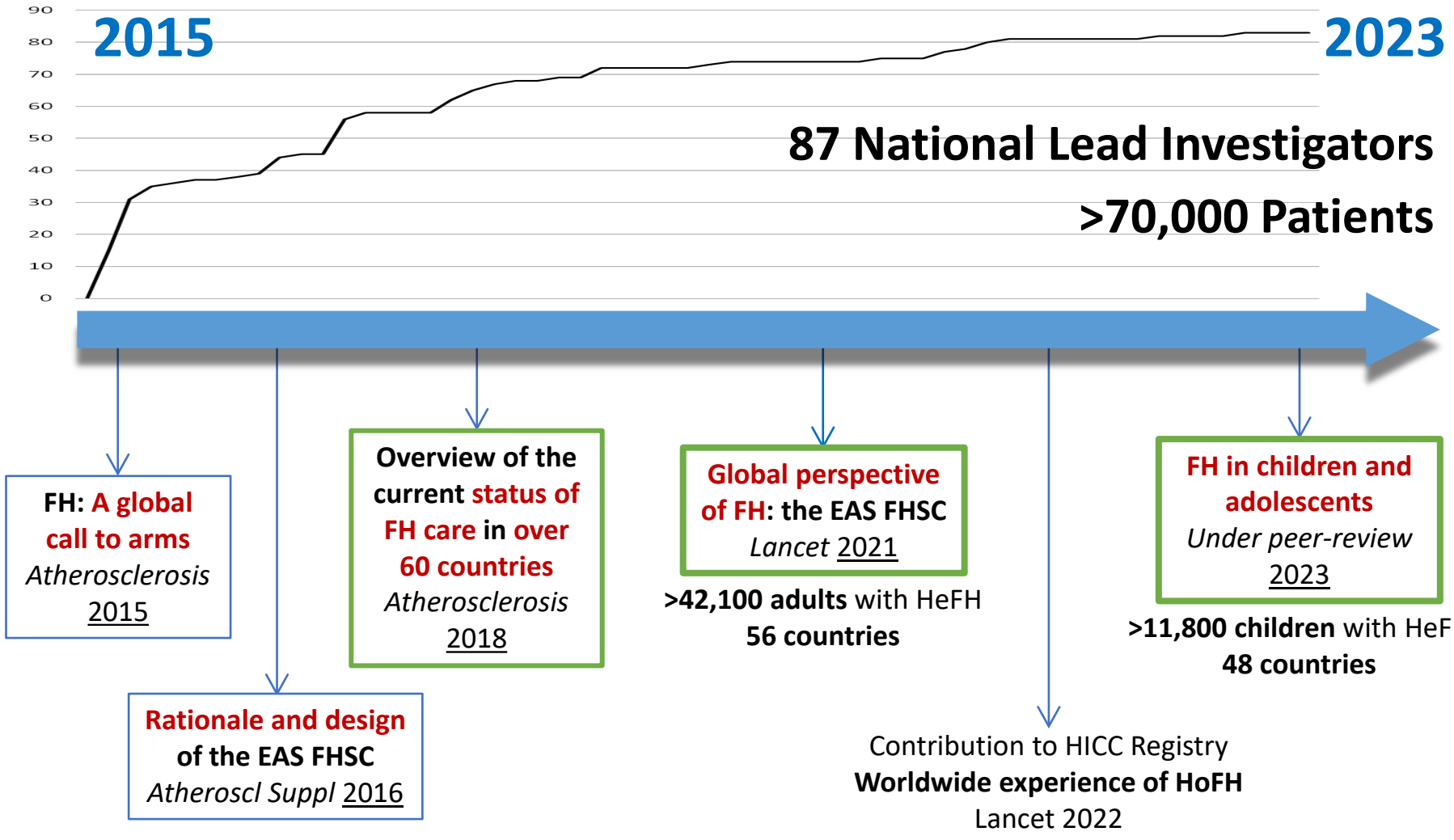
Global perspective of FH: the EAS FHSC
Lancet 2021
>42,100 adults with HeFH
56 countries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Contribution to HICC Registry
Worldwide experience of HoFH
Lancet 2022
FH in children and adolescents
Under peer-review
2023
>11,800 children with HeFH
48 countries

THE LANCET

Articles

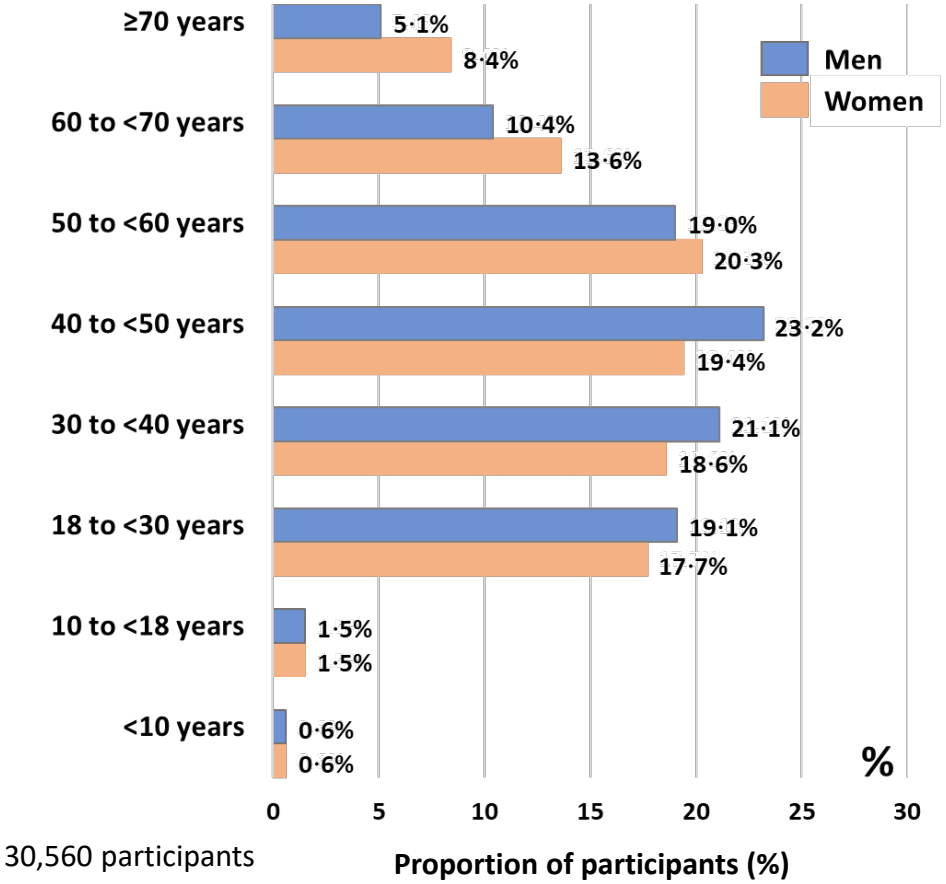
Global perspective of familial hypercholesterolaemia: a cross-sectional study from the EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC)

EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC)*

EAS FHSC Investigators. *Lancet* 2021; 398(10312):1713-1725. doi: 10.1016/S0140-6736(21)01122-3.

