



OVERVIEW OF THE CURRENT STATUS OF FAMILIAL HYPERCHOLESTEROLAEMIA CARE IN OVER 60 COUNTRIES

—

THE EAS FAMILIAL HYPERCHOLESTEROLAEMIA STUDIES COLLABORATION (FHSC)

EAS FHSC Investigators

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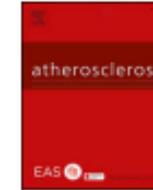


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Overview of the current status of familial hypercholesterolaemia care in over 60 countries - The EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC)



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Methods

Survey among EAS FHSC National Lead Investigators (NLIs)

- 73 NLIs responded
- 63 countries (out of the 68 countries in the EAS FHSC at the time of the survey)

Survey queries

1. Available information on FH in the country
2. FH programmes and initiatives
3. FH management in the country

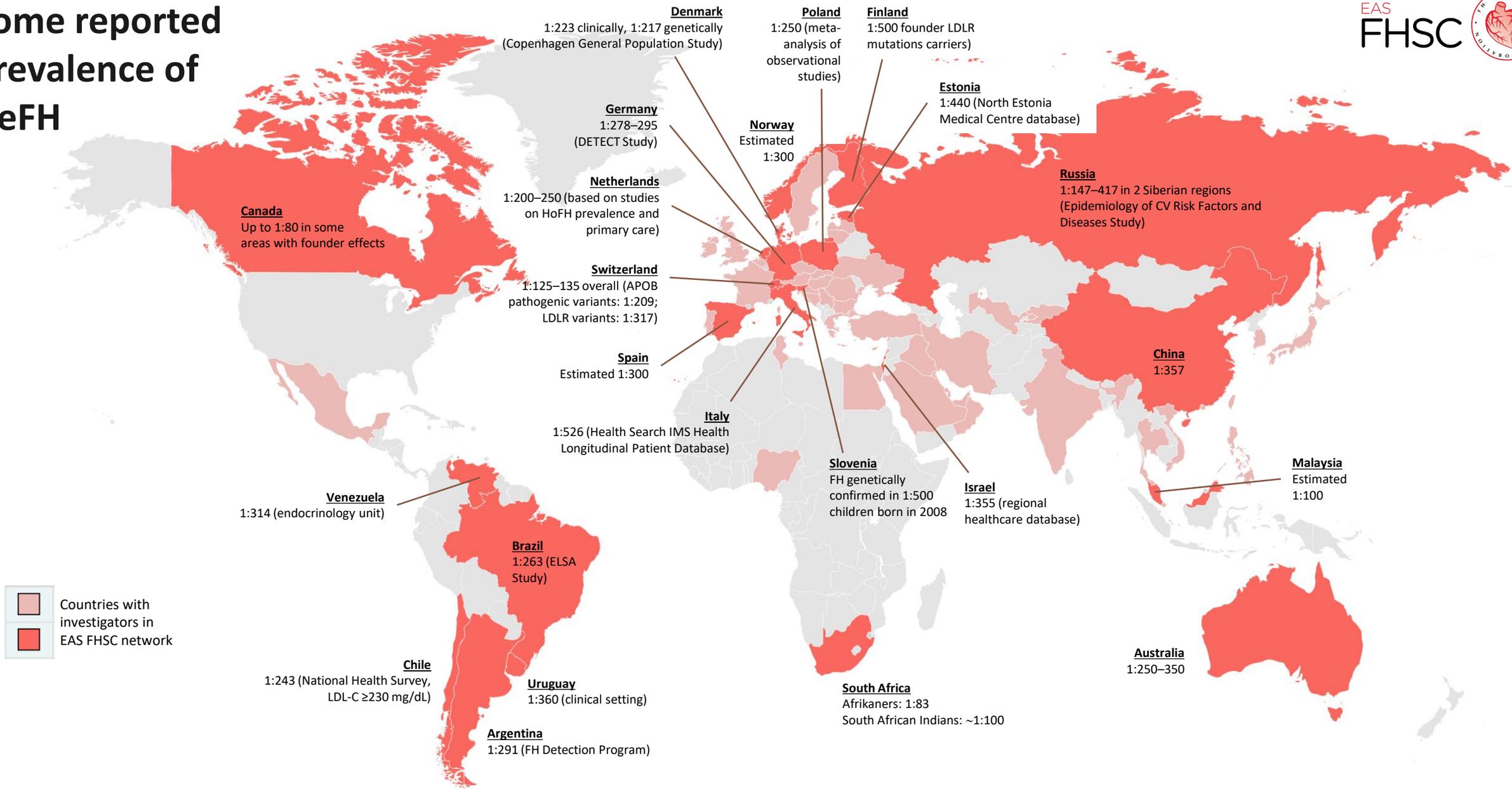
Table 1
FH diagnostic criteria and availability of therapies in the different countries involved in the EAS FHSC network and some reported data on prevalence of HeFH.

