A project of D•A•CH-Gesellschaft Prävention von Herz-Kreislauf-Erkrankungen e.V.

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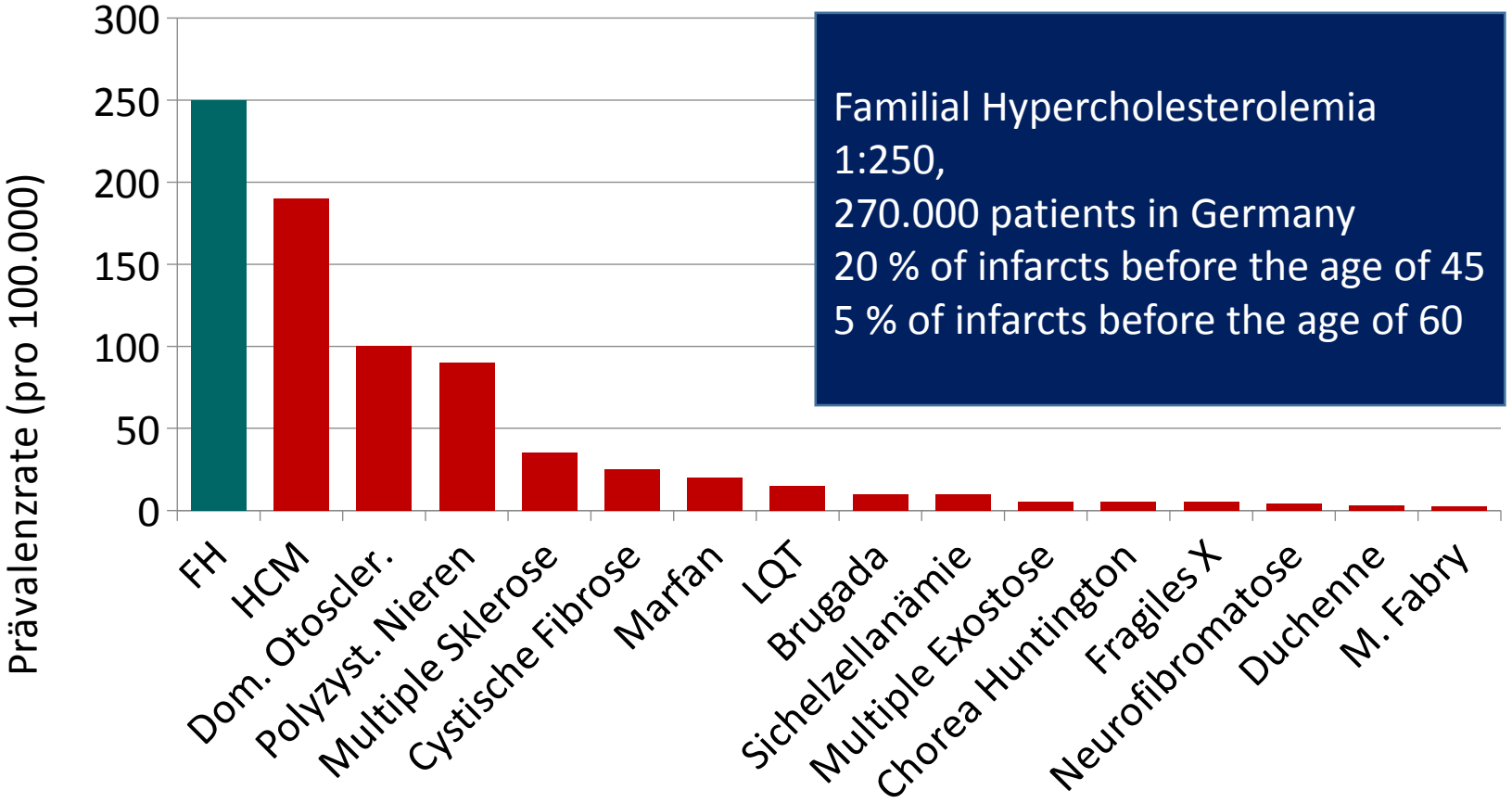
project lead CaRe High
Würzburg, 22.01.2016

What is Familial Hypercholesterolemia?

