Homozygous Familial Hypercholesterolemia

Lessons from a Global Consortium

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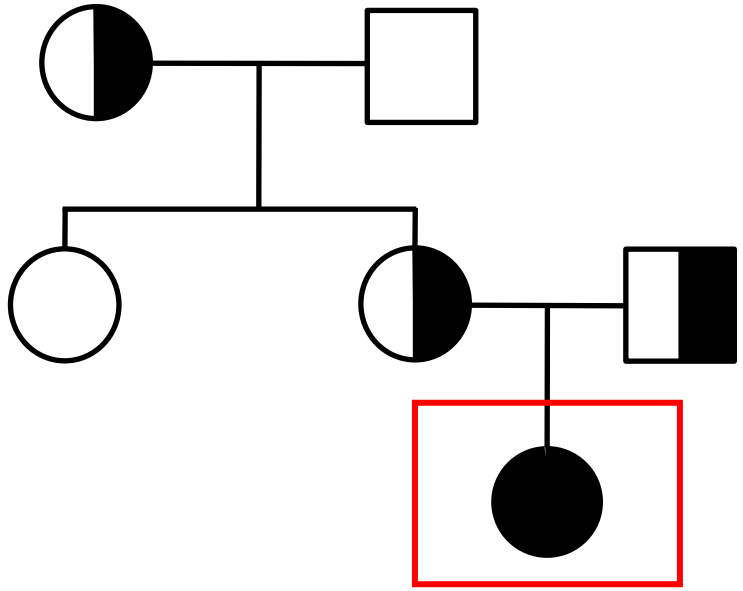
Disclosures

Potentiële belangenverstrengeling	Geen
Voor presentatie mogelijk relevante relaties:	Geen
Sponsoring of onderzoeksgeld	-
Honorarium of andere (financiële) vergoeding	-
Aandeelhouder	-
Andere relatie, namelijk …	-

Homozygous FH is …

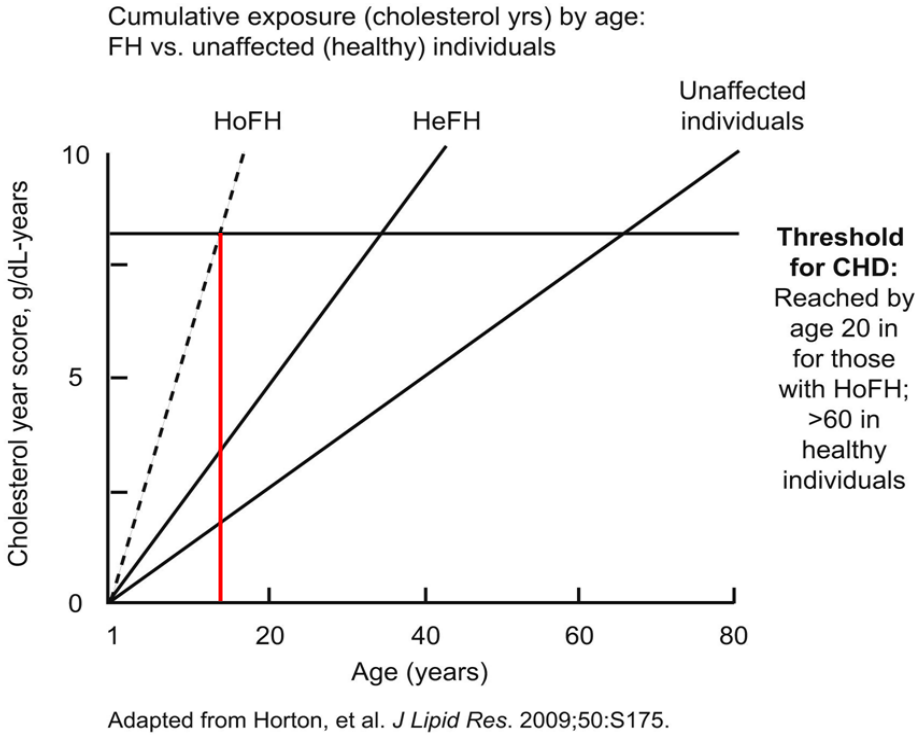
… **rare** (~1 : 360.000)



Homozygous FH is …

… rare (~1 : 360.000)

… the **most severe form of FH**
… characterized by ↑↑↑ **LDL-C and** ↑↑↑ **CVD risk**



Adapted from Horton, et al. *J Lipid Res*. 2009;50:S175.