>42,100 adults with **Heterozygous FH**
56 countries

Age at FH diagnosis among Adults with HeFH



n = 30,560 participants

Age at FH diagnosis

Median 44.4 years (IQR 32.5 – 56.5)

Men	**43.0 years** (32.0 – 54.4)
Women	**46.0 years** (33.0 – 58.3)

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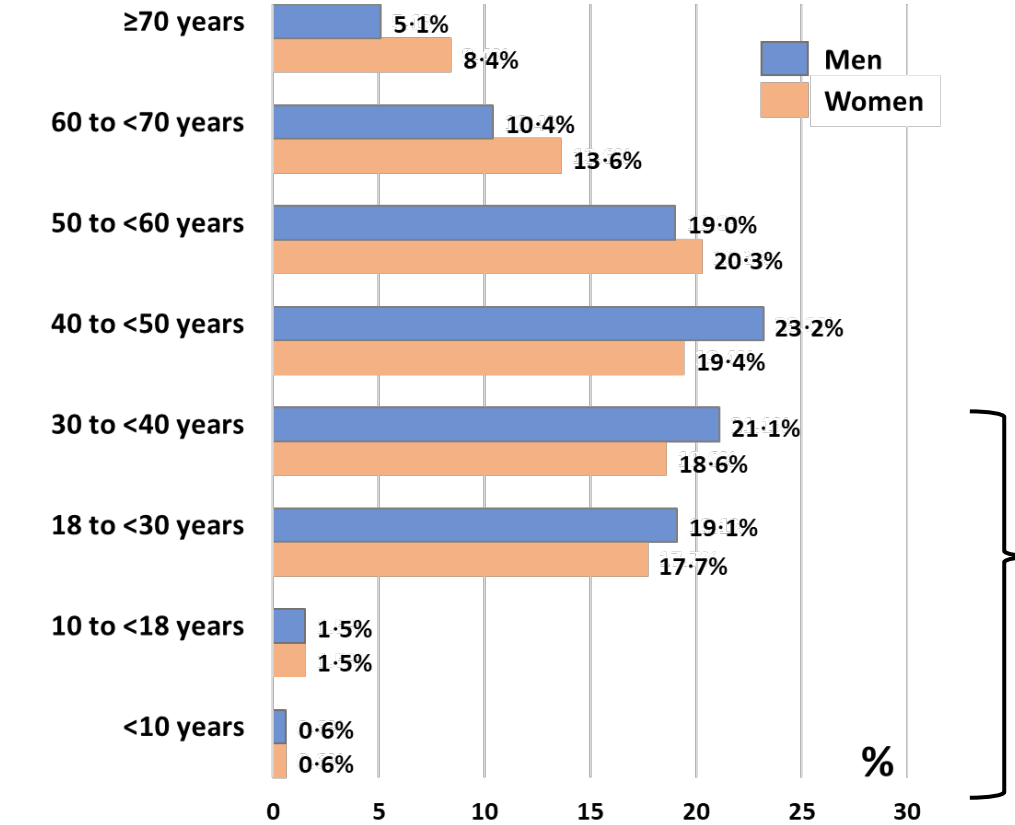

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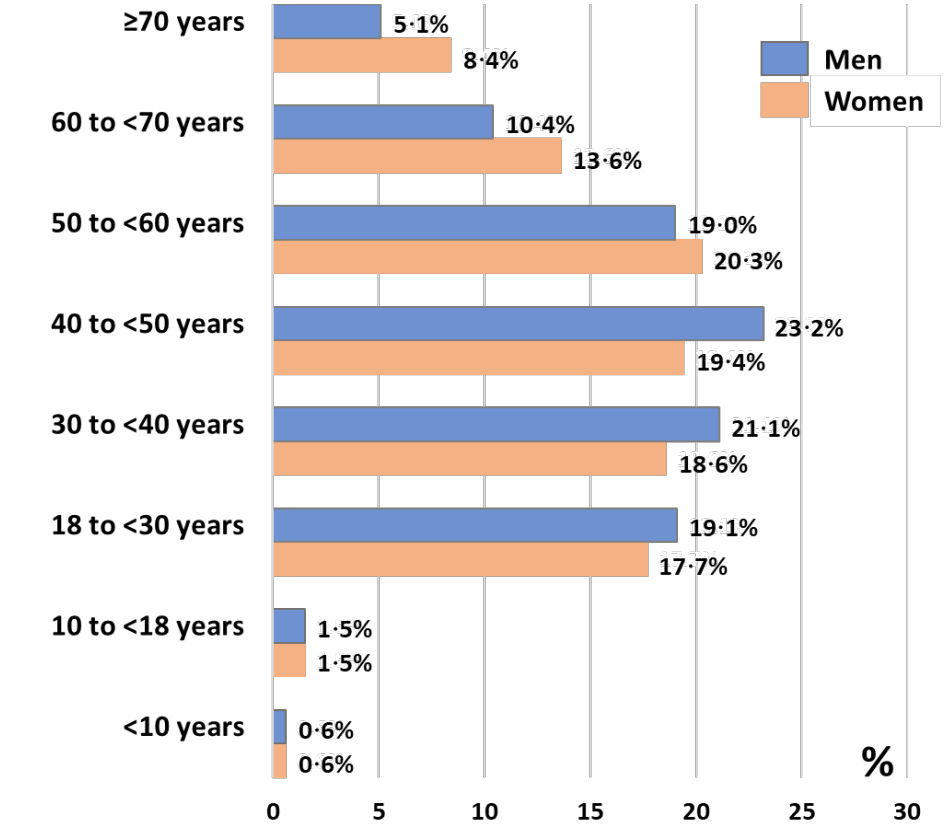

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2.1% diagnosed **age <18 years**

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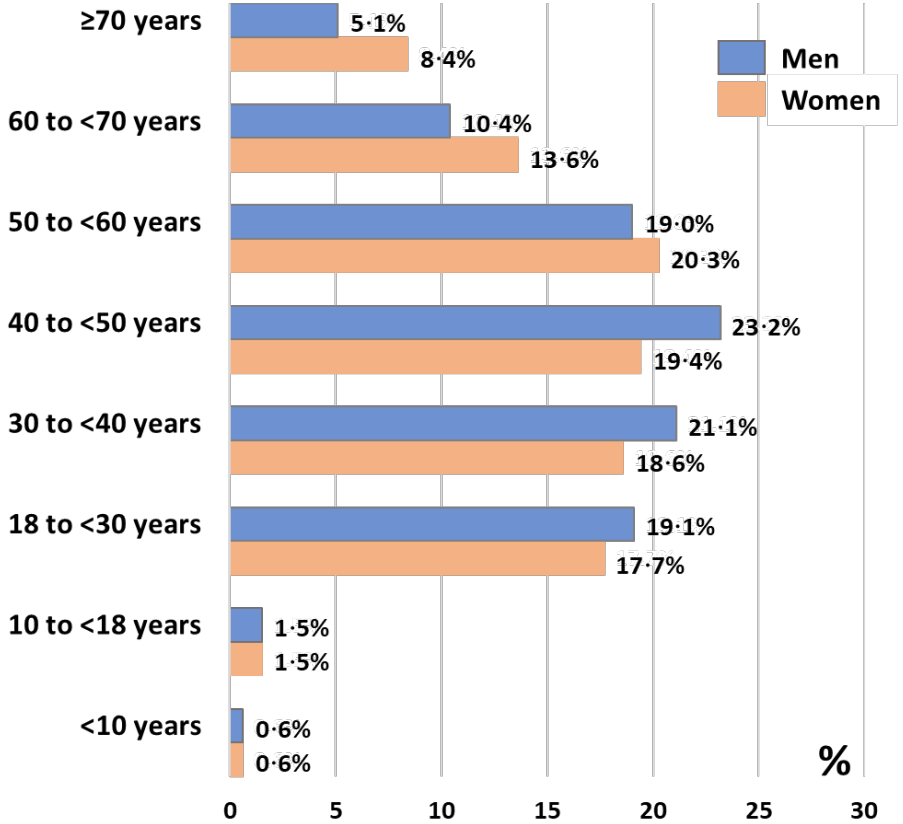
Age at FH diagnosis among Adults with HeFH



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Late diagnosis!

