The FH Foundation welcomes the opportunity to comment on ICER’s Draft Report on Effectiveness, Value, and Pricing Benchmarks for PCSK9 Inhibitors for High Cholesterol, specifically as it relates to the population affected by familial hypercholesterolemia (FH).

The FH Foundation is a 501(c)3 non-profit patient-centered research and advocacy organization dedicated to improving the understanding, diagnosis, and treatment of familial hypercholesterolemia (FH) in order to prevent premature cardiovascular disease and improve patient outcomes in this high-risk population. The FH Foundation’s CASCADE FH Registry is an important component of this effort and we have data to share that can help inform decision makers when it comes to accurately characterizing the FH population.

FH is an autosomal dominant genetic disorder that causes severely elevated LDL cholesterol from in utero and puts those affected at much higher risk for premature heart disease. FH is under diagnosed and under treated in the United States.

Many patients with FH are not able to reach safe levels of LDL-C, even on multiple therapies. There has been an unmet need for additional LDL lowering therapy for these individuals and we welcome the addition of PCSK9 inhibitors and other recently approved therapies to address that need. Our priority is to ensure that people with FH are diagnosed early and treated appropriately, including having access to the care they and their doctors decide is needed to address their risk.

The FH Foundation is concerned that some of the assumptions in the Report will negatively impact FH patient access to they care they need.

For the purpose of your analysis, we would like to highlight the following:

1. Recent studies suggest FH prevalence is approximately 1 in 250 for heterozygous FH and 1 in 160,000 for homozygous FH, rather than the 1 in 500 and 1 in 1 million cited in the Report.
2. Currently, fewer than 10% of individuals with FH are diagnosed in the United States.
3. We do not agree with the definition of the heterozygous FH population as individuals with LDL-C over 250 mg/dL untreated and over 200 mg/dL with

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statin treatment. A clinical diagnosis can be made based on an LDL-C over 190 mg/dL in adults and over 160 mg/dL in children, along with a family history of CVD. Most experts would consider a lower level of LDL-C to suggest possible FH in a person with a family history of known FH. A cut off of 250 mg/dL without statin treatment and 200 mg/dL with statin treatment, as stated in the Report, would miss many people at high risk of CVD due to FH.

4. The risk of CVD associated with FH is not only due to extremely high LDL-C levels, but also to the years of exposure.

5. Heart disease strikes early for FH, affecting men, women, and even children early in life. Left untreated, men with heterozygous FH have a 50% chance of coronary heart disease by age 50 and women have a 30% chance by age 60.

6. The model presented in the Report is of the adult population aged 35 to 74. Unfortunately, individuals with FH are affected earlier in life. This model would not show the benefit of early optimal treatment. The impact of FH can be seen as early as 12 years old, when comparing CIMT results of FH and non-FH siblings. Diagnosis and treatment must start early.

7. A five-year time frame for FH is not adequate to see the benefits of treatment for FH.

8. Left untreated, FH patients in general have a 3-4 times higher risk for CHD compared to unaffected subjects, and CHD events occur one decade earlier.

9. FH patients have higher rates of coronary heart disease, as represented in the CASCADE FH Registry population: Prior CABG, 13.8%; Prior MI, 12.4%; Prior PCI, 17%.

10. We do not agree that LDL-C of 160 mg/dL is an appropriate goal for individuals with heterozygous FH. An appropriate LDL-C goal for individuals with FH is a target range of 70-100 mg/dL or lower. A goal of

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160 mg/dL, as stated in the Report, leaves people at undue risk for CVD given their prolonged exposure to very high LDL-C.

11. For portions of the FH population, treatment strategies would likely include statins, ezetimibe and PCSK9 inhibitors, if needed, rather than ezetimibe or PCSK9 inhibitors as modeled in the Report.

12. The model assumes that “all patients who met the operational definition of FH...received incremental therapy (p.ES10).” Currently, fewer than 10% of individuals with FH are diagnosed. In addition, not every person with FH will need a PCSK9 inhibitor. Many can reach LDL goals on previously available therapies.

13. However, many patients with FH cannot reach optimal LDL-C levels, highlighting the unmet need for additional options. Even with treatment at leading lipid clinics in the United States, the median LDL-C achieved by patients in the CASCADE FH Registry is 143 mg/dL

14. The patient-level burden of illness is very high for FH. FH has an impact on the quality of life for affected individuals, in addition to cardiac events. The CASCADE FH Registry finds that more than half of patients diagnosed with FH are burdened with anxiety associated with their risk for early heart attacks and premature death. Individuals with FH are painfully aware of their risk due to the fact that premature heart disease runs in FH families.

15. While the report states that “differences in CVD risk are less marked between patients with HeFH and those with a prior history of CVD who have elevated LDL-C levels despite other treatment” (p.ES7) this statement does not take into account that a disproportionate number of people with CVD have FH and are undiagnosed. Importantly, it does not consider the advantage of potential primary prevention to avoid CVD for individuals with FH. There is an inherent benefit to primary prevention of CVD events.

Better LDL-C management promises to improve patient outcomes for individuals with FH. Given the high cost, both financial and otherwise, of premature cardiovascular disease, this population must be proactively and adequately treated. FH is known to dramatically increase the risk for early heart disease. It can be detected in childhood when there is still time to prevent the development of atherosclerosis. Diet and lifestyle management will never be enough for this population, as important as it is. Pharmacological therapy is almost always necessary. Our goal is primary prevention of atherosclerosis in patients with FH.


to prevent heart attack, stroke, the need for revascularization, and premature death. It is not enough to prevent the second heart attack once CVD has been established. Our goal must be to diagnose and treat FH in order to prevent the first heart attack so people with FH can live longer, healthier lives.