	FH diagnosis criteria commonly used in clinical practice	Availability of therapies for FH apart from statins (at the time of the present article submission) (statin therapy, including high-intensity statins, available in all countries listed)			Some reported specific data on prevalence of HeFH (see text for details and references)
		Ezetimibe	PCSK9 inhibitors	Lipoprotein apheresis	
AFRICA					
Nigeria	SB	No	No	No	
South Africa	Clinical diagnosis, supported by genetic diagnosis for founder mutations in certain ethnic groups	Yes	No	No	Afrikaner population: 1:83; South African Indian population: approx. 1:100
AMERICAS					
Argentina	DLCN	Yes	Yes	Limited (one private centre)	1:291 (FH Detection Program)
Brazil	DLCN	Yes	Yes	No	1:263 (ELSA Study)
Canada	Canadian FH definition; DLCN; SB	Yes	Yes	Yes	Up to 1:80 in some areas with founder effects
Chile	DLCN	Yes	No	No	1:243 (National Health Survey, LDL-C \geq 230 mg/dL)
Mexico	DLCN; SB	Yes	Yes (only private healthcare)	No	
Uruguay	DLCN	Yes	Yes	No	1:360 (clinical setting)
Venezuela	Clinical diagnosis	Limited	No	No	1:314 (endocrinology unit)
EASTERN MEDITERRANEAN					
Egypt	DLCN	Yes	Yes	No	
Iran	DLCN	Yes	No	No	
Iraq	DLCN	Yes	No	No	
Kuwait	DLCN	Yes	Yes	No	
Lebanon	MEDPED	Yes	Yes	Yes	
Oman	DLCN	Yes	Yes	Yes	
Qatar	DLCN	Yes	Yes	Yes	
Saudi Arabia	SB	Yes	Yes	Yes	

Country	Strategy	Yes	Yes	Yes	Notes
EUROPE					
Austria	DLCN	Yes	Yes	Yes	
Belgium	DLCN	Yes	Yes	Yes	
Bosnia and Herzegovina	DLCN	No	No	No	
Bulgaria	DLCN	Yes	Yes	No	
Croatia	MEDPED	Yes	Yes	Yes	
Cyprus	Definitive diagnosis (TC > 260 mg/dl if < 16 years; TC > 290 mg/dl in adults; LDL-C > 190 mg/dl in adults and tendon xanthoma in patient or 1st/2nd degree relative)	Yes	Yes	Yes	
Czech Republic	Modified MEDPED	Yes	Yes	Yes	
Denmark	DLCN; SB	Yes	Yes	Yes	1:223 clinically, 1:217 genetically (Copenhagen General Population Study)
Estonia	DLCN	Yes	Yes	Yes	1:440 (North Estonia Medical Centre database)
Finland	DLCN	Yes	Yes	Yes	1:500 founder LDLR mutations carriers
France	DLCN	Yes	Yes	Yes	
Germany	DLCN; SB	Yes	Yes	Yes	1:278–295 (DETECT Study)
Greece	DLCN	Yes	Yes	Yes	
Hungary	DLCN	Yes	Yes	Yes	
Ireland	DLCN	Yes	Yes (early access programme only)	No	
Israel	MEDPED	Yes	Yes	Yes	1:355 (regional healthcare database)
Italy	DLCN	Yes	Yes	Yes	1:526 (Health Search IMS Health Longitudinal Patient Database)
Kyrgyzstan	DLCN	No	No	No	
Latvia	DLCN; LDL-C 95th percentile in cascade screening for relatives	Yes	Yes	No	
Lithuania	DLCN	Yes	Yes	Yes	
Malta	DLCN	Yes	Only exceptionally	No	
Netherlands	DLCN	Yes	Yes	Yes	1:200–250 (based on studies on HoFH prevalence and primary care)
Norway	Genetic testing; if negative, clinical diagnosis DLCN	Yes	Yes	Yes	Estimated 1:300
Poland	Genetic testing; DLCN	Yes	Yes	Yes	1:250 (meta-analysis of observational studies in Poland)
Portugal	SB	Yes	No	Yes	
Russia	DLCN	Yes	Yes	Yes	1:147–417 in 2 Siberian regions (Epidemiology of Cardiovascular Risk Factors and Diseases Study)

