

**Cardiology-2018- Cardiovascular Disease and its Risk Factors in Patients with Familial Hypercholesterolemia: A Systematic Review- Gregory Kruse - University of Pennsylvania, USA**

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**Objectives:** Familial hypercholesterolemia (FH) leads to prolonged vascular exposure to high levels of lowdensity lipoprotein cholesterol and subsequent development of atherosclerotic lesions. This study examines additional risk factors in patients with FH and their impact on cardiovascular disease (CVD) risk.

**Methods:** A systematic literature review identified publications describing cardiovascular risk in patients with FH (January-October 2016), extending a previous published review (2004-2015). Each article was assessed for bias by two reviewers using the modified Newcastle–Ottawa assessment scale for non-randomized studies. Additional risk factors studied included age, sex, FH mutations, and previous CVD

**Results:** Three new studies were identified, conducted in the Netherlands, Spain, and Brazil, and reviewed together with the 14 studies identified in the previous review. The study with the lowest bias, comparing patients with versus without FH, reported odds ratios (ORs) for coronary artery disease (CAD) of 10.3 (95% confidence interval [CI]: 7.8–13.8) and 13.2 (95% CI: 10.0–17.4) in patients treated and untreated with lipid-lowering therapy, respectively. The highest risk increases in mortality were observed in the 30–60-yr age band. Most studies found that men with FH had a ~2.5-fold higher CVD risk compared with women, although the magnitude of the difference varied by study. Patients carrying null-mutations had a 68% higher risk of premature CVD (OR: 1.68; 95% CI: 1.10–2.40), and recurrence of cardiovascular events versus patients carrying defective-mutations. Premature CVD was identified as a risk factor for mortality (standardized mortality ratio: 1.62; 95% CI: 1.32–1.93).

**Conclusions:** FH-related CVD risk is high, even in treated patients, and represents an important unmet medical need. Alongside classical risk factors (age, blood pressure, body mass index, smoking, lipid levels), FH-causing mutations are important for

understanding FH-related CVD risk. Other parameters, such as age at which statin therapy is started, require further research.

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