Homozygous FH is …

… rare (~1 : 360.000)

… the most severe form of FH
… characterized by ↑↑↑ LDL-C and ↑↑↑ CVD risk

… either **diagnosed clinically** or **genetically**

Clinical diagnosis

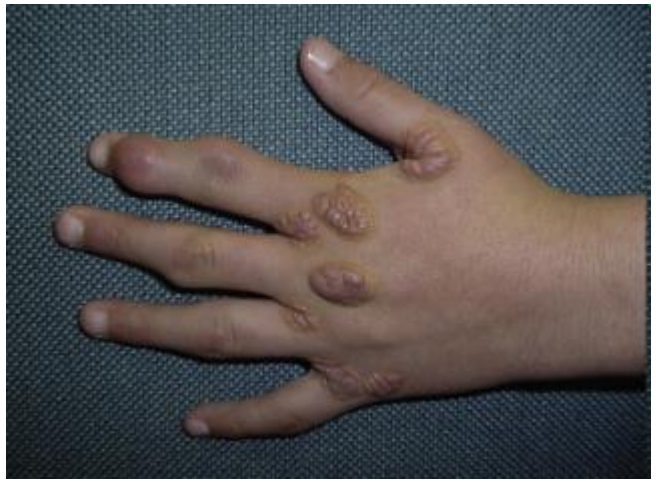
- Untreated LDL cholesterol levels >13 mmol/L (500 mg/dL), or LDL cholesterol ≥8 mmol/L (300 mg/dL) while on conventional lipid-lowering therapies; and,
- Presence of xanthomas before the age of 10 years, or the presence of heterozygous familial hypercholesterolaemia in both parents[1]