- Most frequent co-dominant, monogenic metabolic dysfunction in primary care (previous assumption of prevalence 1:500)
- mutations at LDL-R, ApoB-100, PCSK9
- Up to 10 percent of coronary patients under 55 years of age!
- Founder effect in specific populations
- characteristics:
  - distinctive hypercholesterolemia
  - more than 50 percent cumulative CHD-risk until the age of 50 for men
  - more than 40 percent cumulative CHD-risk until the age of 60 for women

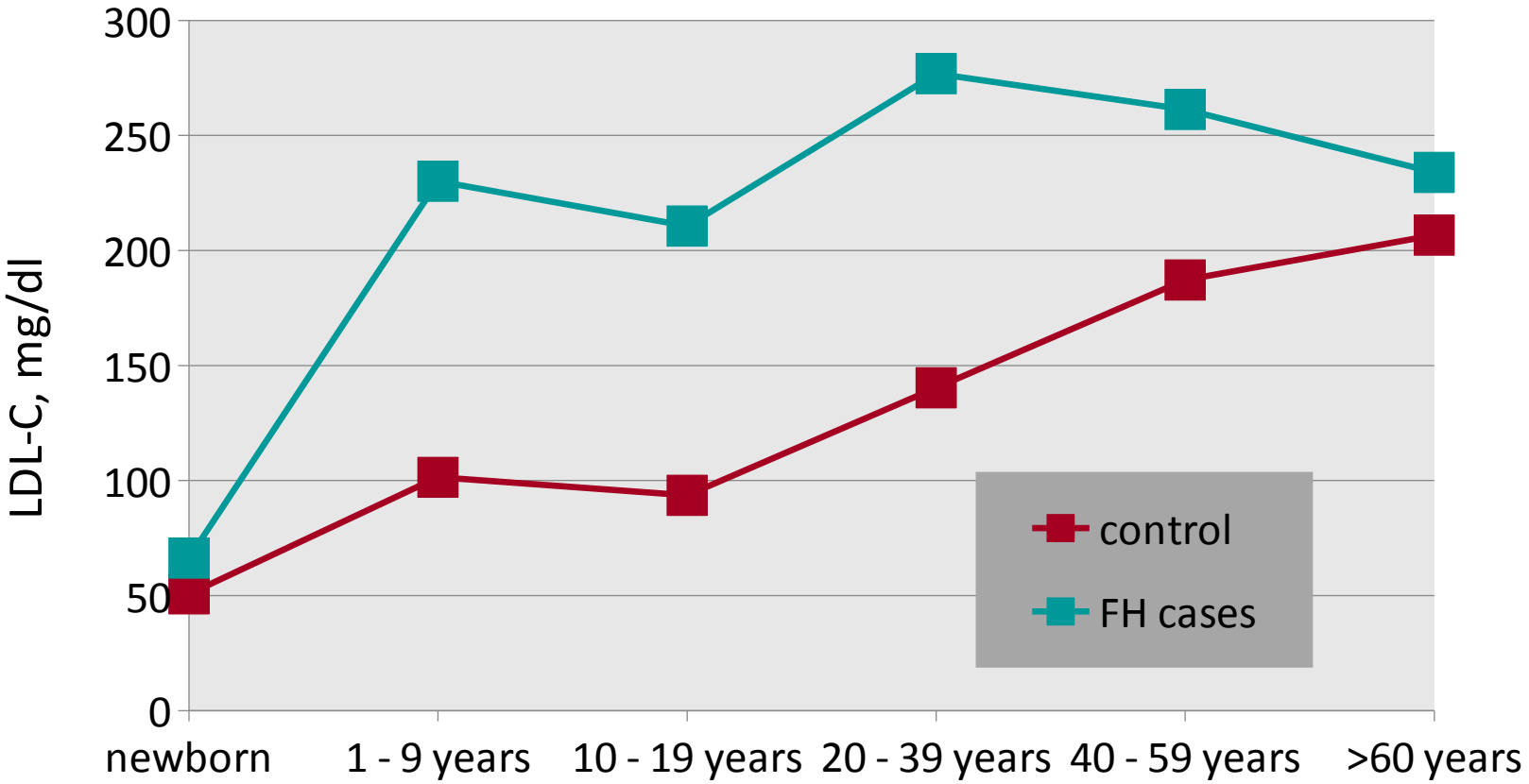
Common (Genetic) Disorders are...