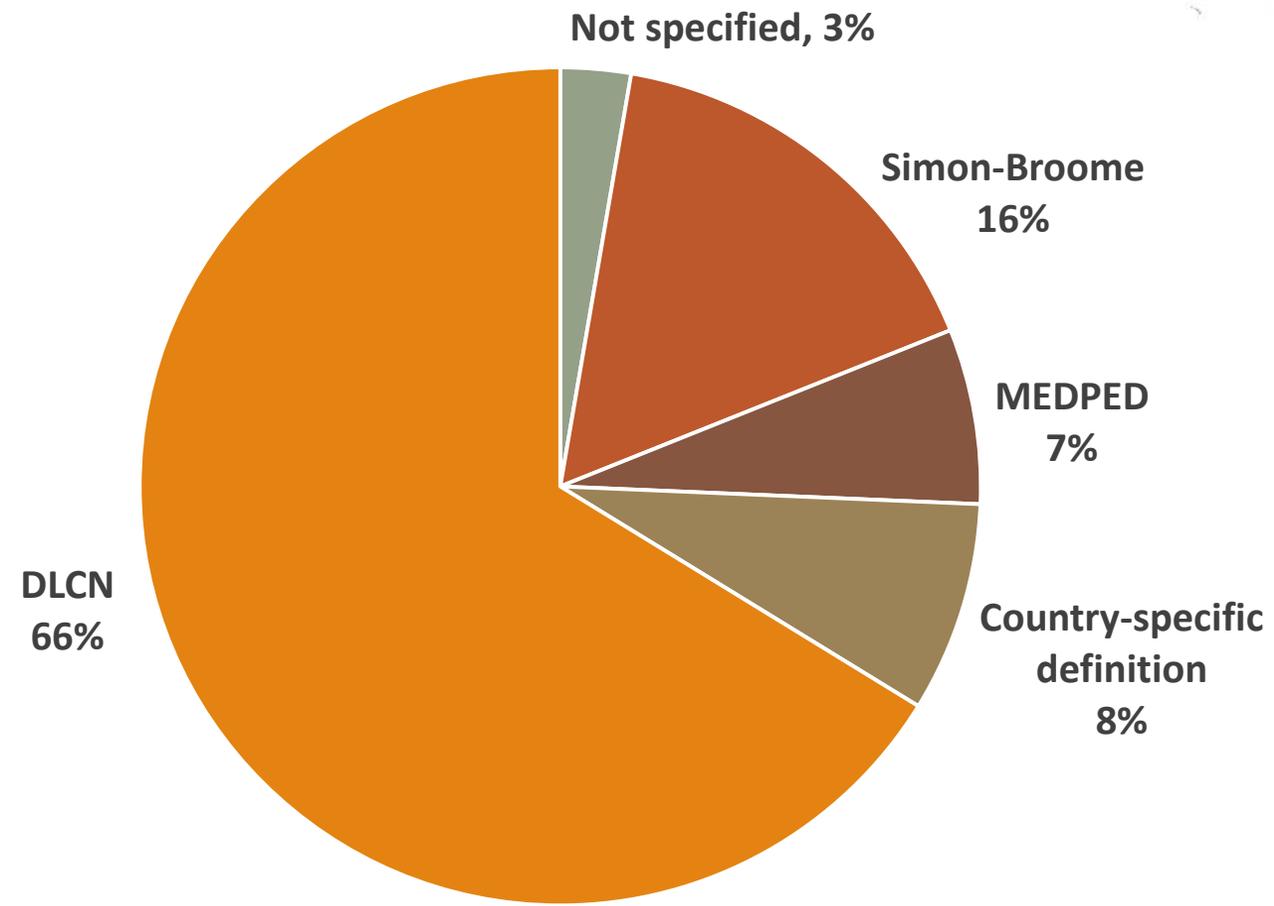
Serbia	DLCN	Yes	Yes	Yes	
Slovakia	DLCN; SB; MEDPED	Yes	Yes	No	
Slovenia	Children: genetic testing; Adults: DLCN	Yes	Yes	Yes	Genetically confirmed FH in 1:500 children born in 2008
Spain	DLCN	Yes	Yes	Yes	Estimated 1:300
Switzerland	Genetic testing (SAPPHIRE-FH Program); DLCN	Yes	Yes (limited)	No	1:125–135 overall (<i>APOB</i> pathogenic variants: 1:209; <i>LDLR</i> variants: 1:317)
Turkey	DLCN	Yes	Yes	Yes	
Ukraine	MEDPED; DLCN	No	Only in trials on HoFH	No	
United Kingdom	SB; DLCN	Yes	Yes	Yes	
Uzbekistan	DLCN	Yes	No	Yes (private clinics)	
SOUTH EAST ASIA AND WESTERN PACIFIC					
Australia	DLCN	Yes	Yes	Yes	1:250–350
China	DLCN; Chinese FH criteria	Yes	No	Yes (limited)	1:357
Hong Kong	DLCN	Yes	Yes	Yes (plasmapheresis)	
India	DLCN; SB	Yes	No	No	
Japan	JAS criteria	Yes	Yes	Yes	
Malaysia	DLCN; SB	Yes	Yes	Yes	Estimated 1:100
Singapore	SB	Yes	Yes	No	
Taiwan	DLCN; Taiwan FH criteria	Yes	Yes	Yes	
Vietnam	DLCN	Yes	No	No	