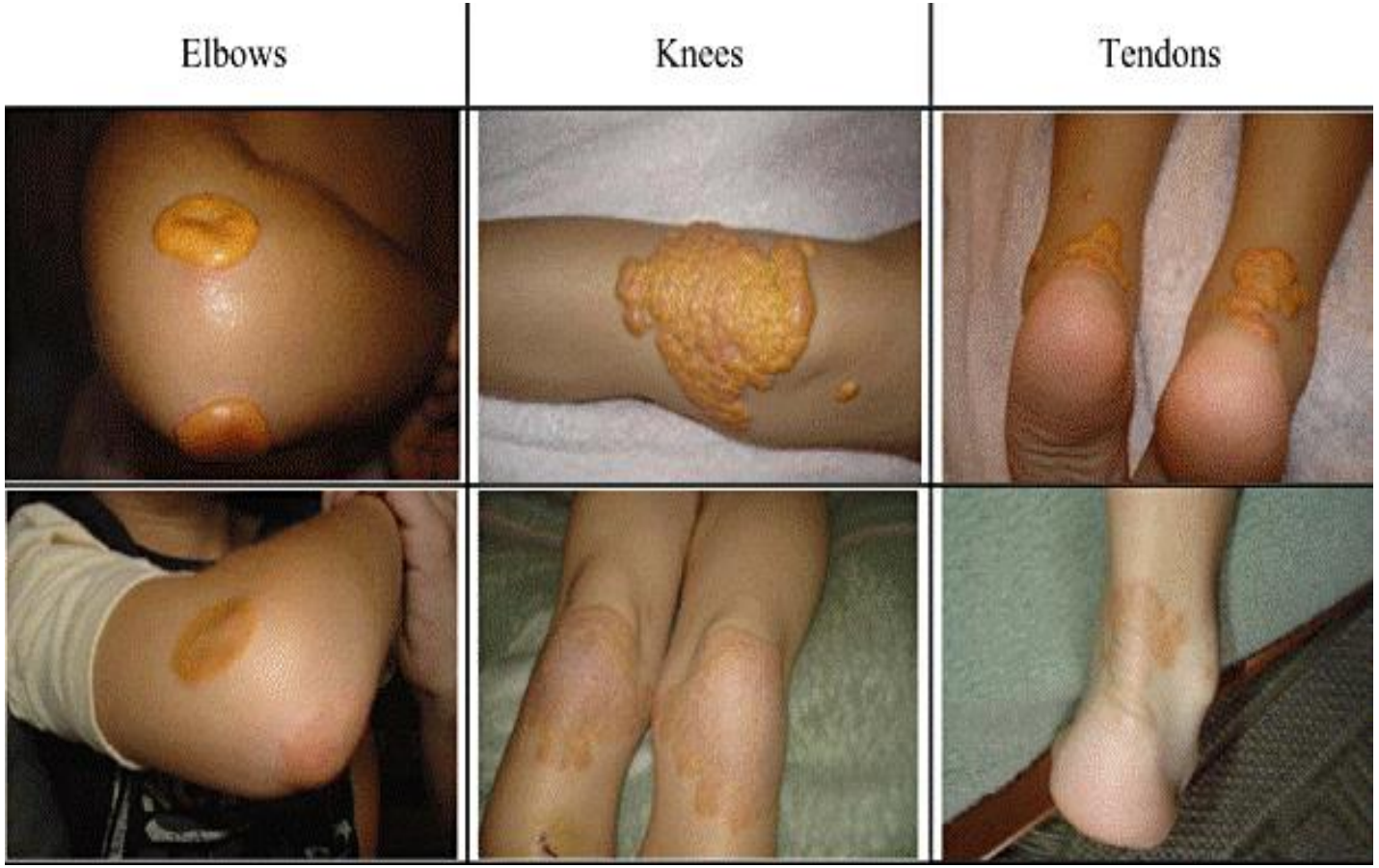
Genetic diagnosis

- Identification of biallelic pathogenic variants at the *LDLR*, *APOB*, *PCSK9*, or *LDLRAP1* gene locus

Cuchel et al. Eur Heart J. 2014 Aug 21;35(32):2146-57

Cutaneous xanthomas
in young patients with HoFH





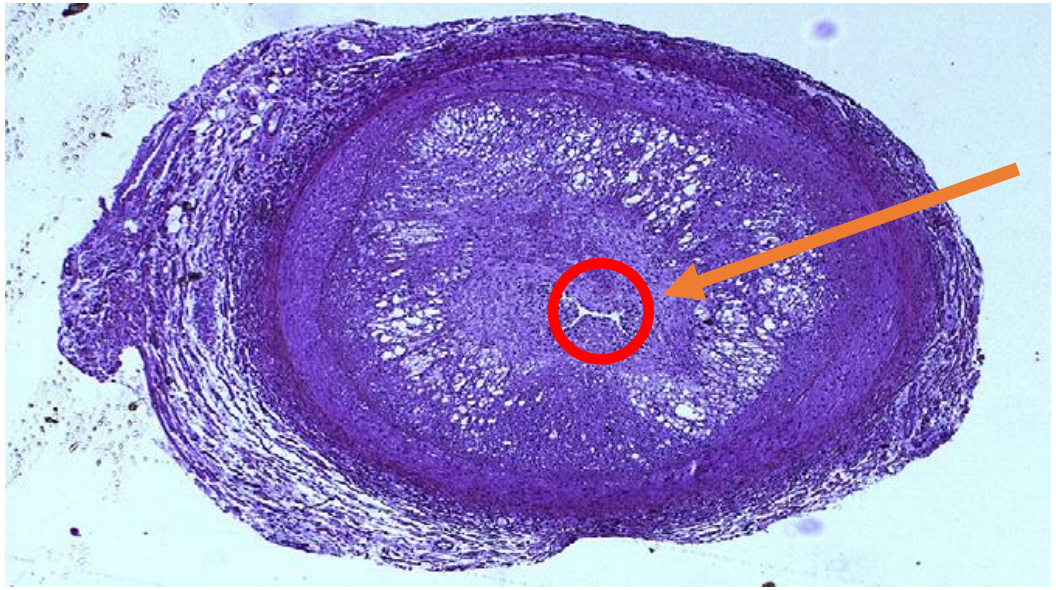
Slide courtesy of prof Stefano Bertolini

Raal FJ et al. Atherosclerosis 2012; 223: 262-268

4-year-old boy with HoFH

- Untreated LDL-C 20 mmol/L
- Died suddenly at age of 4;