40.2% diagnosed **age <40 years**

2.1% diagnosed **age <18 years**

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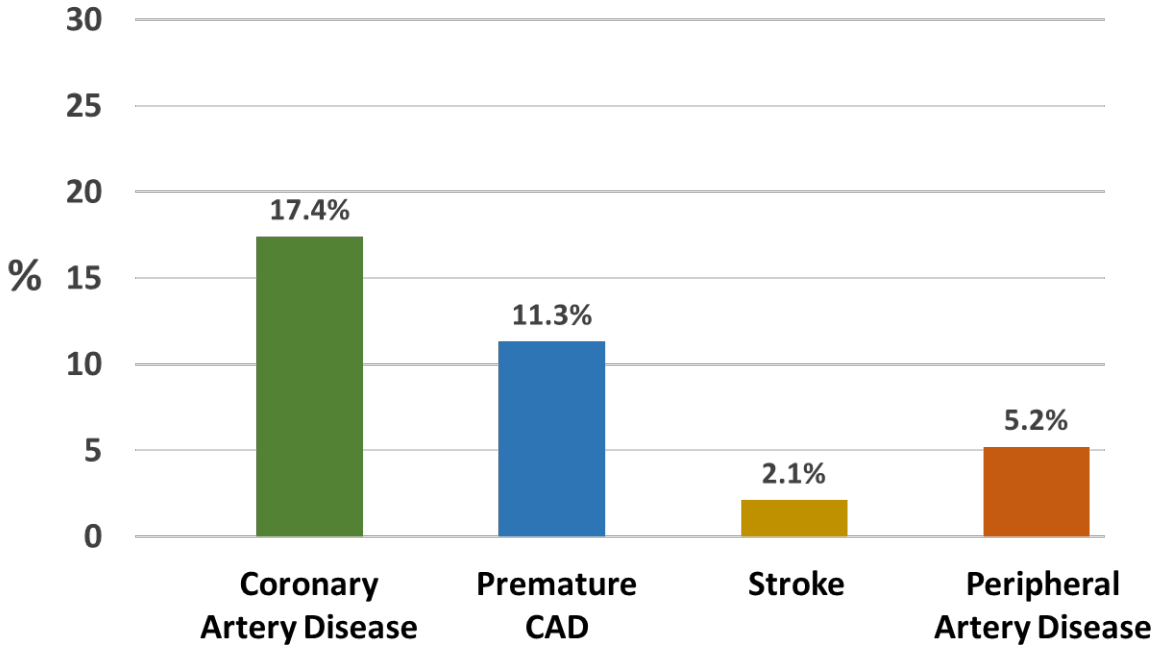
Prevalence of Cardiovascular Disease at entry into the registry

>1 in 6 already has Cardiovascular Disease at registry entry



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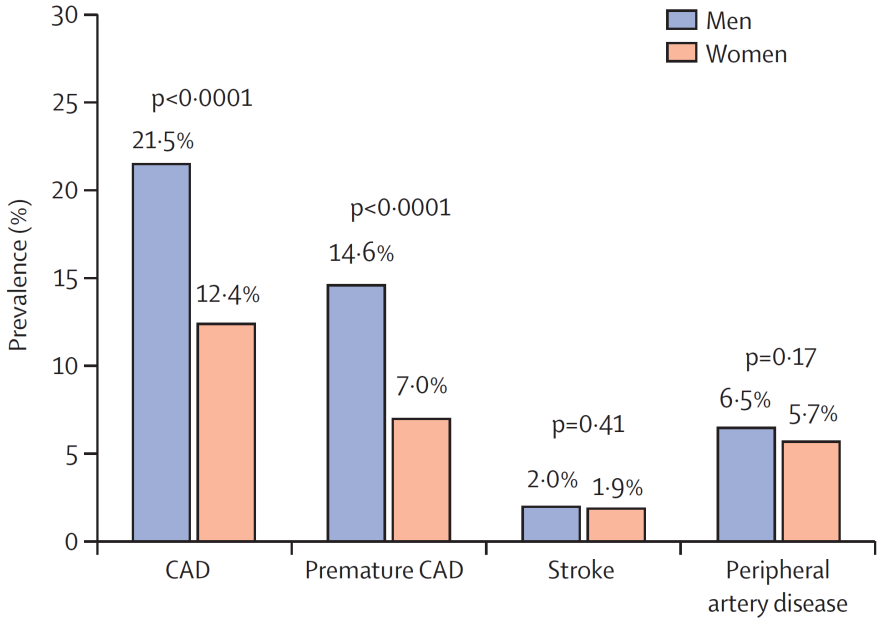
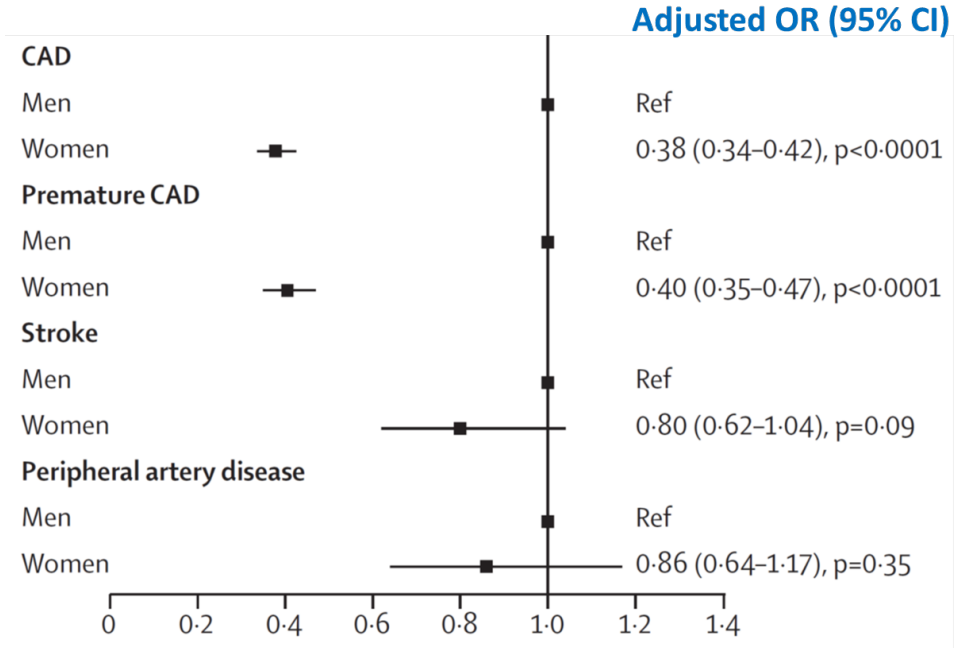
Disparities by sex

Prevalence of CVD stratified by sex



Association of sex with CVD



* ORs adjusted by age, baseline comorbidities (hypertension, diabetes, smoking, and BMI), lipid levels (LDL-C, HDL-C, and log[TG]), LLM, index case, and interaction between LDL-C and LLM.

EAS FHSC Investigators. *Lancet* 2021;398(10312):1713-1725.

LDL-Cholesterol at entry in the registry

High LDL-Cholesterol levels, even if on therapy

Patients Not taking LLM

	Median (IQR), mg/dl
All	**210.0 (167.1 – 259.9)**
Men	206.9 (163.2 – 255.6)
Women	212.7 (170.1 – 264.5)

Patients on LLM

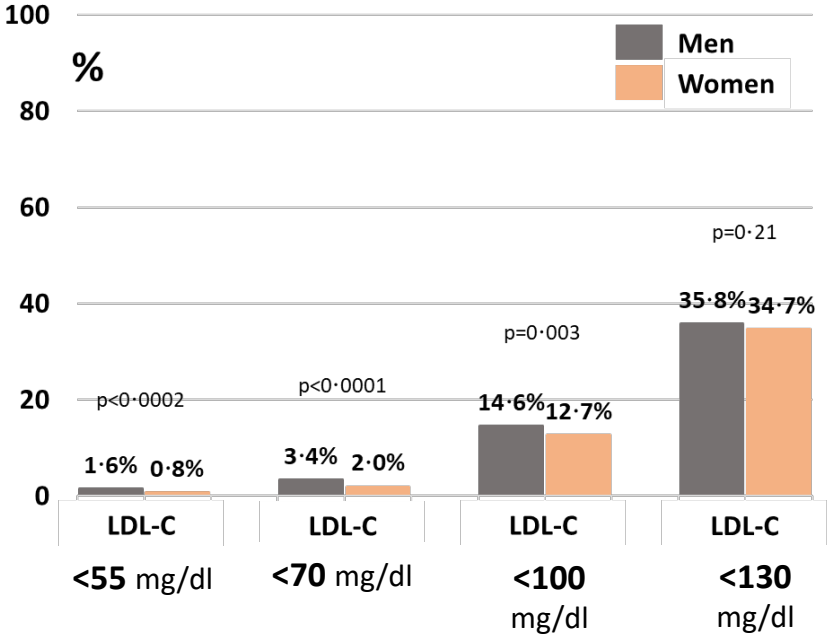
	Median (IQR), mg/dl
All	**163.6 (123.7 – 218.9)**
Men	161.6 (122.2 – 213.1)
Women	164.7 (125.3 – 222.4)