Hopkins et al. J. Clin. Lipidol. 2011; Goldberg et al. J. Clin. Lipidol. 2011;
Sugisawa T et al. J. Atherosclero. Thromb 2012: 19:369. Thompson GR et al Curr Opin. Lipidol 2010;21 492;
Lianage KE et al. Crit. Rev. Clin Lab. Sci, 201148; 1. http://www.geneticalliance .org.uk.esucation3.html

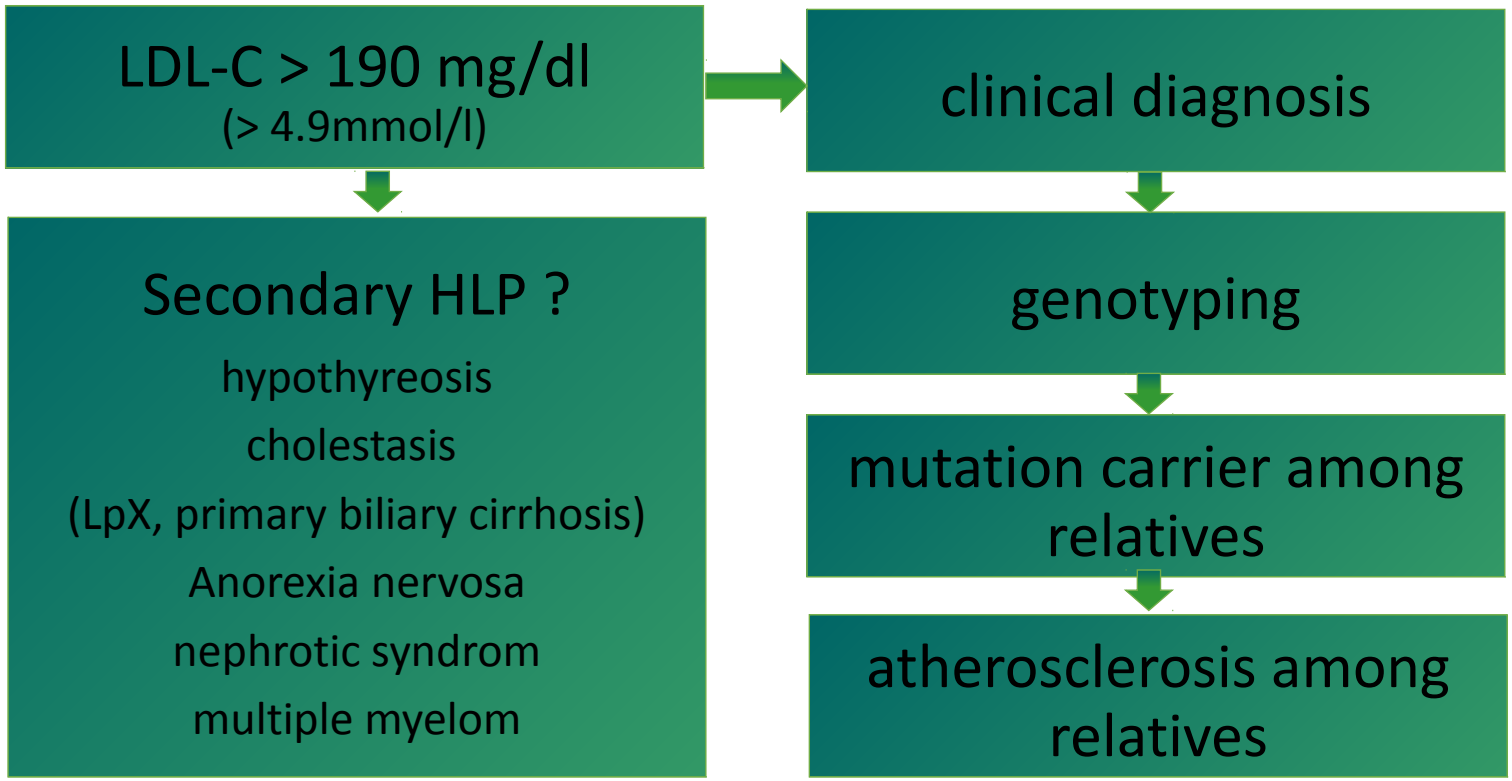
LDL-Cholesterol and Age

Meta-Analysis; 16.221 controls, 1.907 FH-Patients



Wald et al., BMJ 2007;
doi:10.1136/bmj.39300.616076.55

Diagnostic Procedure for Familial Hypercholesterolemia



Dutch Lipid Clinic Network criteria for diagnosis of heterozygous familial hypercholesterolaemia in adults

