

## Statins for Children with Familial Hypercholesterolemia

QUESTION
What is the effectiveness of different statins for children with familial hypercholesterolemia?

CONTEXT	Familial Hypercholesterolemia
<p>Familial hypercholesterolemia (FH) is an inherited metabolic disorder characterized by high cholesterol levels, specifically low-density lipoprotein (LDL) cholesterol. It is most common in heterozygous form, affecting approximately 1 in 500 individuals worldwide. FH is a serious condition because, in untreated patients, it may cause atherosclerosis as early as the second decade of life.</p> <p>Statins are used to treat hypercholesterolemia in adults, including those with FH. This course of treatment seems to be well-tolerated in this population. Recently, however, there have been several clinical trials that evaluate the use of statins in children with FH.</p>	

INTERVENTION	Statins
<p><b>Change in serum LDL cholesterol level:</b> Statins significantly decreased serum LDL cholesterol levels in comparison to placebo. <i>Moderate quality evidence.</i></p>	
<p><b>Change in serum total cholesterol:</b> Statins significantly decreased serum total cholesterol levels in comparison to placebo. <i>Moderate quality evidence.</i></p>	
<p><b>Change in serum HDL cholesterol levels:</b> Statins slightly increased serum HDL cholesterol levels in comparison to placebo. <i>High quality evidence.</i></p>	
<p><b>Change in serum triglyceride levels:</b> Statins slightly decreased serum triglyceride levels in comparison to placebo. <i>Low quality evidence.</i></p>	
<p><b>Liver dysfunction (AST and ALT levels):</b> Statins and placebo did not differ significantly regarding liver dysfunction. <i>Low quality evidence.</i></p>	
<p><b>Adverse events:</b> Statins and placebo did not differ significantly regarding other adverse side effects. <i>Low quality evidence.</i></p>	

<b>Summary of the Evidence</b>	
<b>Benefits</b>	A Cochrane systematic review (date of search: 2010) identified 8 randomized, placebo-controlled trials that evaluated the effectiveness and safety of statins in children with FH [1]. This review found that, compared to placebo, statins significantly decrease serum LDL (5 RCT, RR -32.15, 95%CI -34.90,-29.40) as well as serum total cholesterol (5 RCT, RR -26.53, 95%CI -28.54,-24.51) at end of follow-up (median 24 weeks). It also found that statins slightly increased HDL (5 RCT, mean difference between interventions 3.11, 95%CI 0.55,5.67) and slightly decreased triglycerides at end of follow-up (4 RCT, mean difference between interventions -3.27, 95%CI -12.03,5.50), though not statistically significantly.
<b>Risks</b>	No statistically significant differences were found between statins and placebo regarding increase in aspartate aminotransferase levels (AST) (4 RCT, 4 events RR 2.40, 95%CI 0.29,19.85) or in alanine aminotransferase levels (ALT) (4 RCT, 3 events, RR 2.03, 95%CI 0.24,16.95) at 6 months. There were no differences in global incidence of adverse events (3 RCT, 162 events, RR 1.02, 95%CI 0.85,1.27) at 6 months.
<b>Applicability</b>	Statins are an effective intervention for the reduction of cholesterol levels in children with FH. However, close pediatric follow-up is warranted because of possible hepatotoxicity or myotoxicity. In addition the dosage used across studies varied greatly and duration of follow-up was relatively short (average 1 year).  If the disease is mild, treatment can be delayed until the age of 18.
<b>Commentaries</b>	There is moderate to high level of evidence showing that treatment with statins in children can improve biochemical outcomes such as levels of LDL, HDL and total cholesterol in blood in comparison to placebo. In addition overall incidence of adverse events seems to be similar. More uncertainty exists in the effects of statins on triglyceride levels or liver function.  There is no information on critical outcomes such as the incidence of vascular events or atherosclerosis progression.
<b>Costs</b>	No studies on cost-effectiveness have been identified in the current literature.

1. Vuorio A, Kuoppala J, Kovanen PT, Humphries SE, Strandberg T, Tonstad S, Gylling H. Statins for children with familial hypercholesterolemia. Cochrane Database of Systematic Reviews 2010, Issue 7. Art. No.: CD006401. DOI: 10.1002/14651858.CD006401.pub2.

TABLE		GRADE Evaluation of Clinical Outcomes							
Number of Studies (N)	Outcome	Comparison	Type of Evidence	Quality	Consistency	Direct Evidence	Size of Effect	GRADE	Comments
5 (566)	Change in serum LDL cholesterol level	Statins Placebo	4	0	-1	0	0	Moderate	High heterogeneity
5 (566)	Change in serum total cholesterol level	Statins Placebo	4	0	-1	0	0	Moderate	High heterogeneity
5 (566)	Change in serum HDL cholesterol level	Statins Placebo	4	0	0	0	0	High	
4 (422)	Change in serum triglyceride level	Statins Placebo	4	0	-1	0	-1	Low	High heterogeneity , wide confidence intervals
4 (538)	Liver dysfunction (AST)	Statins Placebo	4	0	0	0	-2	Low	Very low number of events
4 (538)	Liver dysfunction (ALT)	Statins Placebo	4	0	0	0	-2	Low	Very low number of events
3 (416)	Adverse events	Statins Placebo	4	0	0	0	-1	Moderate	Low number of events

Type of evidence: 4 = RCT; 2 = Observational studies; 1 = Non-analytic studies / Expert opinion