LLM = lipid-lowering medication

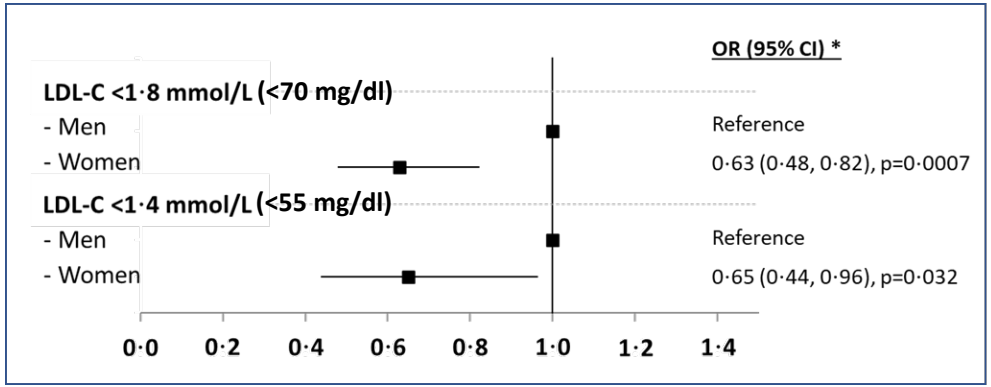
EAS FHSC Investigators. *Lancet* 2021;398(10312):1713-1725.

Low levels of LDL-C goals attainment

% of patients with an LDL-C below different thresholds stratified by gender



Association of gender with having an LDL-C below different thresholds



** OR adjusted by age, baseline comorbidities (HT, DM, smoking, BMI), HDL-C, log(TG), LLM, and index case*

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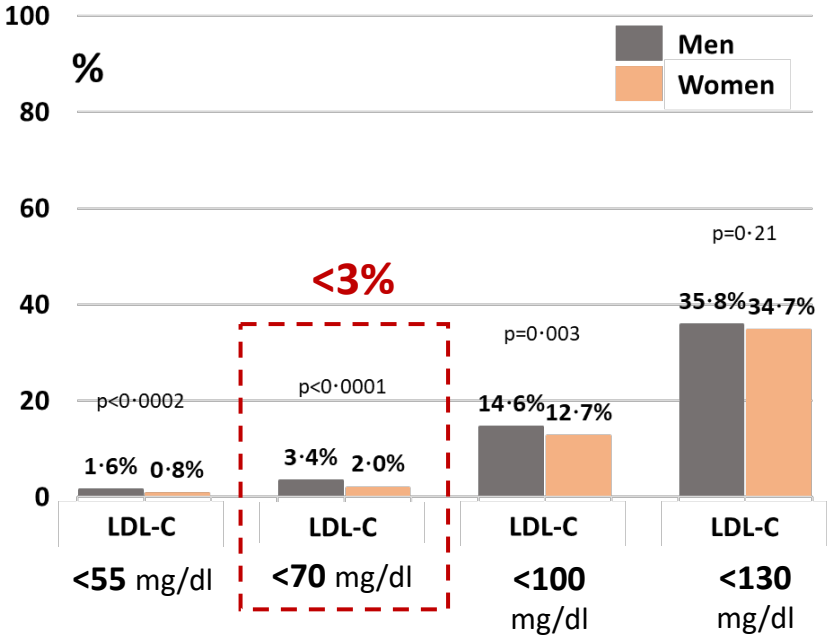

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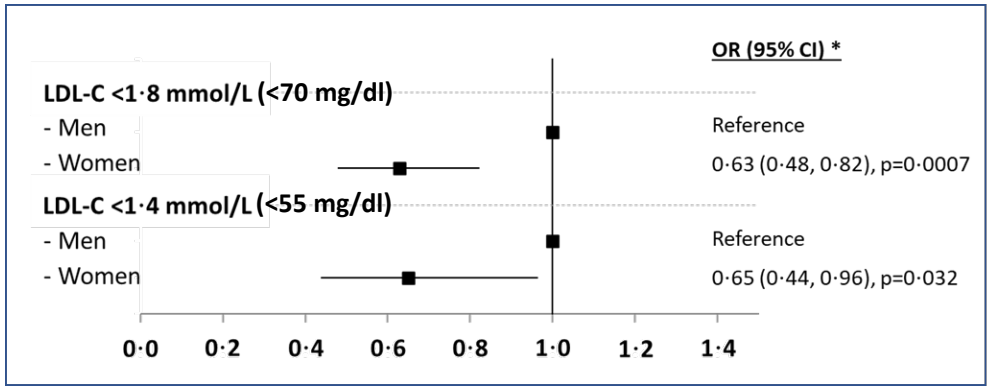

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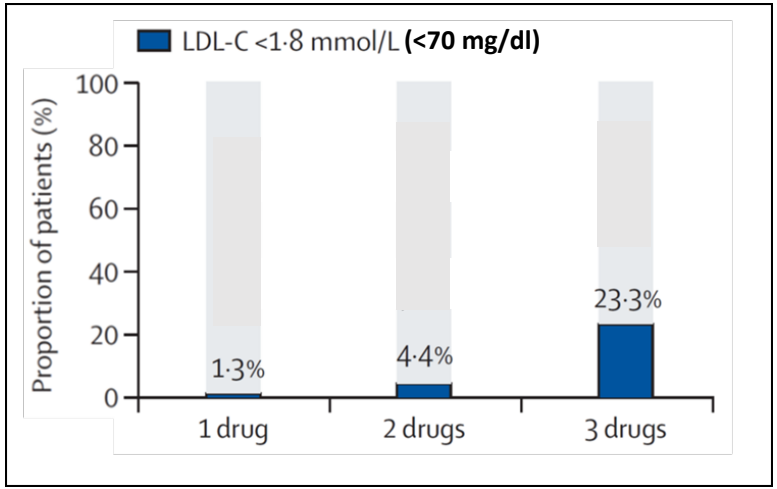
Combination therapy increases LDL-C goal attainment



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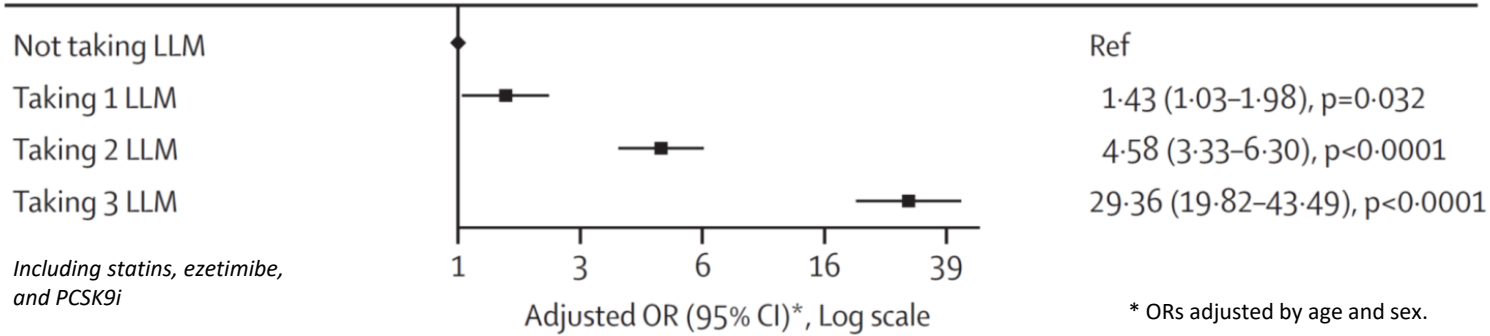
Odds of attaining an LDL-C <1·8 mmol/L (<70 mg/dl) based on the number of LLMs



Including statins, ezetimibe, and PCSK9i

* ORs adjusted by age and sex.