Some reported prevalence of HeFH



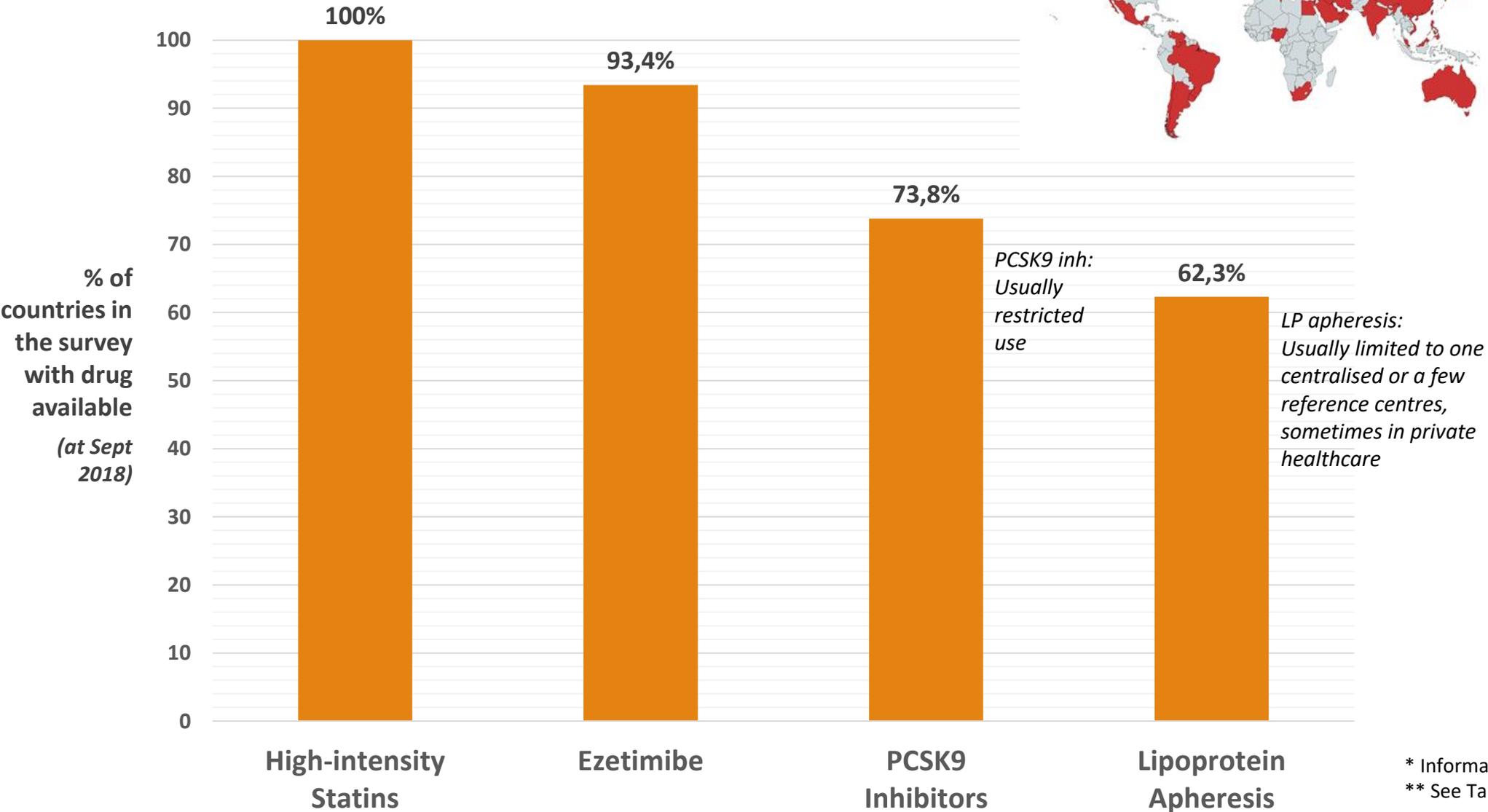
 Countries with investigators in EAS FHSC network
 Countries with investigators in EAS FHSC network

FH diagnosis criteria predominantly used



* Information provided from 61 countries.
** When >1 criteria system were mentioned for the same country, all of them have been included in the graph.
*** See Table 1 in the article for further details.