Group 1: family history	Points
(i) First-degree relative with known premature (<55 years, men; <60 years, women) coronary heart disease (CHD)	1
OR	
(ii) First-degree relative with known LDL cholesterol >95th percentile by age and gender for country	1
(iii) First-degree relative with tendon xanthoma and/or corneal arcus	2
OR	
(iv) Child(ren) <18 years with LDL cholesterol >95th percentile by age and gender for country	2

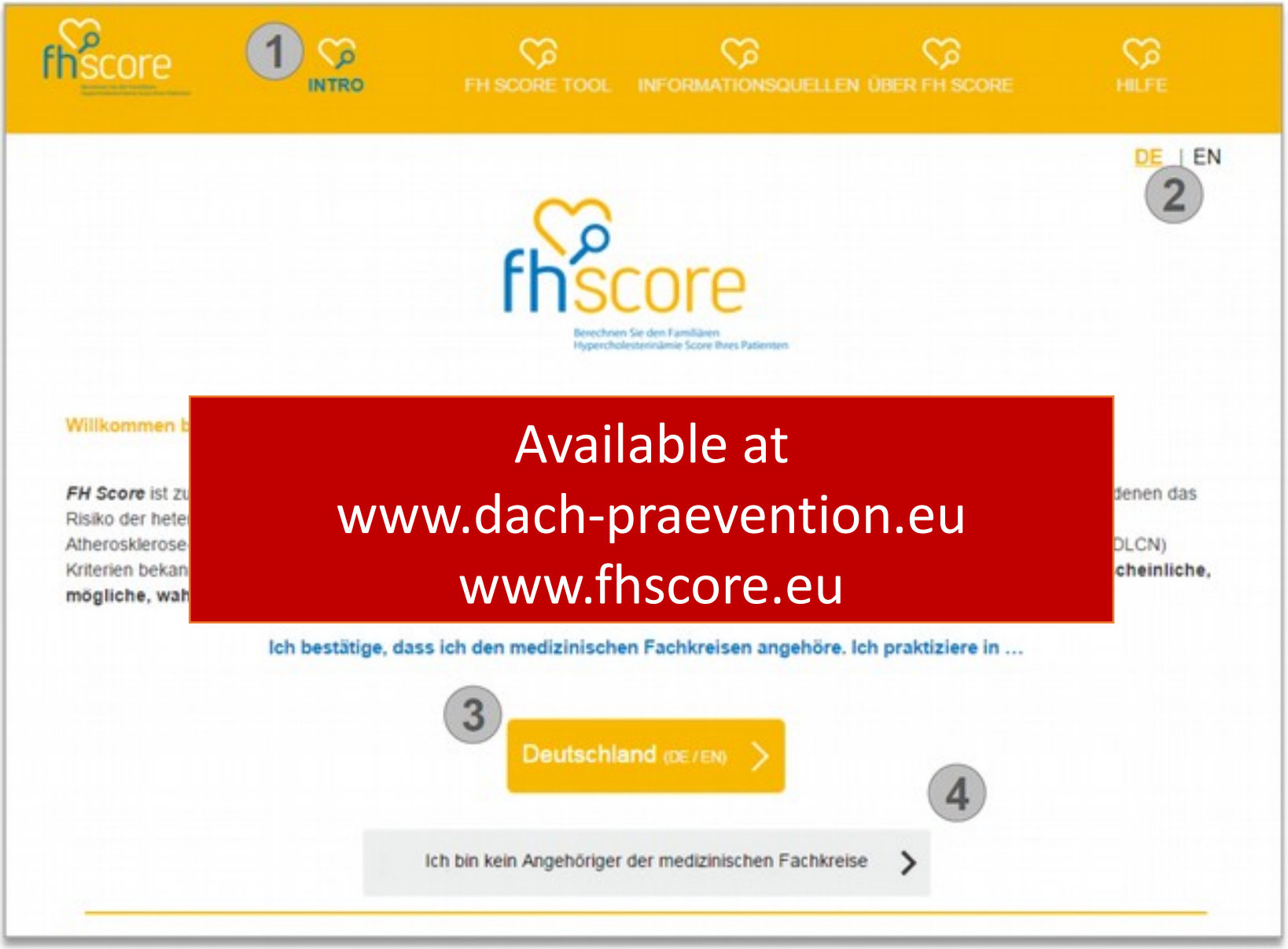
Group 2: clinical history	
(i) Subject has premature (<55 years, men; <60 years, women) CHD	2
(ii) Subject has premature (<55 years, men; <60 years, women) cerebral or peripheral vascular disease	1