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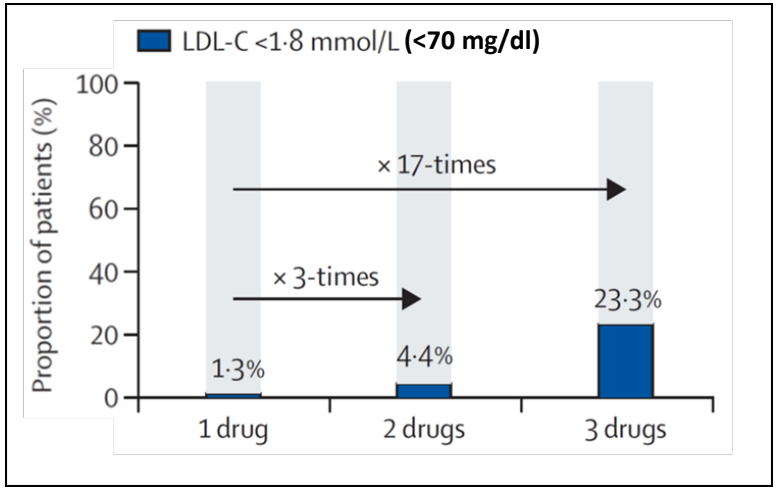

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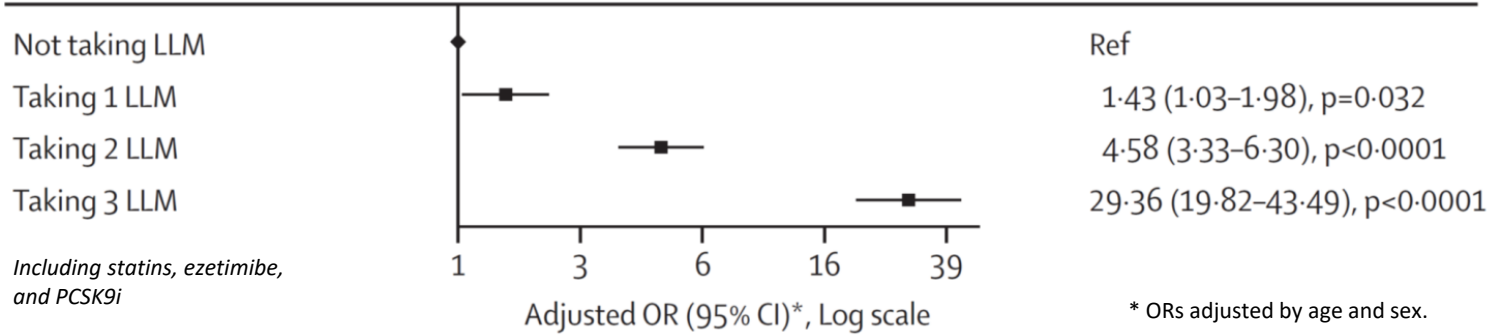

Including statins, ezetimibe, and PCSK9i

* ORs adjusted by age and sex.

Non-Index Cases are younger, with less CV risk factors, and lower LDL-C levels

	INDEX CASES	NON INDEX CASES	
Men	45.4%	46.6%	p=0.058
Age at Baseline (years)	50.0 (39.0 – 59.8)	44.0 (32.1 – 57.7)	p<0.0001
Age at FH Diagnosis (years)	47.8 (36.5 – 57.1)	43.6 (31.6 – 57.1)	p<0.0001
Hypertension	21.1%	12.8%	p<0.0001
Diabetes	5.9%	3.4%	p<0.0001
BMI (kg/m^2)	26.0 (23.3 – 29.2)	24.6 (22.1 – 27.4)	p<0.0001
LDL-C (mg/dL)	-	-	-
▪ Among patients not taking LLM	234.3 (194.9 – 286.2)	178.7 (143.6 – 214.2)	p<0.0001
▪ Among patients taking LLM	181.0 (124.5 – 235.9)	150.4 (120.6 – 190.6)	p<0.0001

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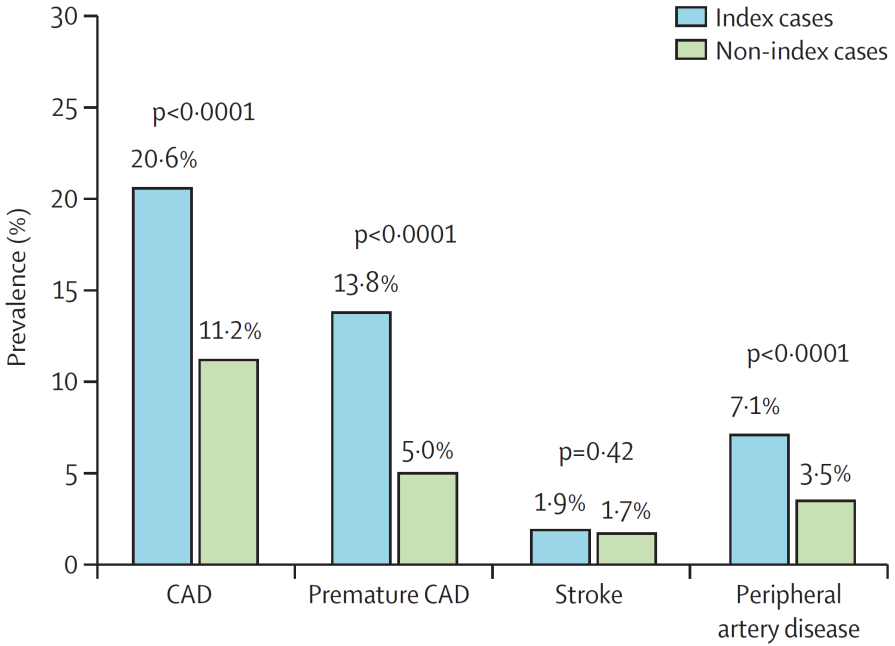
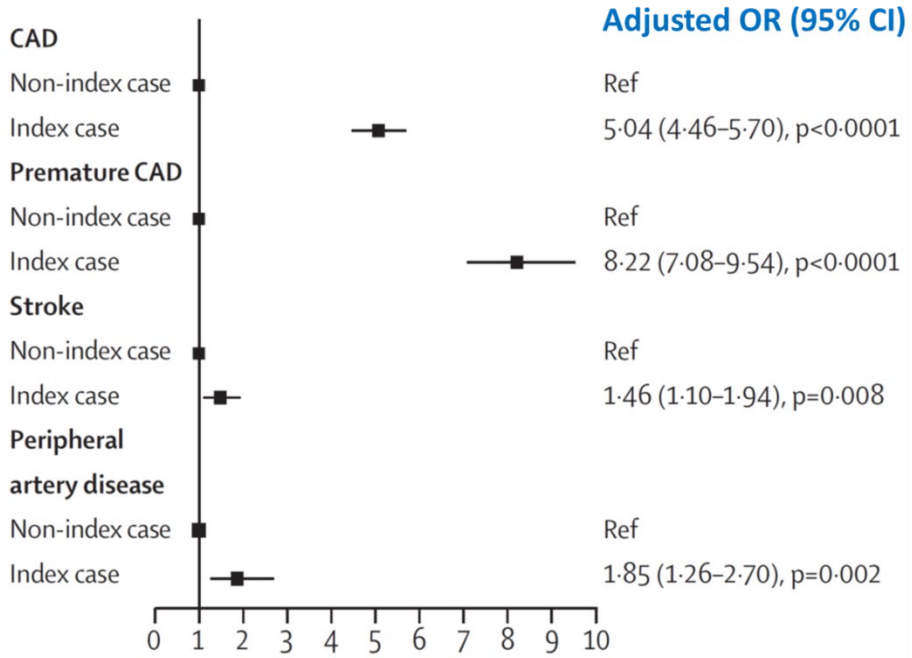
Higher prevalence of CVD among Index Cases

