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Major adverse cardiovascular events in homozygous familial hypercholesterolaemia: a systematic review and meta-analysis

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Lay Summary

Prepared for FH Europe by Dr Liam R. Brunham

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Homozygous Familial Hypercholesterolemia, or HoFH for short, is a severe inherited cholesterol condition causes by inheriting two copies of a defective version of the gene that encodes for the LDL receptor. It is well known that HoFH leads to increased risk of heart disease and death, but the magnitude of the risk and how it has changed over time is unclear. This is in part due to the rarity of HoFH, which affects 1 in 250,000 to 1 in 1 million people. As a result, most of the published studies on HoFH are based on a small number of patients.

We used a technique called systematic review and meta-analysis to identify all of the published studies that reported risk of heart disease in HoFH, and combined all of the results to better understand the risk of this condition. We ended up identifying 94 published studies of 608 non-overlapping patients. Overall, we found that the risk of heart attack in HoFH was very high, occurring in 15% of patients. The risk was slightly higher in the Region of the Americas and Western Pacific Region. The average age of first heart attack was very low at 24.5 years. When we explored how the values changed over time from pre-1990 to post-1990, we found that the prevalence of heart attack remained constant, but the age-of-onset significantly increased from 16 years to 27 years. In other words, the same percentage of patients with HoFH were having heart attacks

were occurring more than a decade later. We found similar trends for the need of procedures to open a clogged blood vessel, as well as death from heart disease.

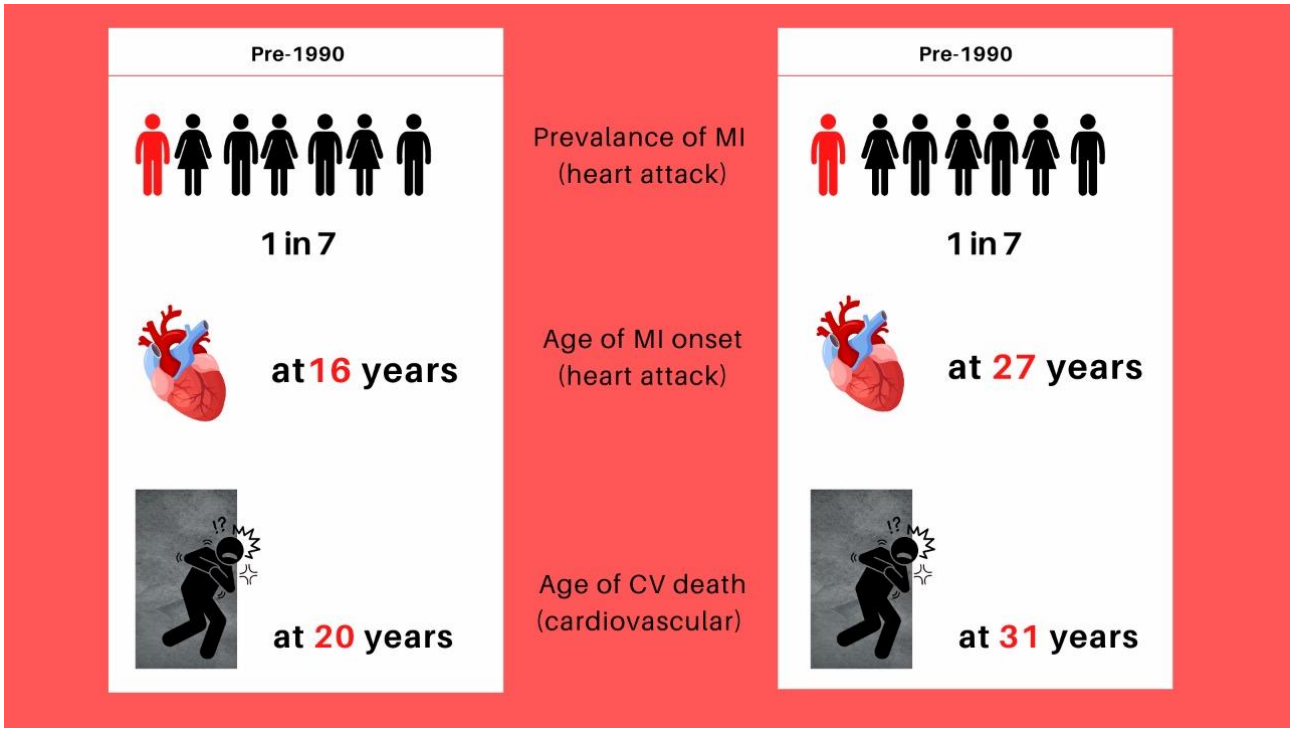

Image adapted from the original publication: Delayed onset of myocardial infarction (MI) and cardiovascular death in patients with homozygous familial hypercholesterolaemia (HoFH) in the statin-era.

The reason we choose 1990 as a time point of interest is that this approximately coincides to when effective cholesterol lowering medication (the statins) first became available and widely used. We therefore interpret the delay in onset of heart disease as reflecting the availability of more effective treatments to lower cholesterol in patients with HoFH.

Overall, these data provide us with a more precise estimate of the magnitude of risk associated with HoFH. While the data strongly reinforce the very high risk with HoFH, they also provide hope that the lives of patients with this condition can be significantly improved with appropriate treatment. With ever more effective therapies on the horizon, we hope that the onset of heart disease in these patients can be further delayed or even prevented.