HoFH WEBINAR TRILOGY

Advancing Knowledge, Care, and Community

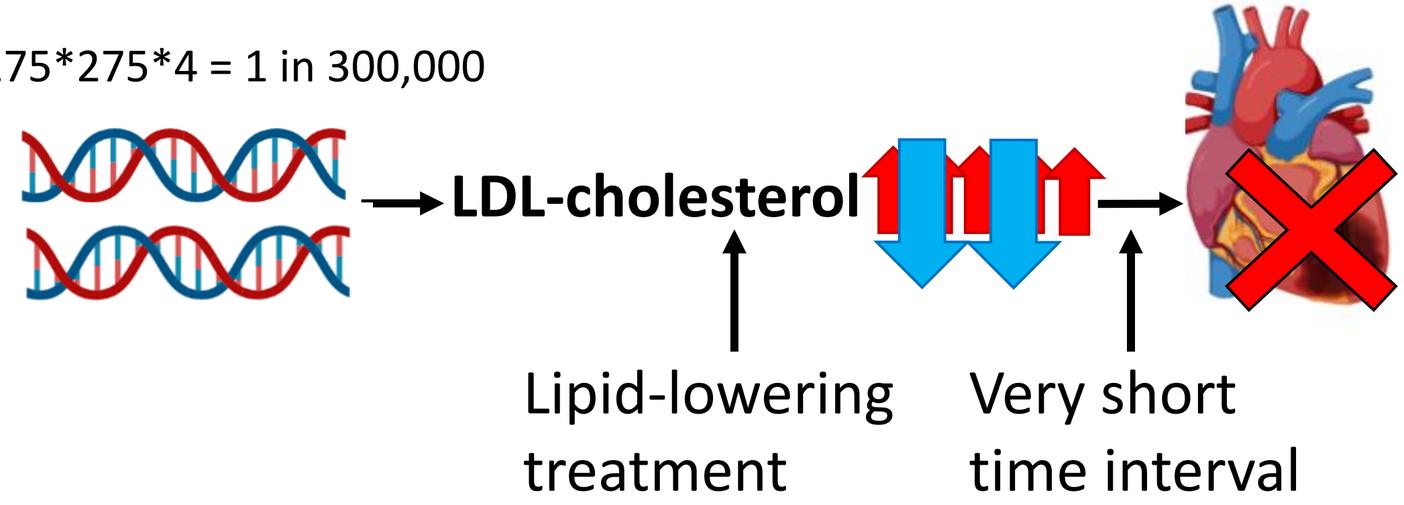
Homozygous Familial Hypercholesterolemia (HoFH)

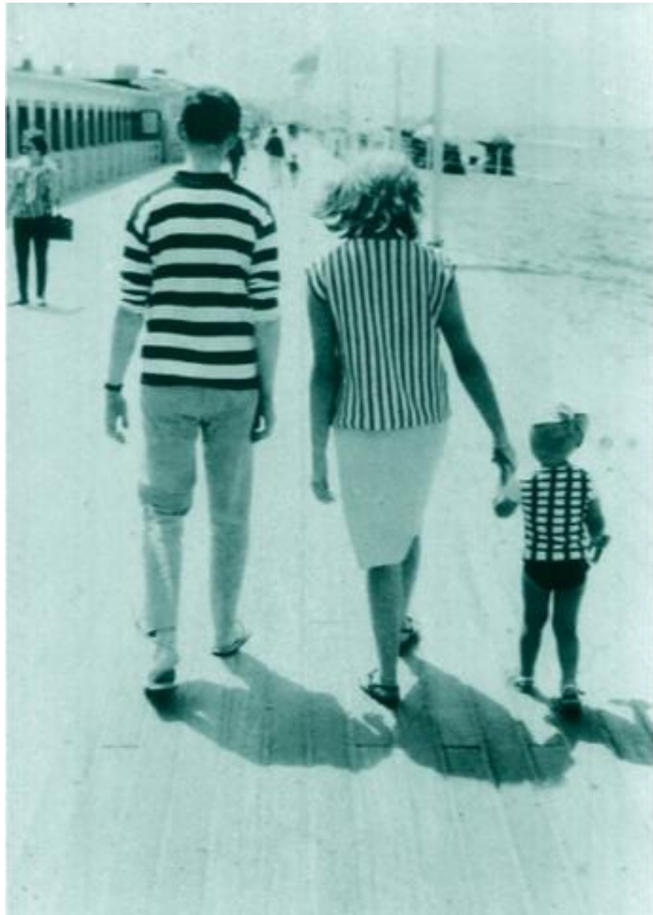
Prof. Albert Wiegman (The Netherlands)