Prevalence of CVD by IC status



Association of Index Case with CVD



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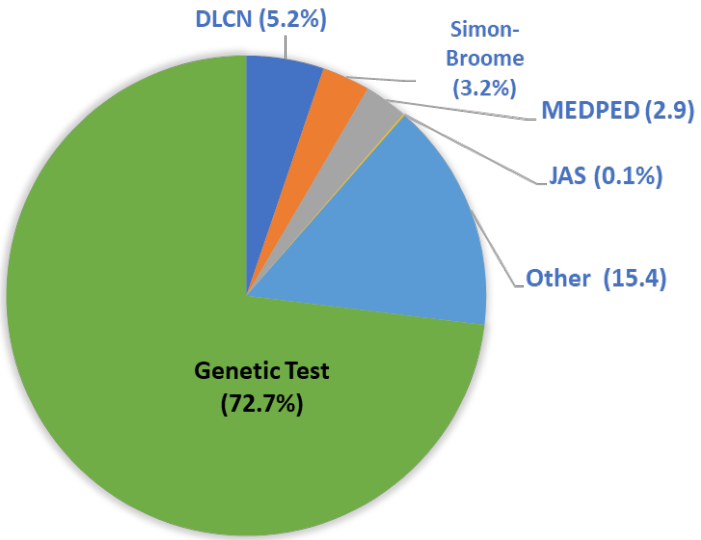
si2021.eu

- ***Broad professional consensus*** *on paediatric FH screening was reached and public policy recommendations developed*
- *The European medical community should step forward and make* ***paediatric screening for FH a standard of care***

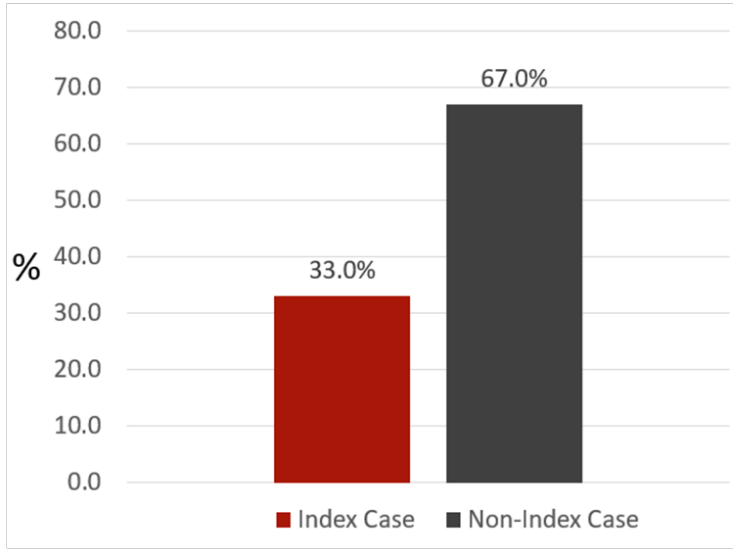
FH in children/adolescents (>11,300 cases)

Children usually not the primary focus of FH identification

Most frequent diagnosis: Genetic testing – family cascade screening



Identified children more frequently non-index cases



Late-Breaking Science EAS Congress 2022
EU Technical Meeting 2021

Identification of FH in children/adolescents

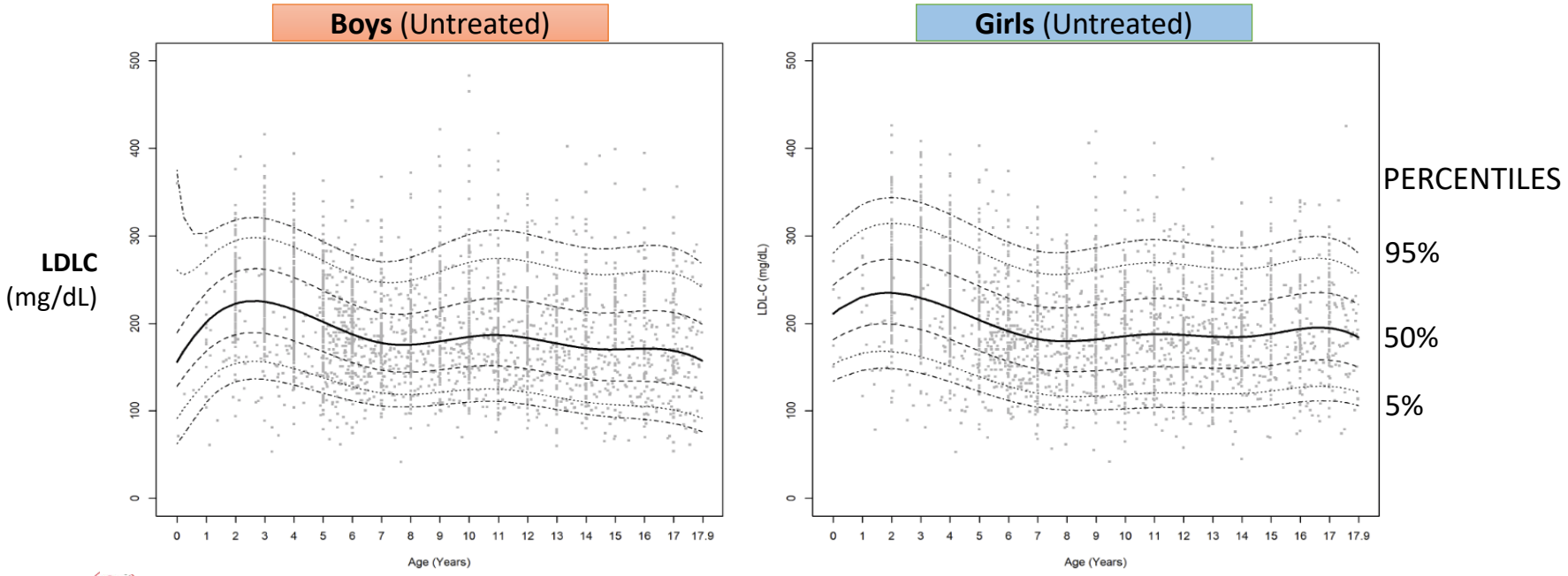
Physical signs and CVD are infrequent
Diagnosis mostly reliant on LDL-C (± genetic testing)

Female	50.0%
Age at FH diagnosis, years	9.1 (5.3 – 13.0)
Xanthomas	2.2%
Corneal arcus	0.9%
Hypertension	0.3%
Diabetes mellitus	0.4%
Coronary artery disease	0.3%