Availability of different therapies for FH



* Information provided from 61 countries.
** See Table 1 in the article for further details.

FH-related initiatives in countries involved in the EAS FHSC network in the Africa and Eastern Mediterranean WHO regions

Egypt: Egyptian FH Research Forum (FHRF), a national initiative endorsed by the Egyptian Association of Vascular Biology and Atherosclerosis (EAVA), currently involving >30 lead investigators from different Egyptian governorates and healthcare centres.

Lebanon: Studies carried out at the School of Pharmacy, Saint-Joseph University of Beirut (LBTM Laboratory-USJ) with collaboration of physicians at Hôtel-Dieu de France Hospital in Beirut.

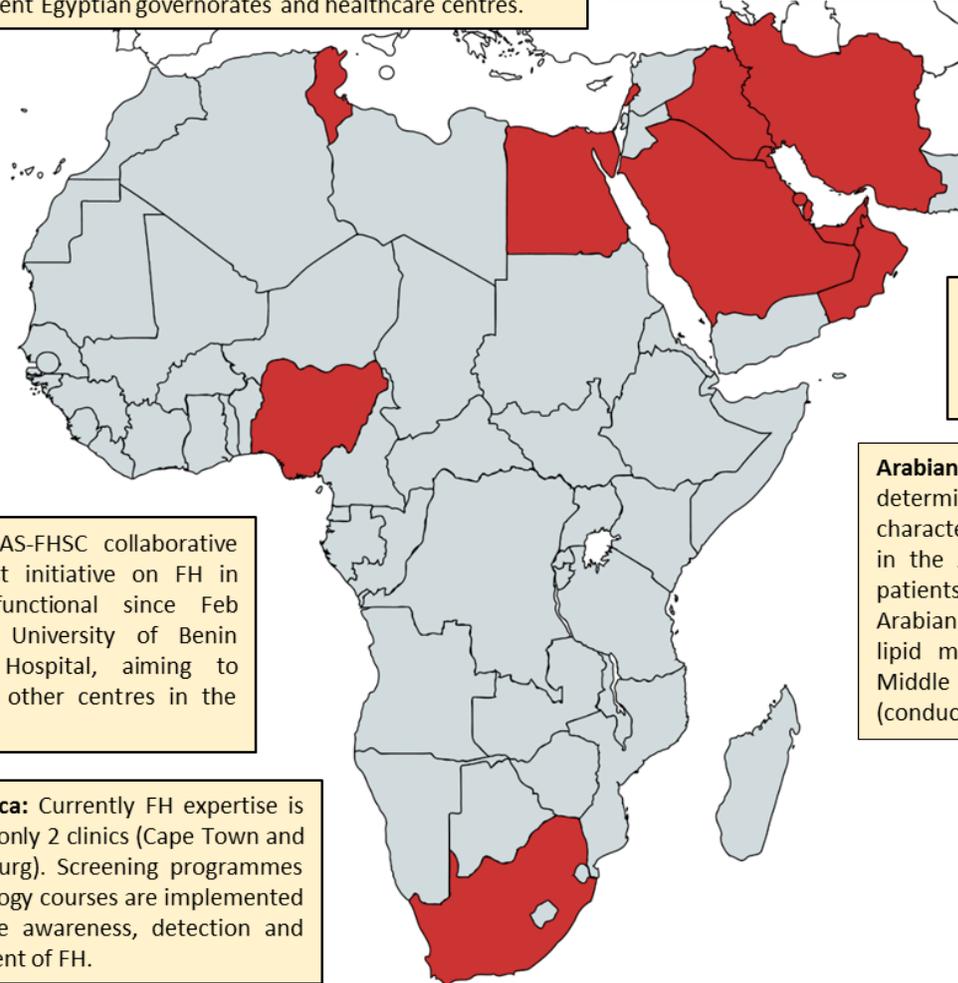
Iran: Initiative to establish a network of paediatric endocrinology experts in different referral centres in the country, aiming to identify index cases, designing uniform data collection criteria, and cascade screening.

Iraq: Network of 10 lipid clinics (Dec-2017) around the country has been established to populate the first Iraqi national registry.

Arabian Gulf: Gulf FH Registry, aiming to determine FH prevalence, genetic characteristics and current FH management in the Arabian Gulf region. It includes FH patients recruited from 15 centres across 5 Arabian Gulf countries. Annual courses on lipid metabolism and severe FH for the Middle East and North Africa region (conducted by IAS and OSLA).

Nigeria: EAS-FHSC collaborative study (first initiative on FH in Nigeria; functional since Feb 2018) at University of Benin Teaching Hospital, aiming to extend to other centres in the country.