FH Europe Foundation

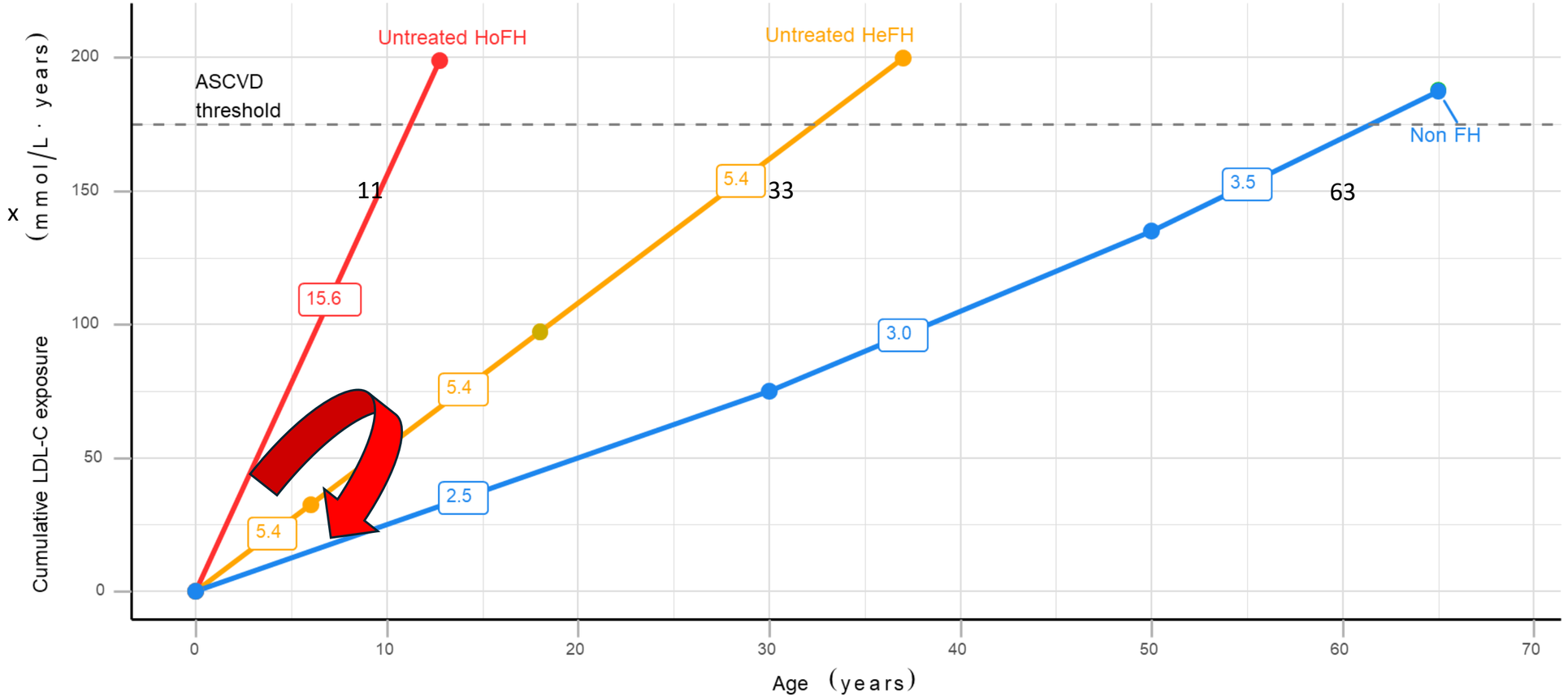
Homozygous Familial Hypercholesterolemia

1 in 275*275*4 = 1 in 300,000





Impact of starting lipid-lowering therapy



Current guidelines:

Start lipid-lowering treatment (LLT) from diagnosis onwards in children with homozygous FH

Graphical Abstract

Schonck et al, *Eur Heart J*, 2026 May 18;ehag357

Improving care for homozygous familial hypercholesterolaemia: key insights and future directions from the global HICC registry

Homozygous familial hypercholesterolaemia

A genetic condition inherited from both parents, leading to extremely high LDL-cholesterol levels from birth and early atherosclerotic cardiovascular disease

HoFH international clinical collaborators

- Collaboration of >160 contributors from over 90 institutions across 45 countries worldwide
- Data on >950 patients living with HoFH

Key insights from HICC

- **At diagnosis:** median age 12 [5.5–27.0] years and 9% ASCVD
- **Median LDL-C:** untreated 14.7 [12–18] mmol/L and treated 7.7 [5–12] mmol/L
- **Treatment:** global disparities in care across country income levels
- **ASCVD:** median age at first MACE 31 [22–42] years and death 37 [20–50] years
- **Sex differences:** lack of age gap in onset of ASCVD between sexes
- **Family planning care:** large variability, particularly around pregnancy

Knowledge gaps and future directions

- **Underdiagnosis:** global detection of HoFH remains markedly low
- **Care inequities:** screening and treatment gaps
- **Novel LLT and imaging:** impact on patient outcomes and best practices
- **ASCVD (risk factors):** e.g. aortic valve disease and lipoprotein(a)
- **Patient outcomes:** experiences with HoFH (e.g. quality of life)
- **Family planning and women's health:** care across the reproductive lifespan