Late-Breaking Science EAS Congress 2022
EU Technical Meeting 2021

LDL-C in children/adolescents with FH at registry entry

High Cholesterol from birth / Screening from early ages



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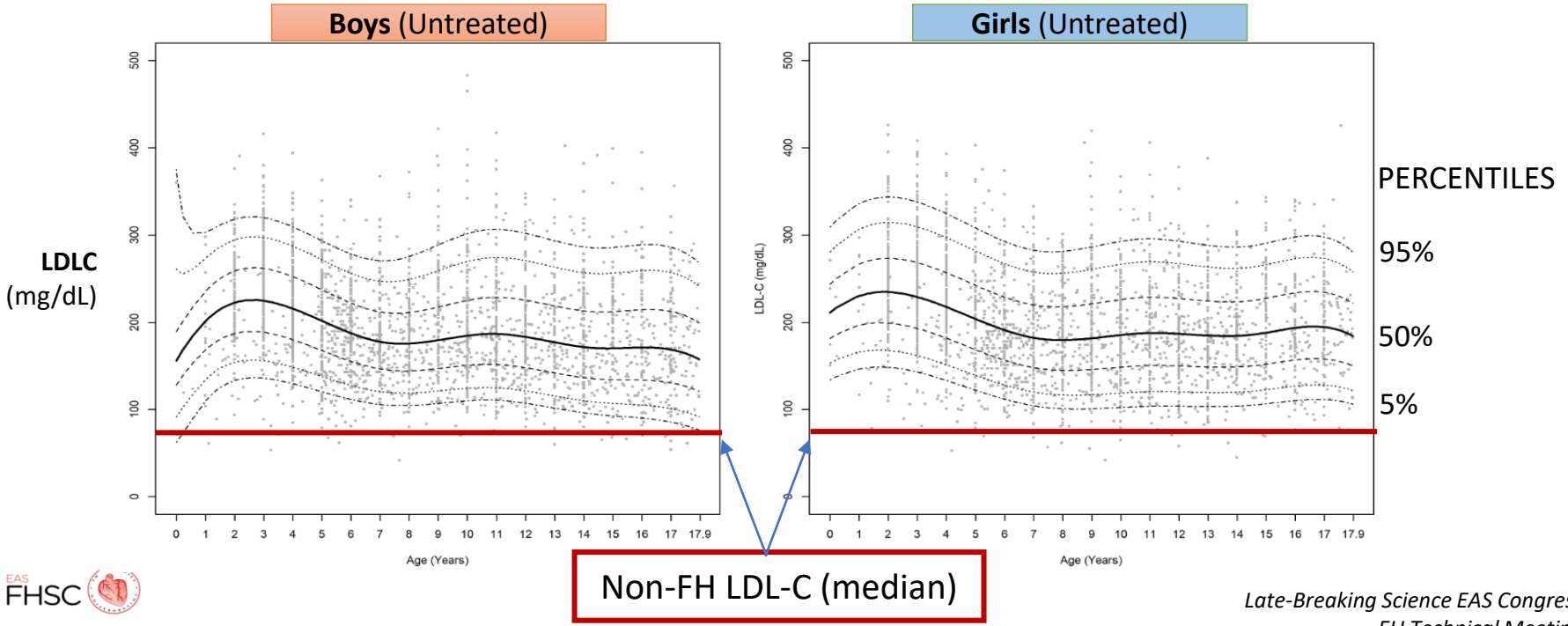

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EU Technical Meeting 2021

Support Logout

PUBLIC HEALTH
Best Practice Portal

European Commission > DG Health & Food Safety > Public health > BP Portal

Welcome to the Best Practice Portal

The Best Practice Portal is designed to help to find reliable and practical information on implemented practices recognized as the best in the area of health promotion, disease prevention, and the management of non-communicable diseases. It also provides an overview of practices collected and transmitted in actions co-funded under the Health Programmes.

Practices can be submitted for assessment through this portal. Every practice, as long as evaluated as "best" against the criteria adopted by the Steering Group on Health Promotion, Disease Prevention and Management of Non-Communicable Diseases (Steering Group), will be published in the portal and might be brought to the attention of Member State representatives for further transfer and broader implementation.

DG SANTE has made it a priority to identify, disseminate and transfer best practices in order to make progress in health promotion and in disease prevention in Europe. DG SANTE also hopes these efforts will help reach the Sustainable Development Goal 3.4 to reduce premature mortality from non-communicable diseases by one-third by 2030, through prevention and treatment, and to also help reach the nine UN/WHO global voluntary targets for health.

Submission

Submit your practice for evaluation.

Database

A database of practices.

Knowledge sharing

Health Promotion and Disease Prevention Knowledge Gateway | EU Science Hub

Implementation

Best practices which have been selected for transfer from one Member State to others.

Marketplaces

Information on marketplace workshops on selected practices

Other portals

EU2022.CZ

FH Europe
The European FH Patient Network

The Prague Declaration

6 Sept 2022

FH Paediatric Screening
Moving Prevention From Evidence to Action:
Overcoming the Barriers to Implementation

Take home messages

FHSC Registry data – contemporary information on FH identification and management

- Late identification – missing years of intervention – impact on prevention
- High LDL-C levels despite therapy – need for combination therapy
- Screening to identify FH individuals early and «healthier»

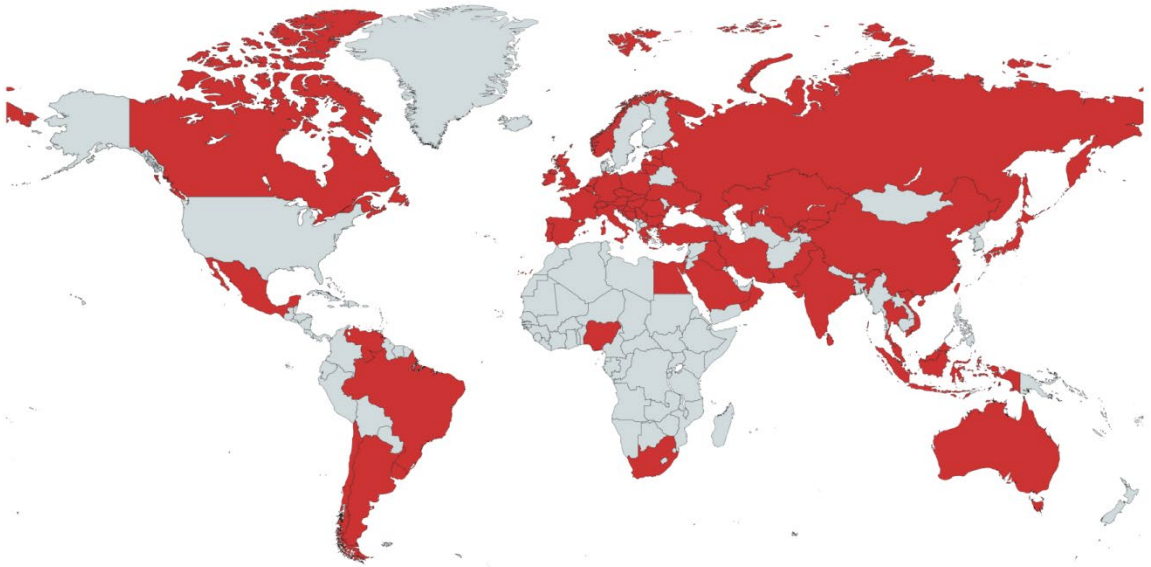
Children & Adolescents

- Physical signs and CVD are uncommon – Diagnosis reliant on LDL-C / genetic testing
- LDL-C in children is high even at lower percentiles and from early ages

➔ Impact on Care and Policy

Acknowledgements

All EAS FHSC Investigators contributing to the FHSC Network and Registry



FHSC Work in progress

Abstracts to the EAS Congress May 2023

- Approaches to **LDL-C management in Children and Adolescents with FH**: Analysis on over 3000 individuals receiving lipid-lowering medication in the FHSC Registry.
- **Lipoprotein (a) and atherosclerotic cardiovascular disease** in adults with heterozygous FH: a cross-sectional study from the EAS FHSC.
- **Obesity and statin use** may impact the **prevalence of diabetes** in FH: A worldwide cross-sectional study by the EAS FHSC.
- Global prevalence of **overweight and obesity** among paediatric and adult patients with **homozygous or heterozygous FH**, and association with coronary artery disease.

Analysis of Genetic data

- **Genetic test data in over 44,500 participants.**

JAMA Cardiology | Special Communication

Reducing the Clinical and Public Health Burden of Familial Hypercholesterolemia

A Global Call to Action

January 2020

Representatives of the Global Familial Hypercholesterolemia Community

Role of Registries

Circulation

ORIGINAL RESEARCH ARTICLE

Prevalence of Familial Hypercholesterolemia Among the General Population and Patients With Atherosclerotic Cardiovascular Disease

A Systematic Review and Meta-Analysis

Meta-analysis ~7.3 million individuals

Prevalence of FH in the General Population

1:311 (95% CI 1:250, 1:397)

Prevalence of FH among patients with CVD

1:17 (95% CI 1:12, 1:24)

JAMA Cardiol. 2020. doi: 10.1001/jamacardio.2019.5173
Hu P et al. Circulation 2020. doi: 0.1161/CIRCULATIONAHA.119.044795

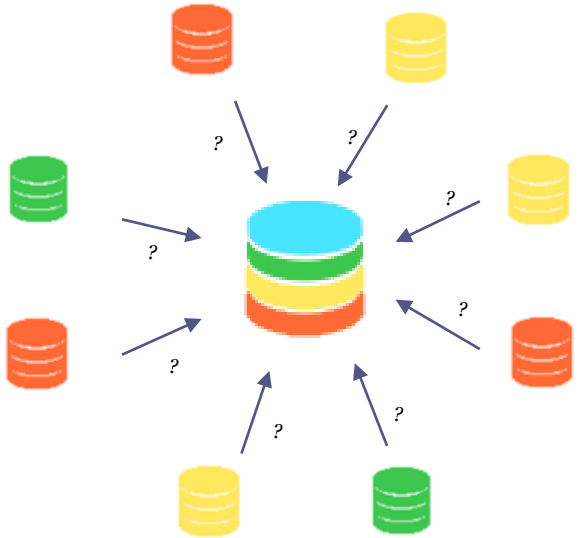
Data management Challenges

Find a solution to merge all local individual registries into one global registry.