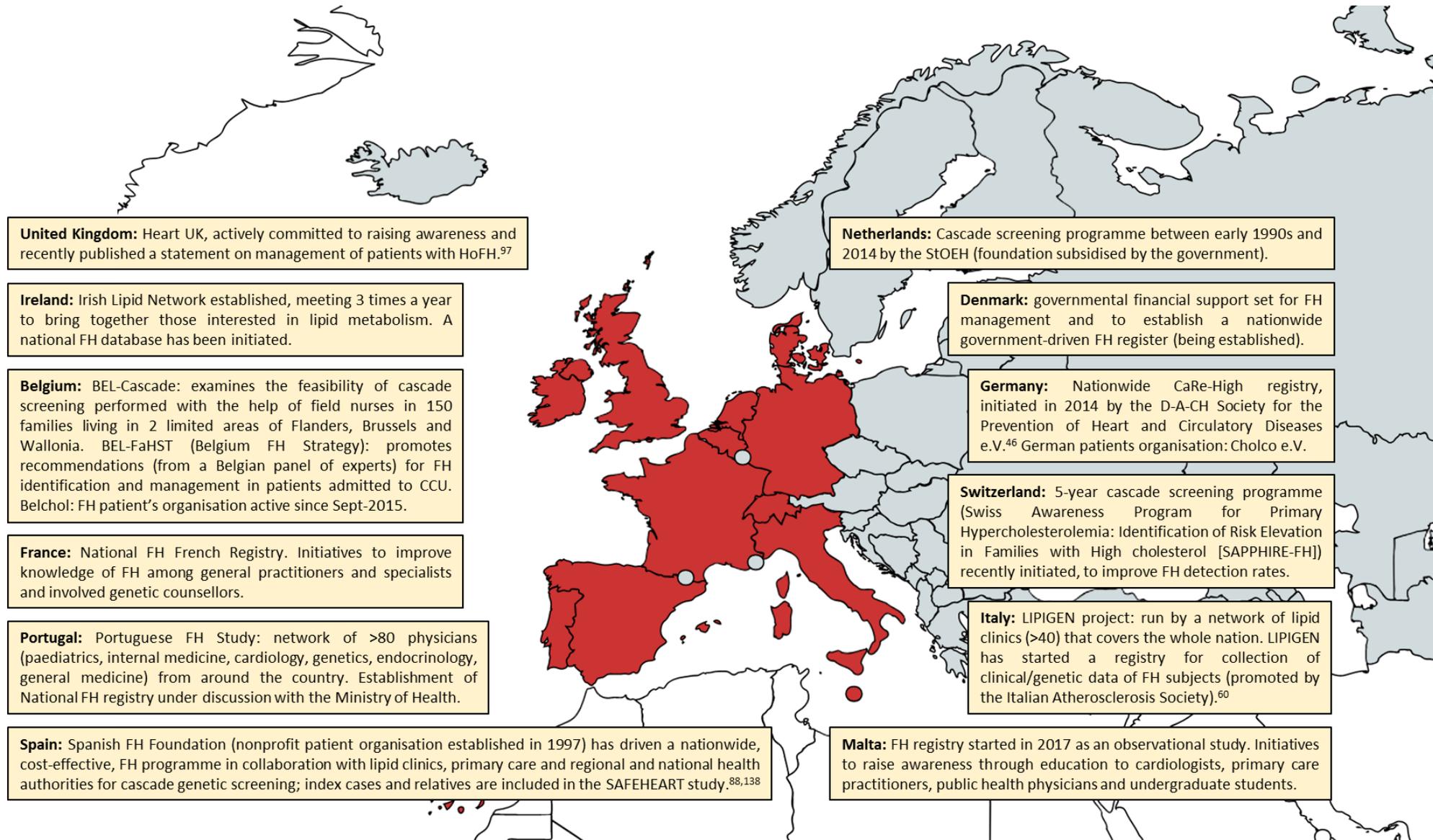
South Africa: Currently FH expertise is limited to only 2 clinics (Cape Town and Johannesburg). Screening programmes and lipidology courses are implemented to improve awareness, detection and management of FH.



FH-related initiatives in countries involved in the EAS FHSC network in the Americas WHO region



FH-related initiatives in countries involved in the EAS FHSC network in the WHO region of Europe



FH-related initiatives in countries involved in the EAS FHSC network in the WHO region of Europe



Poland: National Centre for FH (Gdansk) established in 2017 as a model centre for FH diagnosis and therapy, providing education of FH, diagnosis (clinical and genetic), therapy and apheresis. The Association of FH Patients in Gdansk active since 1999. New Polish Lipid Association FH-Registry (PoLA-FH Registry; www.rejestr-ptl-rh.pl) established beginning 2018.