HoFH still leads to severe morbidity and early mortality in women and men equally, emphasizing the urgent need for earlier diagnosis and equitable, intensified treatment worldwide to improve patient outcomes

ASCVD is a composite of cardiovascular death, myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, ischaemic stroke, carotid endarterectomy, and peripheral artery disease

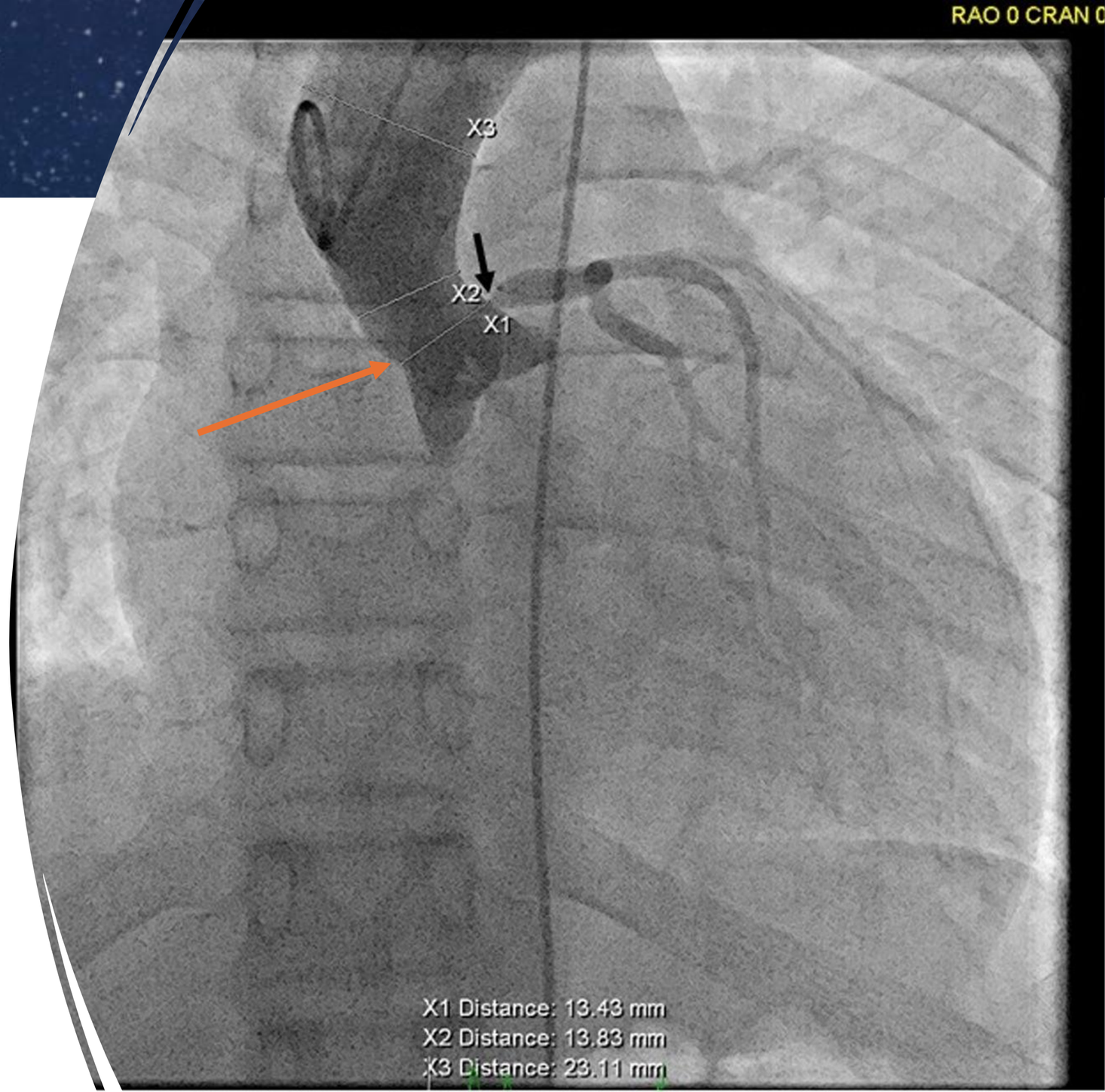
ASCVD, atherosclerotic cardiovascular disease; **HICC**, HoFH international clinical collaborators; **HoFH**, homozygous familial hypercholesterolaemia; **LDL-C**, low-density lipoprotein cholesterol; **LTT**, lipid-lowering-therapy; **MACE**, major adverse cardiovascular events