Which meant to solve the heterogeneity in:

- Data Structures
- Sets of Variables and their definitions
- Data types & measurements units
- Local contexts

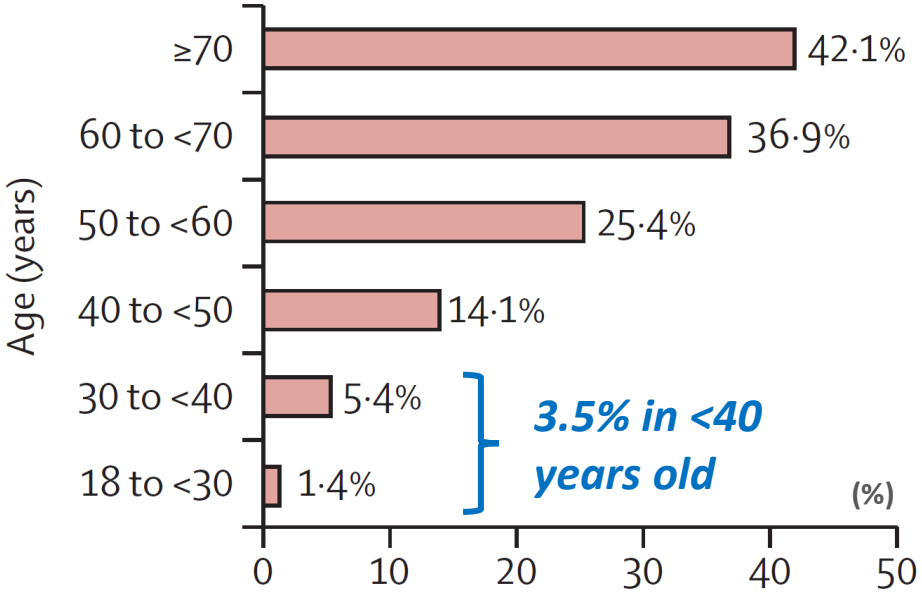
How to merge heterogeneous data?



Missing opportunity to address global CV risk

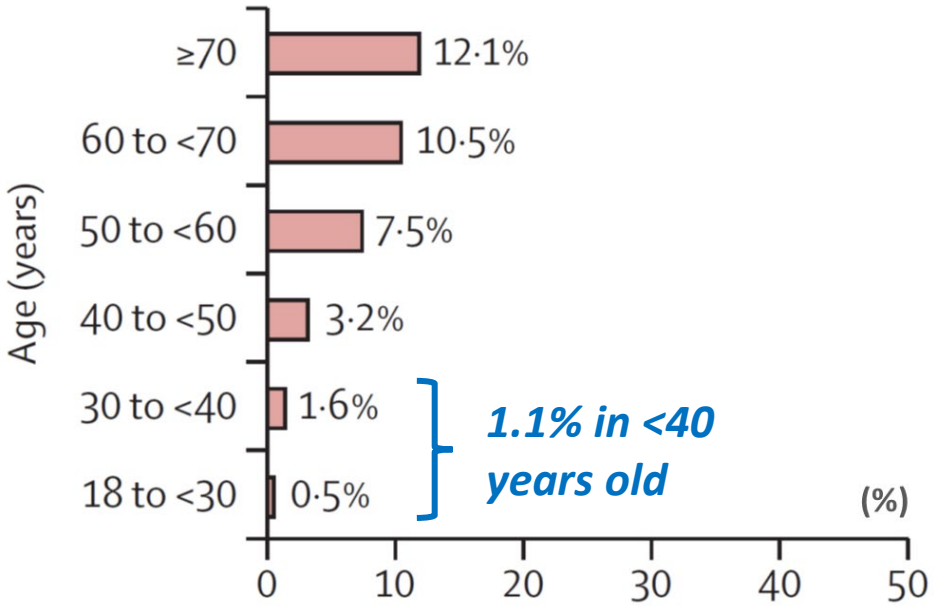
Prevalence of Hypertension

Overall: 19.2%



Prevalence of Diabetes

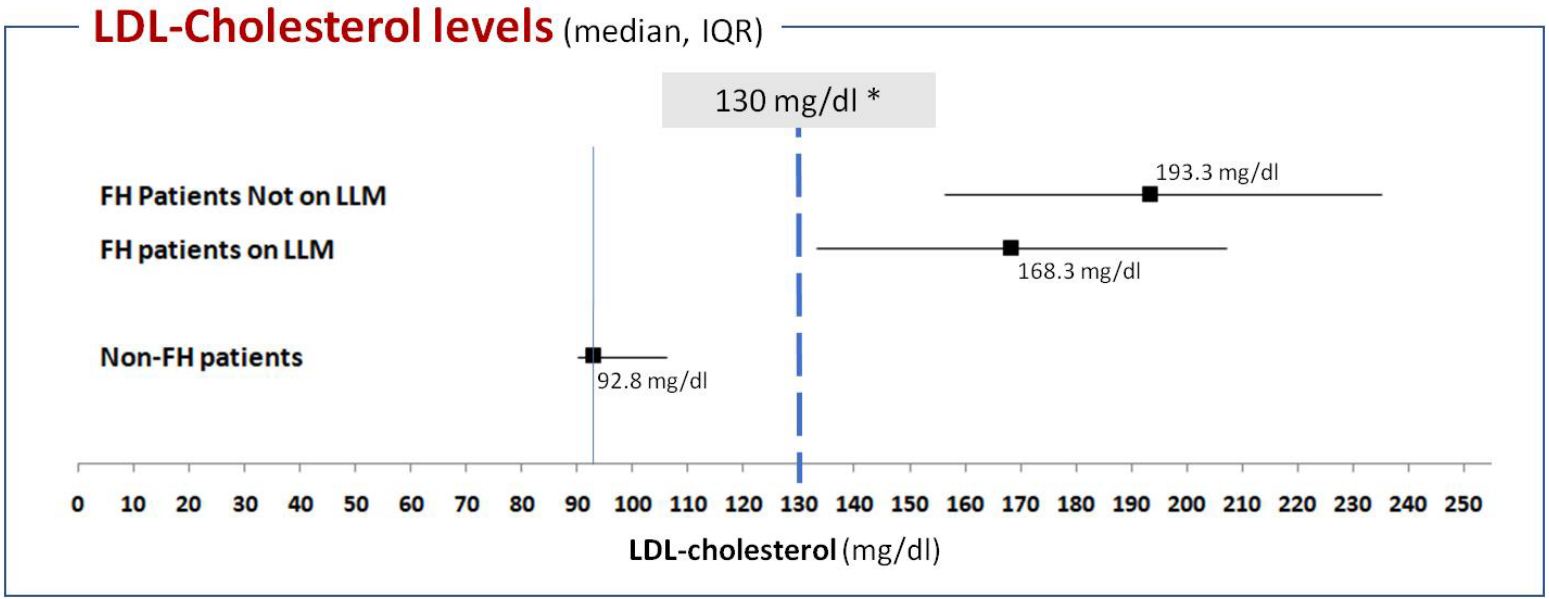
Overall: 5.0%



EAS FHSC Investigators. *Lancet* 2021;398(10312):1713-1725.

FH in children/adolescents (>11,300 cases)

High LDL-C even if on treatment



Late-Breaking Science EAS Congress 2022
EU Technical Meeting 2021

* Wiegman A, et al. Eur Heart J 2015;36(36):2425-37.