Czech Republic: Czech MEDPED network of 69 active centres and collaborators operating throughout the country, under the Czech Atherosclerosis Society umbrella. A patient organisation has operated since 2014.

Austria: Since 2016, enrolment and partly cascade screening in FH registry under the umbrella of the Austrian Atherosclerosis Society (multidisciplinary project at Universities in Vienna, Graz and Innsbruck, planned to expand to other centres across Austria). The project is supported by similar societies, e.g. Austrian Heart Foundation, Austrian FH patient organisation (FHchol Austria). Pilot project FH Kids (selective screening among pre-school children and via school doctors in Vienna).

Slovenia: Universal cholesterol screening in children. Universal screening for CVD risk factors available for adults. National Registry of FH established in 2017, currently including records of ~ 200 children and 200 adults.

Croatia: Croatian Atherosclerosis Society: FH leaflets to all medical personnel on primary care. "FH patient ID card" distributed to patients after their visit to lipid clinic.

Bosnia and Herzegovina: Initiatives for education of doctors and patients through media, lectures, flyers and publishing books on FH. Spreading network of medical centres willing to participate in FH project. Approval from local ethics committee, informing Ministry of health, getting Medical Council support. Working within national Association of Cardiologist/Working Group for Atherosclerosis.

Slovakia: National paediatric cholesterol screening. FH patients' organisation established in 2016. Slovak MedPed FH project: since 1999, using cascade screening approach, led by the Coordination Centre for Familial Hyperlipidemias at Slovak Medical University, Bratislava; 25 outpatient centres throughout the country (4 paediatrics) currently participating; supported by the Heart of Family Foundation and Slovak Association of Atherosclerosis.

Hungary: FH Website to raise awareness and reach both the medical and general community. Regular communication through media. Cooperation with patient organisations including SzívSN.

Serbia: Organisation of a national FH registry in collaboration with clinics throughout the country.

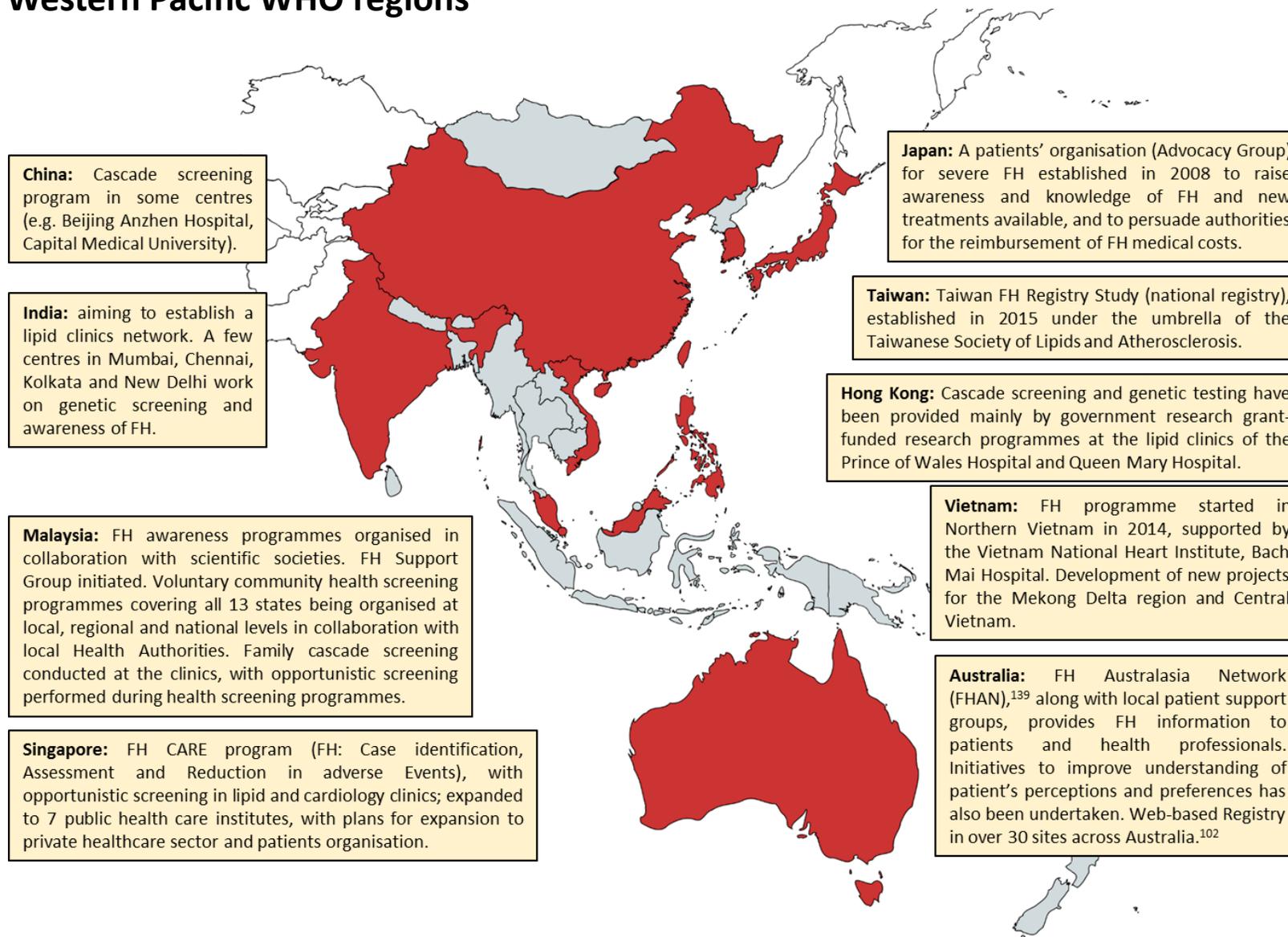
Bulgaria: National FH programme (since 2017) for identification, treatment and control of patients organised by Bulgarian Society of Cardiology; including 7 lipid clinics in the university hospitals in Sofia, Plovdiv, Varna and Pleven. One active patient's organisation.