Group 3: physical examination	
(i) Tendon xanthoma	6
(ii) Corneal arcus in a person <45 years	4

Group 4: biochemical results (LDL cholesterol)	
>8.5 mmol/L (>325 mg/dL)	8
6.5–8.4 mmol/L (251–325 mg/dL)	5
5.0–6.4 mmol/L (191–250 mg/dL)	3
4.0–4.9 mmol/L (155–190 mg/dL)	1

Group 5: molecular genetic testing (DNA analysis)	
(i) Causative mutation shown in the LDLR, APOB, or PCSK9 genes	8

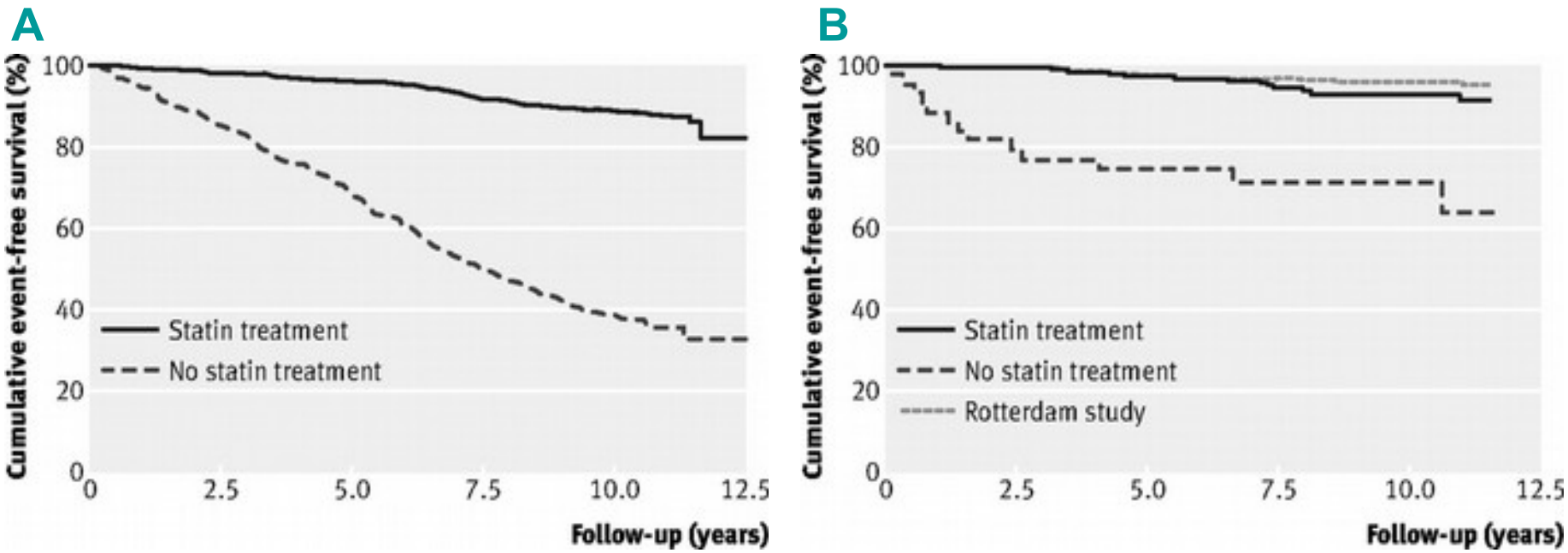
→ > 8 points definite FH; 6-8 points probable FH; 3-5 points possible FH; 0-2 points unlikely FH