Schonck WAM, *et al. European Heart Journal.*

Homozygous FH

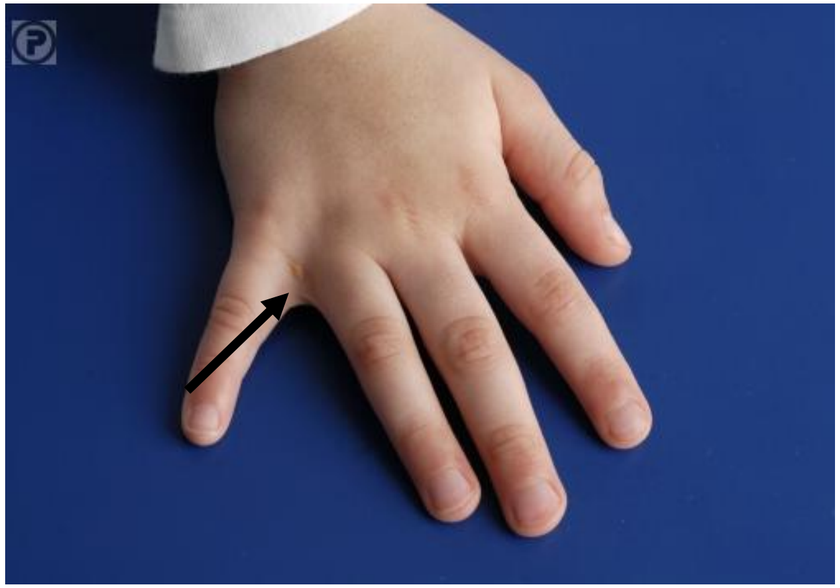
A 9-year-old girl with HoFH

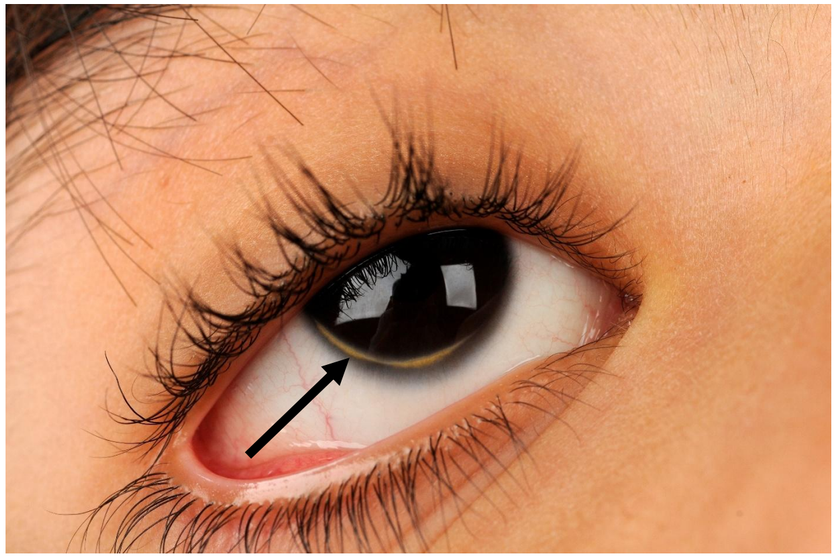
- Since a week, chest pain
- One week prior, presenting with:
  - a cardiac murmur
  - LDL-C 19 mmol/L (735 mg/dL)
- She survived cardiac surgery

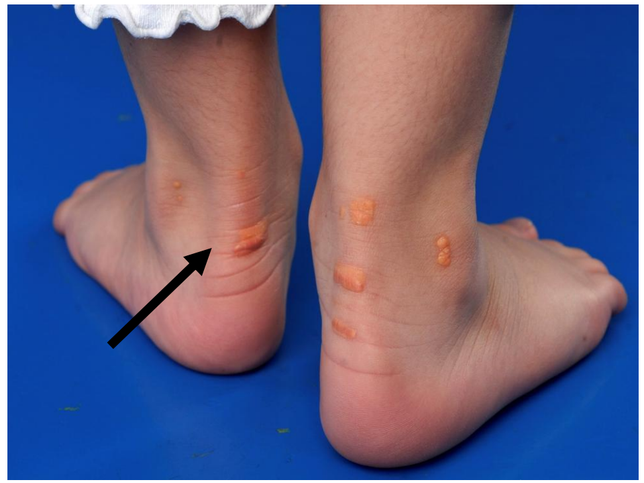


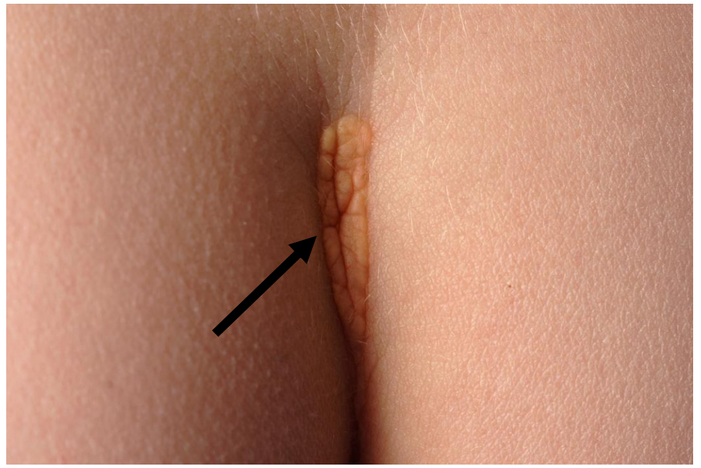
Goel et al, *JACC Case rep* 2024, Aug 7;29:102417