98% occlusion of left coronary artery



2% left where all the blood went through

Slide courtesy of dr Bert Wiegman

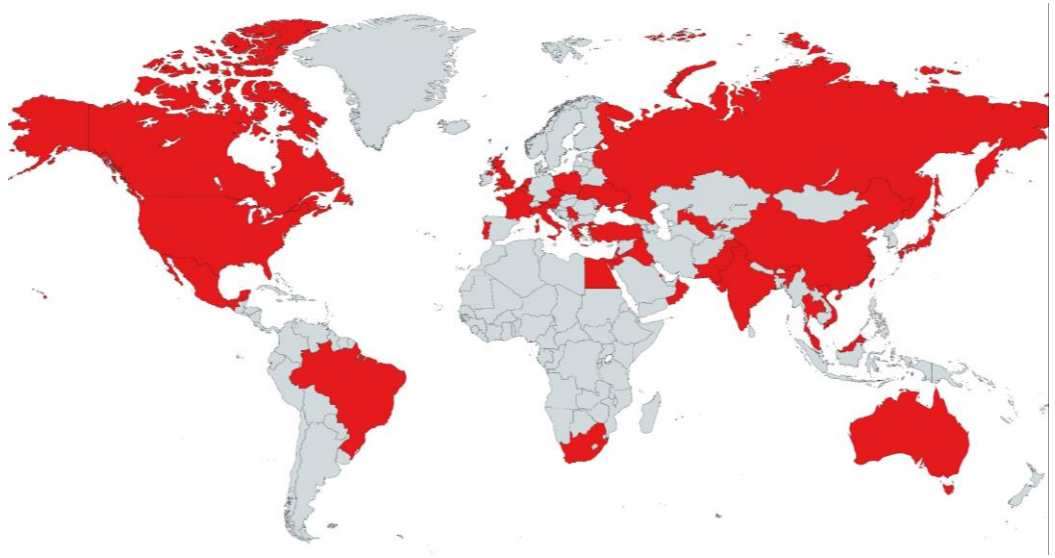
Widhalm K. et al. *J Pediatr* 2011;158:167

HICC

HoFH The International Clinical Collaborators

- Knowledge on HoFH is disjointed and scattered
- Need for robust aggregate data

- Investigator initiated consortium
- 161 collaborators, 38 countries

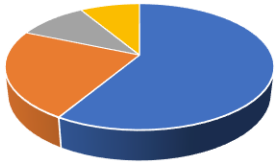


WHAT DATA IS COLLATED ?

Design: retrospective cohort

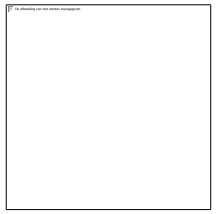
Inclusion criteria:
Clinical or genetic diagnosis of HoFH
Data available 2010 or later

Demographic data

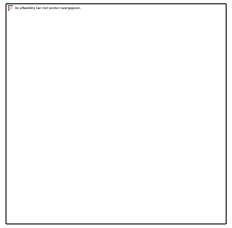


Genetic information

Medical history



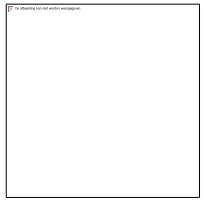
Lipid-lowering medication



Clinical data

Imaging data (summary)

Lab tests (summary)