fhscore
1
INTRO
FH SCORE TOOL
INFORMATIONSQUELLEN
ÜBER FH SCORE
HILFE
DE | EN
2
fhscore
Berechnen Sie den Familiären Hypercholesterinämie Score Ihres Patienten
Willkommen b
FH Score ist zu
denen das
Risiko der hete
Atherosklerose
DLCN)
Kriterien bekan
cheinliche,
mögliche, wah
Available at
www.dach-praevention.eu
www.fhscore.eu
Ich bestätige, dass ich den medizinischen Fachkreisen angehöre. Ich praktiziere in ...
3
Deutschland (DE / EN)
4
Ich bin kein Angehöriger der medizinischen Fachkreise

Benefit of Molecular Diagnostics

- carrier of mutations among relatives (children!) with low LDL-C
- via LDL-C 25% wrong classification among relatives
- cascade screening: 1 index patient -> 20 relatives -> 8 more patients
- common risk scores (PROCAM, Framingham, SCORE) underestimate CHD risk
- early start of therapy (prevention)
- improved therapy compliance
- stratification based on molecular defect
- cost efficient (NICE)

Statin Treatment Improves Prognosis for FH Patients



Better prognosis for FH patients under statin treatment (A)

… even if the treatment starts at age 55 (B)

Versmissen j, BMJ. 2008 Nov 11;337:a2423. doi: 10.1136/bmj.a2423.

Guidelines for treatment targets?

FH

ESC CVD Prevention

risk		LDL-C target (mg/dl)
low	SCORE < 1 %	< 115
moderate	SCORE 1-5 %	< 115
high	FH, hypertension, diabetes without RF and without organ damage, CKD (GFR 30-59 ml/min), SCORE 5-10 %	< 100
very high	CHD, PVD, CVE, diabetes with RF or organ damage, CKD (GFR < 30 ml/min), SCORE > 10 %	< 70

Perk J. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012) European Heart Journal 2012; 33, 1635–1701 doi:10.1093/eurheartj/ehs092

Familial Hypercholesterolemia in Europe

Situation in Germany

- prevalence about 1:300→ more than 270.000 patients in Germany, less than 10% diagnosed and properly treated
- half of the relatives of a FH-patient are at risk
- early diagnosis and treatment decreases the risk for CHD
- until 2014 there was no specific prevention program for FH in Germany
- At the end of 2014 we started a cascade screening program and registry for FH patients in Mannheim, which we expanded to more regions of Germany over 2015.

Benn, M., Watts, G. F., Tybjaerg-Hansen, A., & Nordestgaard, B. G. (2012). Familial Hypercholesterolemia in the Danish General Population: Prevalence, Coronary Artery Disease, and Cholesterol-Lowering Medication. The Journal of Clinical Endocrinology & Metabolism, 97(11), 3956–3964. doi:10.1210/jc.2012-1563

Nordestgaard, B. G., Chapman, M. J., Humphries, S. E., Ginsberg, H. N., Masana, L., … Descamps, O. S. (2013). Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease: consensus statement of the European Atherosclerosis Society. European Heart Journal, 34(45), 3478–90a. doi:10.1093/eurheartj/eht273

Project Aims

- investigating the state of therapy and care of patients with FH
- identify / recruit more FH patients
- Assessing the effectivity of a cascade screening for FH in a german cohort
- Setting up a nation-wide registry for FH-patients
- improving the medical care situation for FH patients

Study Inclusion Criteria

- LDL-C (without treatment) above 190 mg/dl
- cholesterol above 290 mg/dl
- patients with tendon xanthomas
- positive family history of hypercholesterolemia
- positive family history for myocard infarct under 50 years of age for grandparents, uncles, aunts or under 60 years of age for parents, siblings or children
- first and second degree relatives of FH patients regardless of LDL-C-Level

Cascade Screening

- Identification of index patients by physicians and lipid clinics by the means of already existing blood levels and inclusion criteria
- further diagnostics (incl. genetic screening) and treatment of the index patient by the attending physician
- Patient questionaire issued by a study assistant
- Support with contacting and informing relatives about FH
- Inclusion (voluntarily!) of the index patient and relatives in the FH registry