Greece: National HELLAS FH Registry, coordinated by the Hellenic Atherosclerosis Society and including 12 participating lipid clinics.⁴⁷

FH-related initiatives in countries involved in the EAS FHSC network in the WHO region of Europe



FH-related initiatives in countries involved in the EAS FHSC network in South-East Asia and Western Pacific WHO regions



Discussion (I)

- **Data on FH prevalence lacking in most countries**
 - Where available, it tends to align with recent estimates suggesting a higher frequency than traditionally considered.

- **Overall low rates of FH detection reported across all regions**

- **Several factors influence estimations of burden of disease (prevalence, identification, etc):**
 - Population characteristics (including genetics, consanguinity rates, population cholesterol levels...)
 - FH awareness (community, healthcare professionals, policy-makers)
 - Socio-cultural factors (e.g. disease visibility, social acceptance)
 - Diagnostic criteria and adjustment to the specific populations
 - Accessibility to genetic testing
 - Presence and coverage of screening programmes
 - Variability in clinical practice
 - ...

- **National registries**
- **International/cross-regional registries (e.g. FHSC)**
- **Educational programmes**
- **Support (authorities, scientific societies...)**
- **Funding**

Discussion (II)

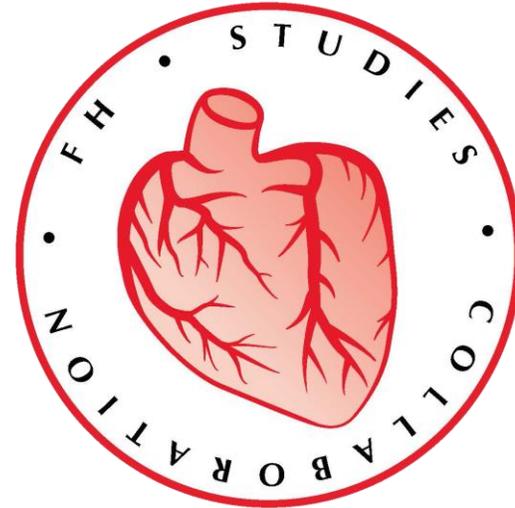
- **Management varies across countries**
- **Clinical diagnosis is predominantly made by DLCN in most countries.**
- **Traditional dx criteria: how well do they fit with contemporary populations and from different regions ??**
 - **Region/country-specific criteria for FH diagnosis ??**
 - **Only a minority of countries have regionally-modified criteria**
- **Genetic testing often available but not widely implemented (cost issues, self-funded, only in research...)**
- **Genetic cascade screening in approx 1/3 countries, usually on a regional basis**
- **Only few nationwide coverage, only a minority “national government programmes”**
- **Variability management: primary care / non-lipid specialists / lipid clinics**

Discussion (III)

- Under-treatment is common
- Therapy not universally reimbursed, criteria vary across countries
- High-intensity statins – available in all countries in the survey (limited access in some)
- Ezetimibe – not available in 4 countries
- PCSK9 Inhibitors – available in approx 2/3 countries, restricted use, criteria vary
- Lipoprotein apheresis – offered in approx 60% countries, usually limited to one or few reference centres



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