Find homozygous FH early on physical signs





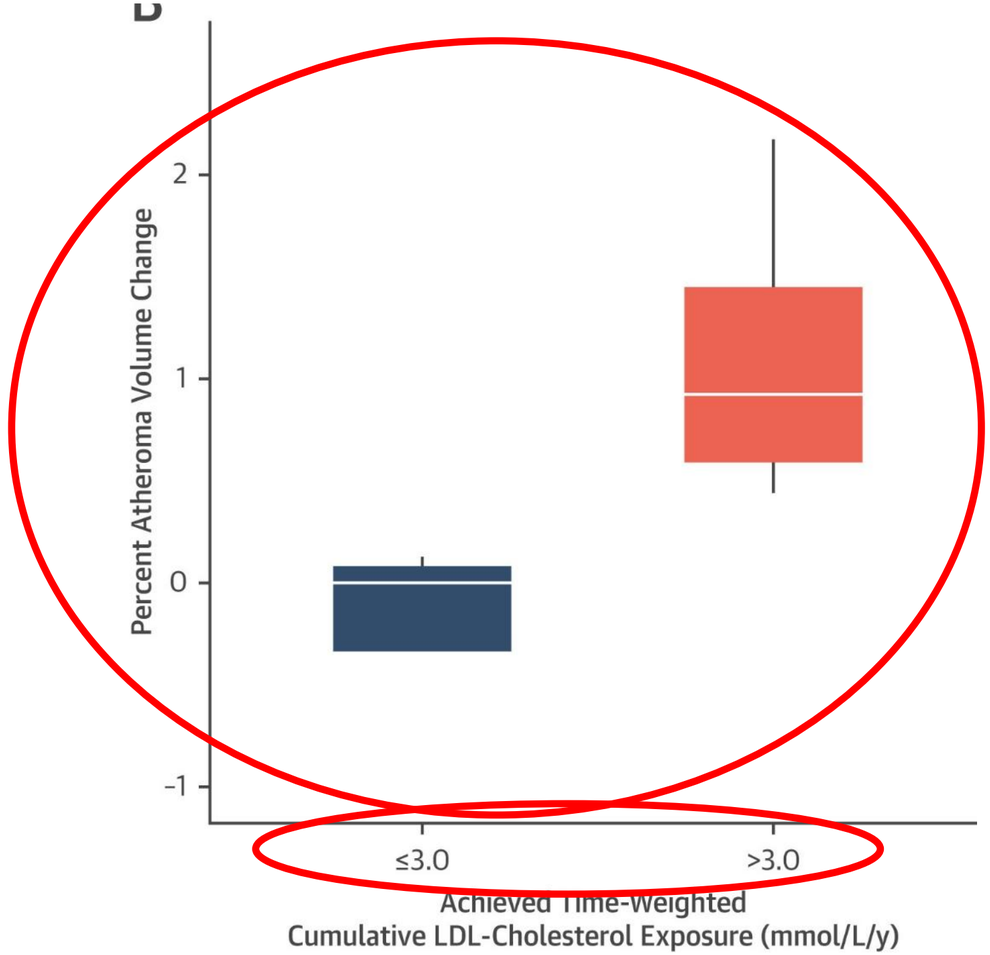




Wiegman - Unpublished - With consent of patients

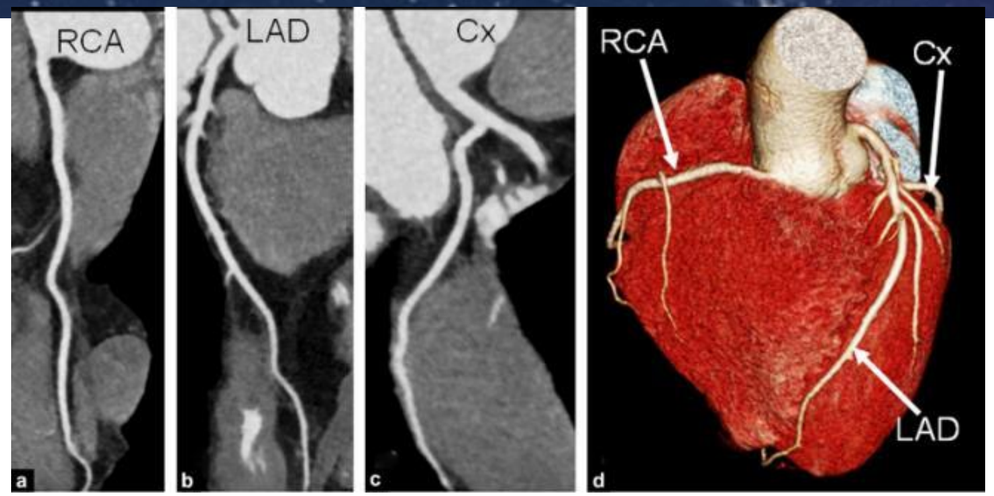
Decreased LDL-C Exposure Following ANGPTL3 Inhibition Reduces Coronary Plaque Development in HoFH

