

Facts on Familial Hypercholesterolemia (FH) and Coronary Heart Disease (CHD)

- **FH is a dominantly inherited disease affecting 1 in 500 individuals.**
 - Half of all first degree relatives of a patient with FH also suffer from FH.
- **FH increases the risk of CHD, especially the risk of premature CHD.**
 - [Austin et al \(2004\) Am J Epidemiol 160:421.](#)
 - About 12% of acute myocardial infarction under the age of 60 is due to FH.
[Dorsch et al \(2001\) BMJ 322:111.](#)
 - About 85% of CHD in severely hypercholesterolemic subjects under the age of 40 is due to FH.
[Nybo et al \(2007\) Clin Biochem; Epub ahead of print](#)
 - 50 fold (in men) to 125 fold (in women) increased risk of fatal myocardial infarction before age 40
[\(1999\) Atherosclerosis 142:105.](#)
- **Atherosclerosis associated with FH starts in childhood.**
[Wiegman et al \(2004\) Lancet 363:369-70.](#)
- **Timely treatment with statins can delay or prevent CHD.**
 - Statin therapy in FH patients leads to lowering of cholesterol and regression of atherosclerosis.
[Kane et al \(1990\) JAMA 264:3007.](#) [de Sauvage Nolting et al \(2002\) Am J Cardiol 90:181.](#) [Smilde et al \(2001\) Lancet 357:577.](#) [Hedman et al \(2005\) J Clin Endocrinol Metab 90:1942.](#) [Wiegman et al \(2004\) JAMA 292: 331.](#) [Rodenburg et \(2007\) Circulation 116:664.](#)
 - Two-year studies indicate that statin treatment is safe in children.
[Hedman et al \(2005\) J Clin Endocrinol Metab 90:1942.](#) [Wiegman et al \(2004\) JAMA 292: 331.](#)
- **FH is typically not diagnosed and not treated until middle age**
[Neil et al \(2000\) BMJ 321:148.](#)
- **Family testing for FH can improve diagnosis and treatment levels in children, adolescents, and young adults**
 - Dutch, Norwegian, and Portuguese programs for screening relatives of FH patients identified on average 2 to 3 affected relatives per index patient and increased treatment levels in recognized patients to 90%.
[Umans-Eckenhansen et al \(2001\) Lancet 357:165.](#) [Fouchier et al \(2005\) Hum Mutat 26:550.](#) [Leren et al \(2004\) Semin Vasc Med 4:75.](#) [Bourbon M et al \(2007\) Atherosclerosis; Epub ahead of print](#)
- **The majority of FH is caused by mutations in the genes *LDLR* or *APOB*.**
[Austin et al \(2004\) Am J Epidemiol 160:421.](#) (and references therein)
- **Genetic testing can confirm clinical diagnosis, facilitate family testing, and inform prognosis.**
 - Genetic testing shows close to 100% sensitivity and specificity in identifying affected relatives of any age. In contrast, sensitivity and specificity of diagnosis based on LDL-cholesterol levels varies with age.
[Leren \(2004\) Clin Genet 66:483.](#) [Wald et al \(2007\) BMJ 335:599.](#)
 - Genetic testing can determine the type of mutation, which may impact the risk of CHD.
[Junyent et al \(2008\) Arterioscler Thromb Vasc Biol 28:580-6.](#)
- **AHA guidelines consider genetic testing the “criterion standard” for diagnosis of FH in children.**
[McCordle et al \(2007\) Circulation 115:1948.](#)



The Impact of FH in the US*

- FH affects an estimated 600,000 Americans.
- With proper diagnosis and treatment, using a combination of targeted genetic testing and lipid-lowering drug therapy:
 - FH related heart attacks could be prevented in 200,000 of these individuals
 - FH-related deaths could be prevented in 50,000 of these individuals.

*Estimates are based on [Heart Disease and Stroke Statistics – 2006 Update, American Heart Association](#), [WHO-Human Genetics Programme. Report of a second WHO consultation: Geneva, 1999](#), [Austin et al \(2004\) Am J Epidemiol 160:421](#), [Fouchier et al \(2005\) Hum Mutat 26:550](#), [Leren et al \(2004\) Semin Vasc Med 4:75](#), [Austin et al \(2002\) Genet Med 4:275](#).