KEY POINTS

- Familial hypercholesterolemia (FH) confers a very high risk for atherosclerotic cardiovascular disease (ASCVD) with a significant burden on public health from lifetime exposure to LDL-cholesterol if untreated. Poor adherence to lipid-lowering treatment (LLT) is a major challenge for achieving guideline treatment goals in FH.
- Misunderstanding of perceived and actual risk of FH and the benefits of LLT, inadequate knowledge, lack of standardization of treatment, insufficient monitoring of LDL-cholesterol level and inequalities in healthcare resources have negative impacts on adherence to LLT in FH.
- Implementation strategies to improve adherence should be patient-centred, country-specific and contextualised to a given healthcare system, including support from family, community and peer groups, patient and healthcare provider education, lifestyle and behavioural interventions, potent combination therapy, simple treatment and long-acting regimens, subsidies for essential therapies, regular patient followed up and monitoring of treatment.

REVIEW CRITERIA

A search for original and review articles was performed in the PubMed database using the following key terms: 'cardiovascular disease', 'barriers', 'enablers', 'FH', 'LDL-cholesterol', 'lipid-lowering therapy', 'medication adherence', 'primary hypercholesterolemia' and 'statins' either alone or in combination. All articles selected were in the English language, full-text articles, with no restriction applied to the date of publication.

LIPID-LOWERING TREATMENT: BENEFITS AND GOALS IN FAMILIAL HYPERCHOLESTEROLEMIA

Composite evidence strongly supports that earlier lifestyle management and robust cholesterol-lowering therapy can maximally lower lifetime exposure to LDL-cholesterol and lead to a greater reduction in risk of ASCVD in FH [1,2▪▪,8▪,9,10▪]. Observational studies confirm that reductions in LDL-cholesterol lower the risk of coronary events in younger [11] and older patients with FH [12]. In the CHARON study, rosuvastatin treatment for 2 years resulted in significantly less progression of carotid intima-media thickness in children with heterozygous FH compared with their untreated unaffected sibling [13]. In a long-term follow-up study, children commenced on low-to-moderate intensity statin had a 1% incidence of ASCVD events compared with 26% in their affected parents who were treated with statins later in life [11]. These findings strongly support the early use of LLT in FH.

Current guidelines recommend a relative reduction in plasma LDL-cholesterol of more than 50% in all patients with FH, followed by an absolute goal of less than 55 mg/dl (<1.4 mmol/l) and less than 70 mg/dl (<1.8 mmol/l) for adult FH patients with and without ASCVD, respectively [2▪▪,3]. In children with heterozygous FH, an LDL-cholesterol goal of less than 135 mg/dl (<3.5 mmol/l) or approximately 50% reduction is considered in patients with no additional risk factors for ASCVD, whilst an LDL-cholesterol goal of less than 2.5 mmol/l is recommended in those with additional risk factors for ASCVD [2▪▪,14▪]. However, more than 80% of FH patients treated with conventional LLT (mostly statins and/or ezetimibe) do not achieve recommended LDL-cholesterol goals. For example, the Spanish (SAFEHEART) registry showed that more than 95% of adult FH patients with ASCVD receiving LLT failed to achieve guideline recommended LDL-cholesterol targets [15] and less than half of the children (<18 years) with FH attained treatment goals [16]. In another study from Norway, only 43% of 302 FH children achieved an LDL-cholesterol treatment goal of less than 135 mg/dl (≤3.5 mmol/l) [17]. Data from the European Atherosclerosis Society (EAS) Familial Hypercholesterolaemia Studies Collaboration (FHSC) global registry showed that only 2.7% of FH patients achieved LDL-cholesterol levels less than 70 mg/dl [18▪]. Other studies have also demonstrated low rates of LDL-cholesterol goal attainment in FH [19,20,21▪]. Likewise, more than 50% of FH patients fail to attain recommended LDL-cholesterol goals even when additionally treated with PCSK9 inhibitors [22▪]. Poor patient adherence to LLT is the major contributor to the lack of LDL-cholesterol goal attainment [2▪▪,8▪].

ADHERENCE TO LIPID-LOWERING TREATMENT

Medication adherence is defined by the WHO as 'the degree to which the patient's behaviour corresponds with the agreed recommendations from a healthcare provider' [23▪▪] and is reported in terms of the percentage of prescribed doses taken for the defined period of time. Medication persistence is a parameter measured in units of time, and represents the time from initiation to discontinuation of therapy. Nonadherence to medication can be primary or secondary. Primary medication nonadherence occurs when the patient does not initiate the medication or an appropriate alternative within an