Patients who achieved cumulative LDL-C exposure below ≤3.0 mmol/L/year showed significantly lower % atheroma volume change after at least 6 months evinacumab.

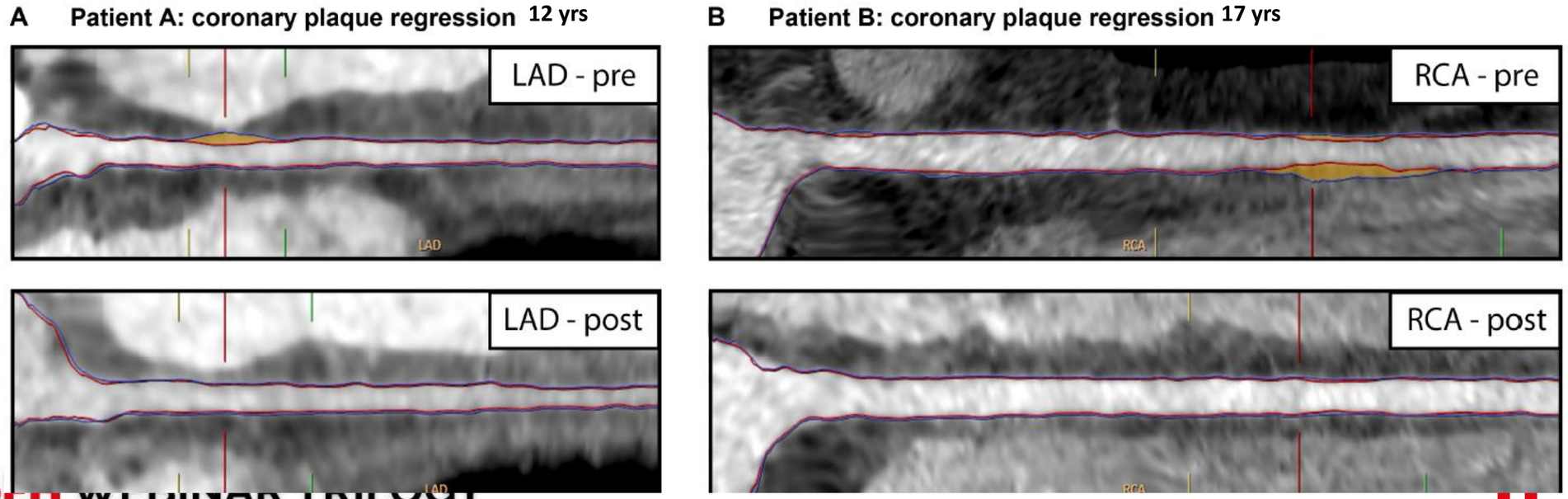


Schonck et al, *JACC Cardiovasc Imaging* 2024;17:1258-60