The CaRe High Team

Mannheim, Rhein-Neckar-Region, Southern and West Germany (sponsored by AMGEN GmbH, Munich)

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Data Manager

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Data Manager

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Implementation of the Cascade Screening

- ✓ compiling of all study documents
- ✓ Ethical approval from the ethics committee Baden-Württemberg
- ✓ Further ethical approval from the ethics committees in Saarland, Bremen, Rhineland-Palatinate, Hessen, Bayern, Berlin
- ✓ Implementation of the data bank and screening software PASS Clinical FH
- ✓ Recruiting of participating physicians and lipid clinics in the Rhine-Neckar Region and in Germany

Cooperations

CaRe High

Gesundheitsnetz Rhein-Neckar-Dreieck e.V.

Dr. med. Claus Köster

GGM Gesundheitsprojekt Mannheim e.G.

Dr. med. Werner Besier
Dr. med. Manfred Mayer

CholCo e.V. Cholesterin & Co

Michaela Wolf

Boehringer Ingelheim

Dr. med. Michael Schneider
Company Medical Service
Project „Fit im Job – Fit im Leben“

nutriCARD
COMPETENCE CLUSTER for NUTRITION and CARDIOVASCULAR HEALTH

Dr. rer. nat. Christine Dawczynski
Prof. Dr. Stefan Lorkowski
Friedrich-Schiller-Universität Jena

Participating Physicians in Mannheim and Vicinity

- Praxis Dr. med. Manfred Mayer, Mannheim, 4 patients
- Praxis Dr. med. Jürgen Merke, Bensheim, about 20 patients
- Praxis Dr. med. Cornelius Müller, Mannheim, about 5 patients
- Praxis am Lanzgarten, Frau Dr. med. Füllgraf-Horst, Mannheim, 4 patients
- Nierenzentrum Mannheim, Dr. Frank Leistikow, Mannheim, at least 10 patients
- Diabetologische Schwerpunktpraxis, Herr Dr. med. Thomas Segiet, Speyer, at least 2 patients
- Praxis Frau Dr. med. Melanie Schüler, Hirschberg, at least 2 families
- Praxis Dr. med. Friebe, Gernsheim, at least 1 patient
- Lipidambulanz Uniklinikum Heidelberg, OA Dr. med. Stefan Kopf, about 10 new patients per month

Cooperations with Lipid Specialists I

Prof. Dr. med. Ulrich Laufs,
Universitätsklinikum des
Saarlandes, Homburg

Prof. Dr. med. Elisabeth
Steinhagen-Thiessen,
Lipidambulanz Charité Berlin

Prof. Dr. med. Gerald Klose,
Bremen

Cooperations with Lipid Specialists II

Prof. Dr. med. Ulrich Julius
Innere
Medizin/Stoffwechselkrankheiten
Medizinische Klinik und Poliklinik III
Universitätsklinikum
Carl Gustav Carus Dresden

Dr. med. Britta Otte,
Lipidambulanz Universitätsklinik
Münster

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Deutsches Herzzentrum, München

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Stoffwechselambulanz,
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Klinikum der Universität München

Prof. Dr. med. Klaus Parhofer,
Medizinische Klinik und Poliklinik II
Klinikum der Universität München

Main Problems and Challenges

- recruiting of participating physicians is difficult (cold calling)
- time between first contact and signing of the cooperation contract: 8 to 10 weeks
- time between signing the contract and first patient inclusion: 2 weeks to up to one year
- only indirect contact to the relatives of an index patient is allowed

Future Tasks

- securing ethics approvals for Westfalen-Lippe, University Heidelberg, LMU München, University Clinics Dresden, University of Cologne
- economic evaluation of the project
- further recruiting of physicians and lipid clinics


рахмат
danke
謝謝
ngiyabonga
teşekkür ederim
Баярлалаа
спасибо
taafetai lava
mersi
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dank je
misaotra
blagodaram
vinaka
kiitos
dankie
dhanyavad
thank you
gracias
tapadh leat
paldies
хвала
asante
mochchakkeram
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hvala
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ありがとう
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terima kasih
rahmet
diolch
dhanyavadagalu
shukriya
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merci