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# Familial hypercholesterolaemia: A global call to arms

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A.J. Vallejo-Vaz et al. / Atherosclerosis 243 (2015) 257-259

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## ARTICLE INFO

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Familial Hypercholesterolaemia (FH) is the commonest autosomal co-dominantly inherited condition affecting man. It is caused by mutation in one of three genes, encoding the low-density lipoprotein (LDL) receptor, or the gene for apolipoprotein B (which is the major protein component of the LDL particle), or in the gene coding for PCSK9 (which is involved in the degradation of the LDLreceptor during its cellular recycling). These mutations result in impaired LDL metabolism, leading to life-long elevations in LDLcholesterol (LDL-C) and development of premature atherosclerotic cardiovascular disease (ASCVD) [1–3]. If left untreated, the relative risk of premature coronary artery disease is significantly higher in heterozygous patients than unaffected individuals, with most untreated homozygotes developing ASCVD before the age of 20 and generally not surviving past 30 years [2-5]. Although early detection and treatment with statins and other LDL-C lowering therapies can improve survival, FH remains widely underdiagnosed and undertreated [1], thereby representing a major global public health challenge.

Whilst the prevalence of heterozygous FH has been traditionally estimated as ~1:500, contemporary data suggest an overall frequency of ~1:200-300, implying that >30 million individuals could be affected worldwide [1,3,4,6]. Furthermore, the burden of the disease is even higher in subpopulations with gene founder effects or within communities where consanguineous marriages are common [7]. Available information suggests that <5% of those affected are diagnosed, with higher detection rates reported among countries with formal screening programmes [1]. Similarly, homozygous FH is now considered to have a higher prevalence of 1:160,000-300,000 (calculations based on suggested heterozygous frequency of ~1:200-300) instead of the historical figure of 1:1,000,000 [1,2,8]. Additionally, FH is either insufficiently treated or treated late and, even with current best therapies (high-dose statins and cholesterol absorption inhibitors), only ~20% of individuals attain guideline-recommended LDL-C goals [1,9,10]. These factors are also compounded by a general lack of public health policies aimed specifically at FH, lack of uniformity among various initiatives for remediating the gaps in care, and the absence of a specific WHO "International Classification of Diseases" code for FH itself (currently included together with other disorders within the heading "pure hypercholesterolaemias" [ICD-10 code E78.0]) [11]. For example, the identification of new FH subjects is mainly based on clinical criteria in most regions, whereas in others genetic confirmation of the diagnosis in index cases and relatives according to a cascade testing strategy is utilised [1]; additionally, although a cascade screening strategy has been found to be cost-effective [12] and may promote risk reduction by early initiation of therapy, only a few regions/nations have implemented it widely (Suppl. material 1).

To overcome the existing gaps in care and reduce the preventable global burden of disease arising from FH, major efforts are needed to institute early detection and effective treatment. Central to these efforts is increasing awareness, dissemination of information and promotion of education among healthcare providers, policy makers and patients. The generation of high-quality and reliable data on current clinical practice and policies and their consequences on health outcomes may help support decisionmaking by demonstrating the gaps in existing levels of healthcare and geographical inequalities. Collaboration and partnership between healthcare professionals, patient organizations, healthcare providers and policy makers are essential to develop a scalable and sustainable best standard of care of patients and families with FH. FH has no geographical boundaries, and each country will face its specific challenges in delivering the best care for FH. Therefore, establishing priorities, identifying short and long-term goals, and implementing and evaluating models of care are essential for shaping and developing the most effective health policy on FH. Different approaches may be required and availing all resources should be explored in order to achieve these objectives (Fig. 1).

To fill the current gap in public health initiatives on FH, both professional and patients organizations have initiated programmes to address the aforementioned gaps in care (Suppl. material 1), occasionally at an international level, but more frequently at national or regional levels, including screening programmes, educational and awareness activities, consensus statements or accessibility to therapies. The current challenges and need for large-scale information to support the best evidence-based care and policies suggest, however, that the time is ripe for an international call-to-action that integrates efforts across the world to tackle the health burden and gaps in care of FH.

In this context, the European Atherosclerosis Society (EAS) FH Studies Collaboration (FHSC) has been launched as an ambitious global initiative that, through a consortium of major FH registries worldwide, aims to generate large-scale robust data on how FH is detected and managed and the clinical implications thereof. The ultimate aims are to disseminate this information in order to empower the medical, global and lay community to seek changes in their respective countries or organizations to improve the care of patients and families with FH (Suppl. material 2). A number of leaders in the field have agreed to contribute to this international initiative (Suppl. material 3) resulting in a global network that will ultimately generate novel data to inform future guidelines on FH management. Under the auspices of the EAS FHSC, a recent "patient advocacy group" meeting brought together patients' organizations representatives and clinicians (Suppl. material 4). The key aims and objectives identified were raising awareness and education (with a special focus on primary care providers), improving health policies, establishing networks among different regions including patients

258

A.J. Vallejo-Vaz et al. / Atherosclerosis 243 (2015) 257-259



**Fig. 1.** Familial hypercholesterolaemia (FH) poses important global public health concerns, being globally underdiagnosed and undertreated. Key aspects to be covered to face the FH burden include early diagnosis of the disease and screening strategies, generation of large-scale reliable data (e.g. by means of registries) and encouraging research on FH, raising awareness and education within healthcare professionals, policy makers, patients and families, development of policies aimed specifically to FH, and the establishment of early and effective treatment (including facilitating access to therapies, also to novel drugs). These actions should be led by professional bodies within their scope of action in partnership with patients' organizations and health authorities. See Suppl. material 1. CV: cardiovascular. EAS: European Atherosclerosis Society. FH: familial hypercholesterolaemia. FHSC: FH Studies Collaboration. IAS: International Atherosclerosis Society.

and professional organizations, and accessibility to treatments, among others.

The FH awareness week/day (24th September) intends to emphasize the health burden and major challenges in care posed by FH by undertaking different awareness-raising activities to make healthcare providers, policy makers, and patients and families more aware of the need to take action to fight the problem of FH.

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#### Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.atherosclerosis.2015.09.021.

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