Evinacumab in adolescents with homozygous FH



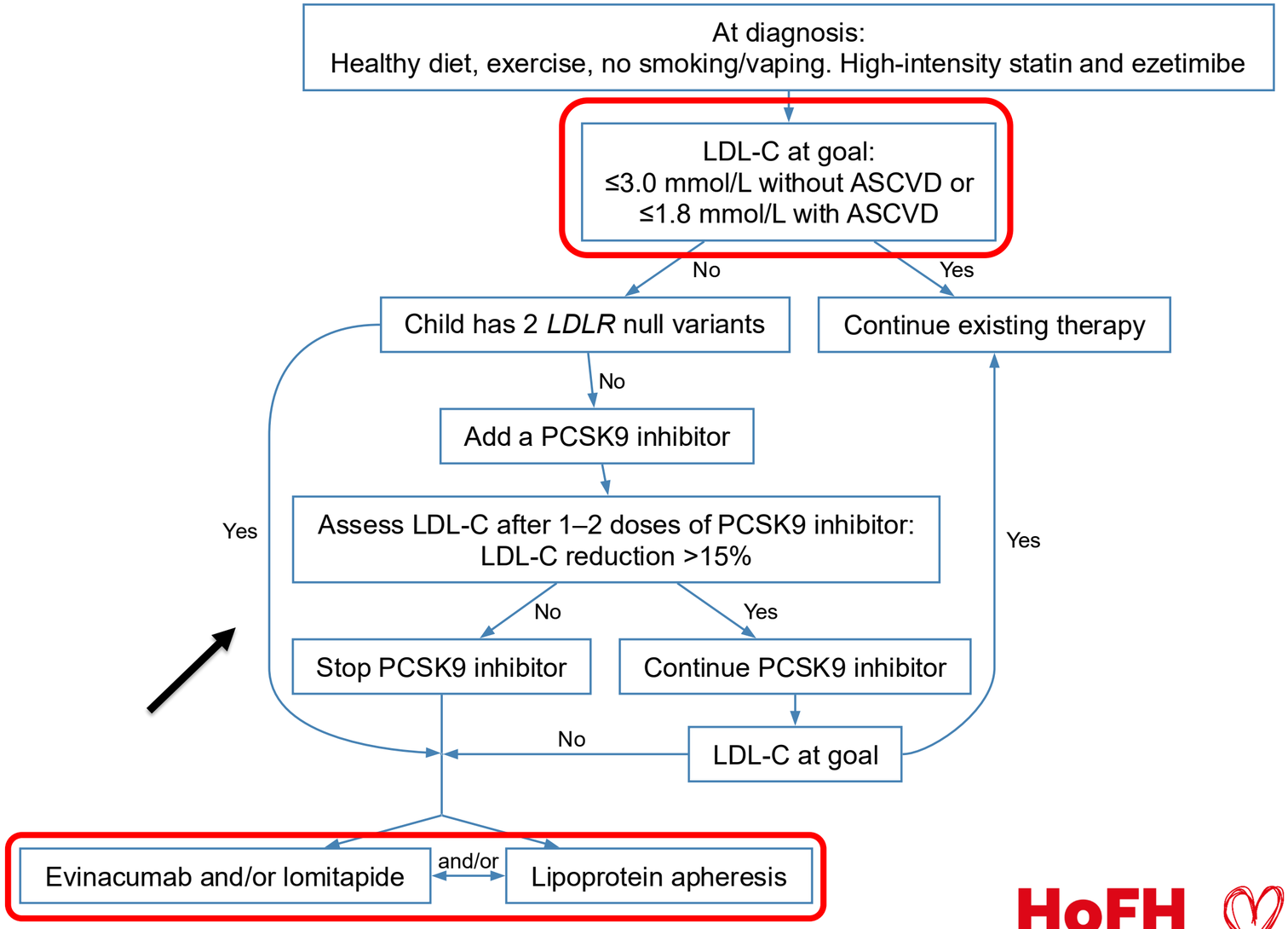
Coronary CT angiography



Plaques disappeared

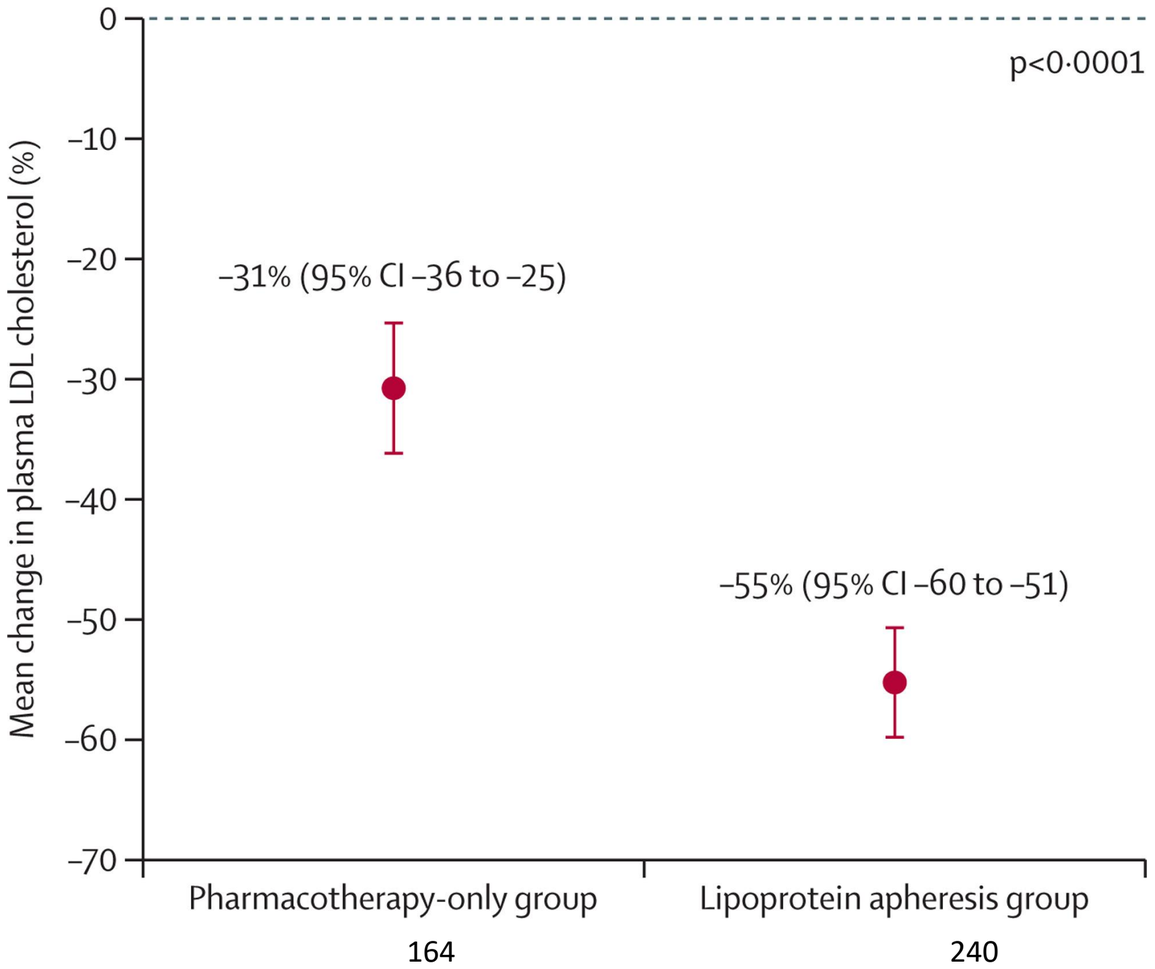
Reeskamp et al, *Atherosclerosis* 2021;327:13-7