Family history

Study population

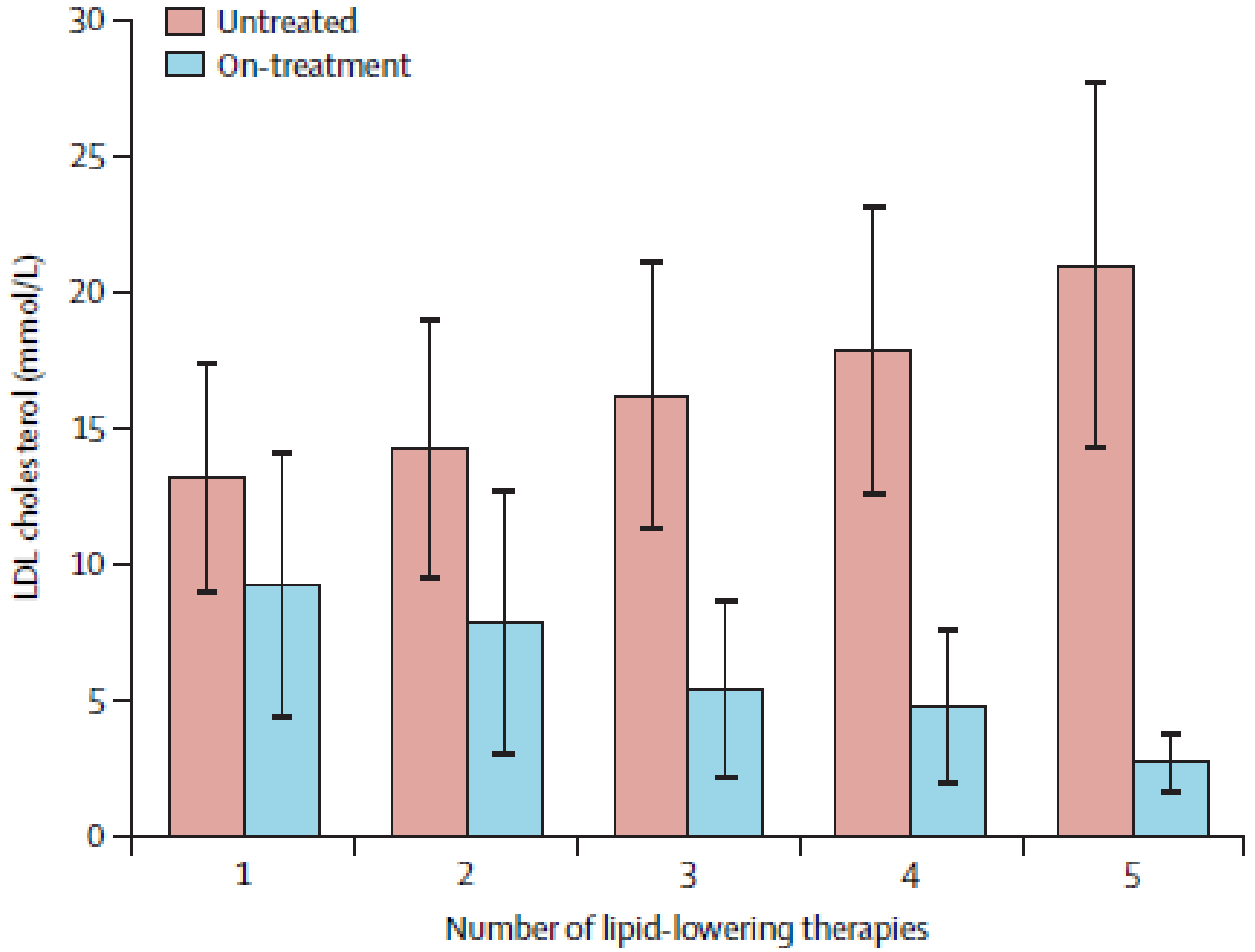
N = 751

- 48% male
- 53% from high-income countries
- 75% genetic diagnosis
- Median untreated LDL-C 14.7 (11.6-18.4) mmol/L