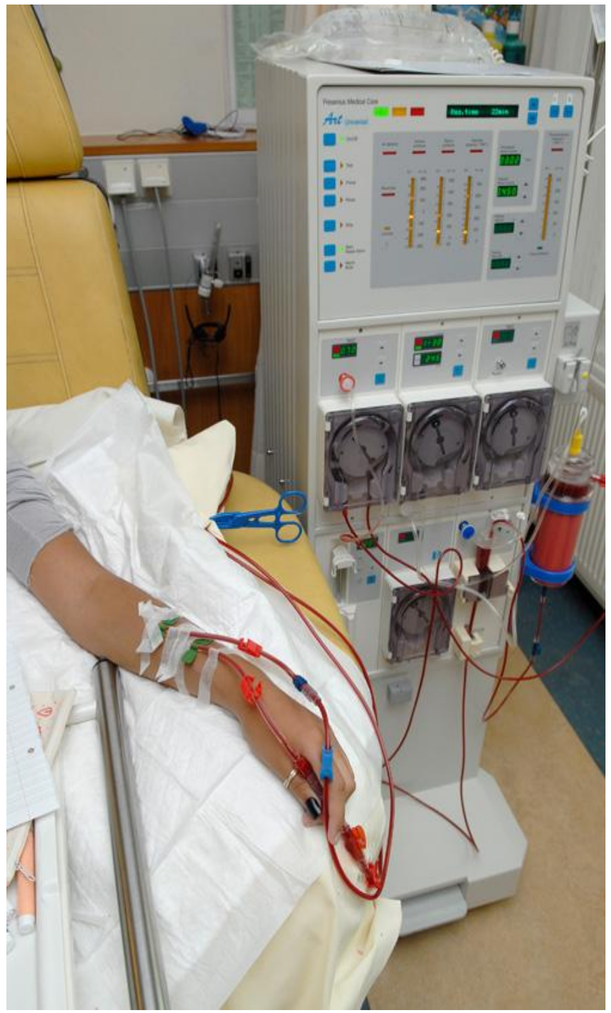
Treatment algorithm for children with HoFH



Wiegman et al, *Eur Heart J* 2026 May 25:ehag382

CV outcomes in patients with homozygous FH on LA initiated during childhood





Reijman et al, *Lancet Child Adolesc Health* 2024;8:491-9

LDLR-independent therapies in HoFH

Evinacumab

ANGPTL3 inhibitor:

- ↓ LDL-C independent of LDLR (effective in LDLR null/null patients)
- >48% LDL-C ↓ (children 5–17 yrs) on top of LLT

Approved:

- EMA from 6 months
- FDA from 12 months

Considerations:

- Intravenously once per 4 weeks

Lomitapide

MTP inhibitor:

- ↓ LDL-C independent of LDLR (effective in LDLR null/null patients)
- >50% LDL-C ↓ (children 5–17 yrs) on top of LLT

Approved:

- FDA from 2 years
- EMA from 5 years
- Oral daily

Considerations:

- Requires low-fat diet
- Hepatic & gastrointestinal side effects

LDLR-independent therapies enable **effective LDL-C reduction even without LDLR activity**

Wiegman et al, *Eur Heart J* 2026 May 25:ehag382