HoFH is diagnosed late

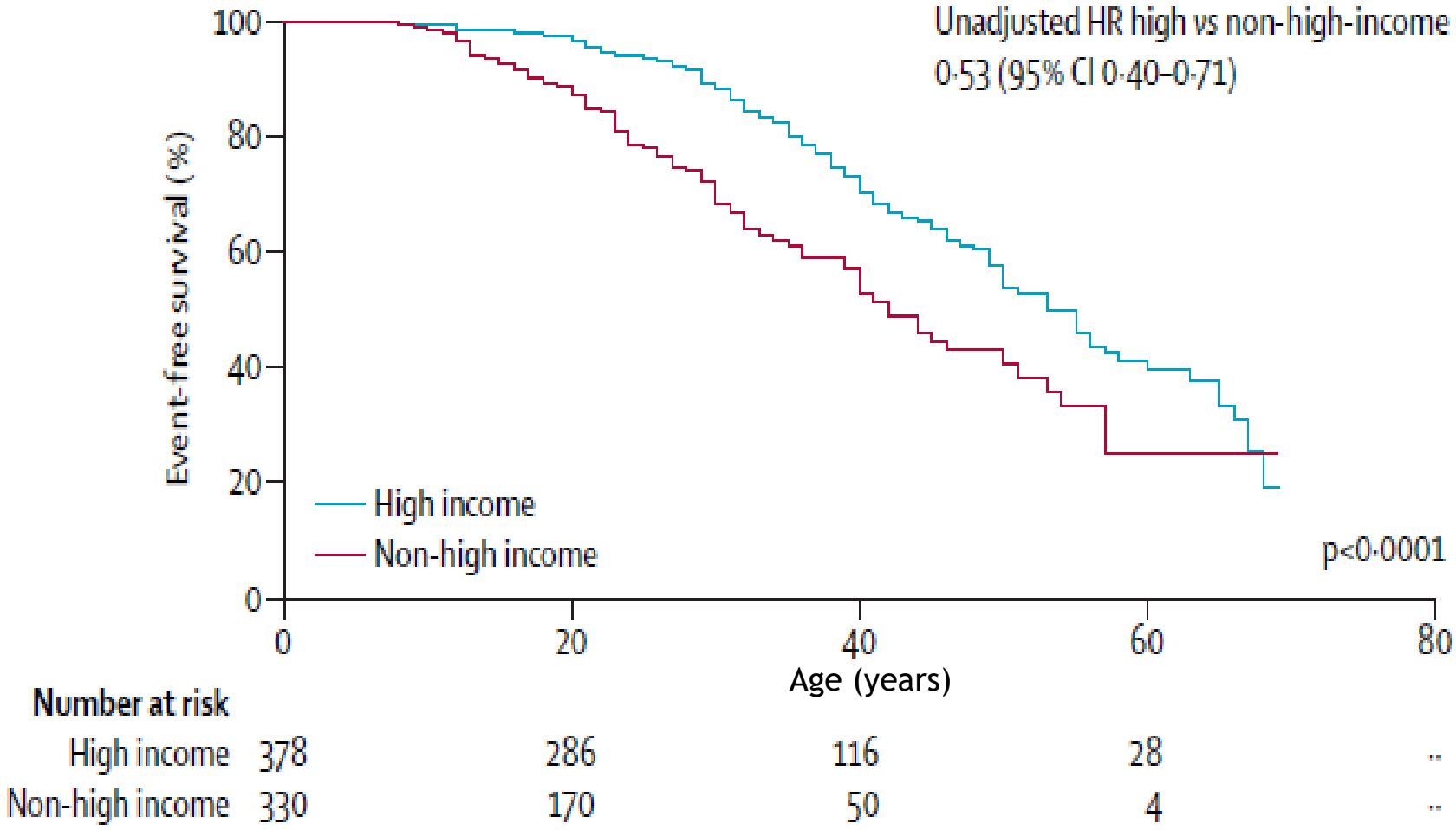
at a median age of 12 [6-27] years old
when nearly 1 in 10 already has cardiovascular disease

Tromp TR and HICC *Lancet* 2022



HoFH is undertreated: only 10.9% reach LDL-C goal

Tromp TR and HICC *Lancet* 2022



Tromp TR and HICC *Lancet* 2022

Take-home messages

- HoFH is a rare, life-shortening and difficult to treat lipid disorder
- With combination therapy, LDL-C goal attainment *is possible*
- We show a large global inequity in treatment and outcomes of HoFH

- Data-driven concerted action is required to reduce barriers to early diagnosis and effective treatment

HICC HoFH The International Clinical Collaborators

Acknowledgements

HICC Steering Committee

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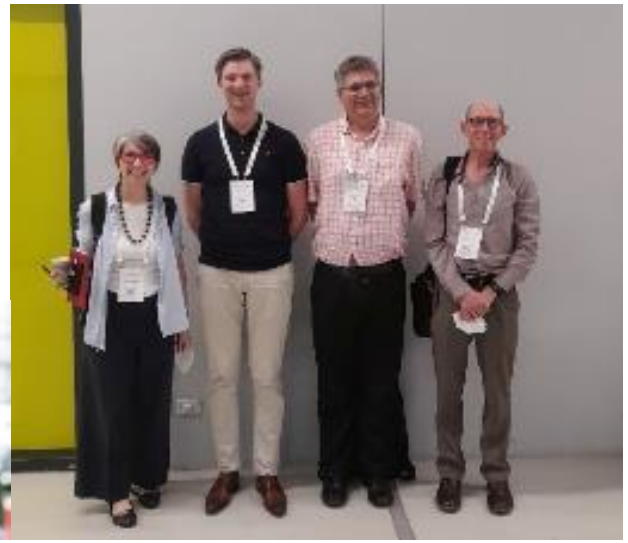

Homozygous Familial Hypercholesterolaemia International Clinical Collaborators:
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