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RESEARCH LETTER
Cardiovascular disease

Individuals with familial hypercholesterolemia have excess risk of eating disorders: a prospectively matched cohort study

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Suffering from an eating disorder (ED) is commonly understood as having a troublesome relationship with food, body and weight.[1] It is described as a mental disorder that can limit one's life due to all-consuming thoughts about what to eat, when to eat, and how much to eat.[2] Thus, an ED can have severe consequences for the individual, both physically and mentally, as well as impacting the whole family negatively.[2–4]

The underlying mechanisms and causes of developing an ED are many and complex.[1] Potential triggering factors have been suggested, such as having a chronic disorder, experiencing loss of family members, and being limited to a restrictive diet.[1] Studies show that children with diet-treated chronic disorders are associated with a higher likelihood for developing EDs.[3,5]

Familial hypercholesterolemia (FH) is a hereditary chronic condition that causes a predisposition for premature atherosclerotic cardiovascular disease and death.[6–8] Ideally, from a young age, treatment includes both pharmaceutical medications and a heart-healthy diet with a particular focus on fat quality. Hence, individuals with FH may be more vulnerable than the general population for developing an ED.[7]

No previous studies have investigated the risk of EDs in individuals with FH. The purpose of this study was therefore to investigate if individuals with genetically verified FH, who are likely to have received extensive diet and lifestyle counselling, have a higher risk of incident EDs compared with age- and sex-matched controls. The Regional Committee of Medical and Health Research Ethics South-Eastern Norway has approved the study (reference 2011/1343 South-East B).

This prospective matched cohort study during 2008–18 includes individuals with genetically verified FH (diagnosed between January 1992 and May 2014) and age- and sex-matched controls (1:20 ratio) obtained from the general population ($N = 110\,526$) (*Figure 1*). The FH population ($N = 5602$) consisted of 52% women and 48% men from the Unit for Cardiac and Cardiovascular Genetics database at Oslo University Hospital (*Figure 1*).[9] In Norway, 94% of FH mutations are in the LDLR gene, 5.4% in the APOB gene, and 0.6% in the PCSK9 gene.[10]

Individuals in the FH and control populations had their personal identification numbers linked to the Norwegian Patient Registry and the Norwegian Cause of Death Registry. Here, a case of ED was defined as having at least one contact with specialized healthcare, with the diagnosis F50 according to the International Classification of Diseases, Version 10, as the main or secondary diagnosis. The majority of the ED diagnoses were from Mental Health Services (69%) or a contract specialist within Mental Health Services (10%). The remaining were from somatic hospitals (20%) or a contract specialist within these hospitals (1%).

The follow-up time was calculated from the start of follow-up (registration date of FH diagnosis or 1 January 2008) until the endpoint, death, or 31 December 2018 (whichever occurred first). Individuals in the control cohort within each matched set had the same date for the start of follow-up as the FH person in the set. Incidence rates were presented per 1000 person-years. The risk of ED was analysed using Cox regression (matched analysis) and expressed as an hazard ratio (HR). All analyses were performed in Stata Version 16.

The mean age at the start of follow-up was 37.5 years in the FH population and similar (37.2 years) for controls. In total, 35 individuals with FH and 424 controls were diagnosed with an ED during follow-up. Of the 35 cases of EDs in the FH population, 33 were women (94.3%). In the control group with 424 cases of EDs, 375 were women (88.4%). The calculated ED incidence rates per 1000 person-years were 0.64 [95% confidence interval (CI): 0.45–0.88] for the FH population and 0.39 (95% CI: 0.36–0.43) in the control population. This corresponded to a significantly higher risk of ED in the FH population compared with that in the control population using matched analysis

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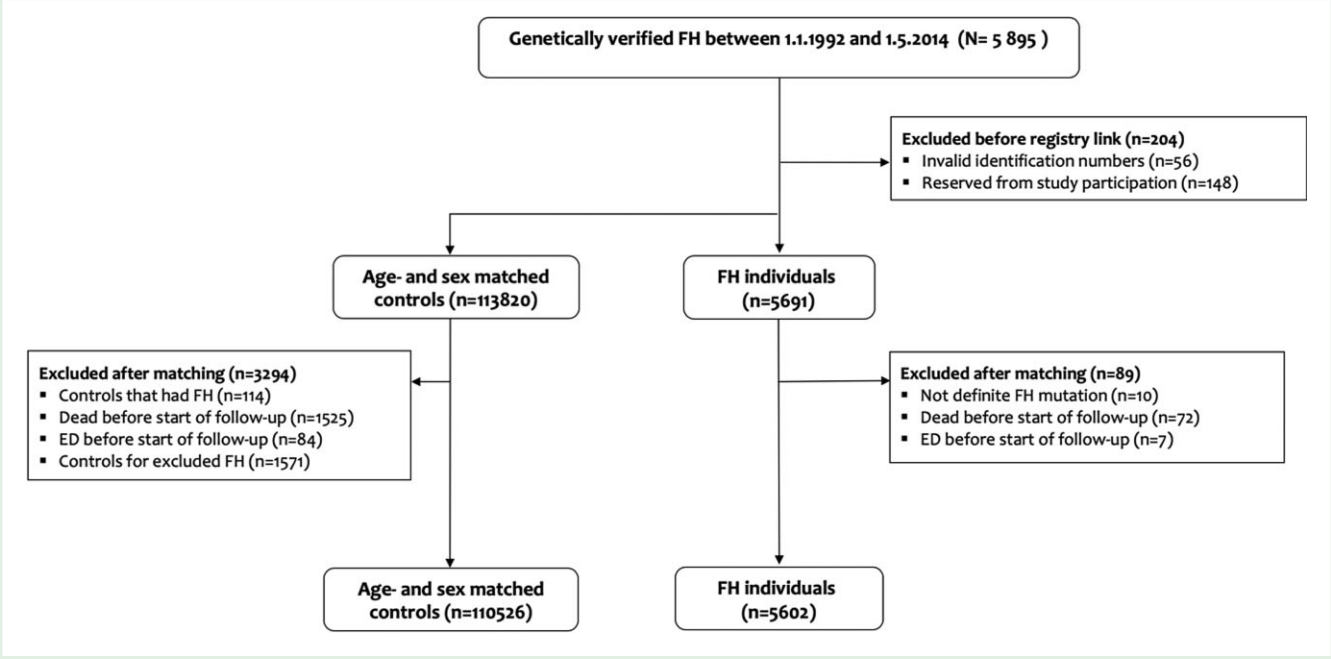

Figure 1 Flow chart of individuals with familial hypercholesterolemia and age- and sex-matched controls included in the study.

Table 1 Incidence rates and risk estimates for eating disorders between individuals with familial hypercholesterolemia and age- and sex-matched controls during 2008–18

	Number of events	Person-years per 1000 (95% CI)	Incidence rate per 1000 person-years (95% CI)	Hazard ratio (95% CI)
Total				
Control	424	1083.2	0.39 (0.36–0.43)	1 (reference)
FH	35	54.8	0.64 (0.45–0.88)	1.67 (1.18–2.35)
Women				
Control	375	561.9	0.67 (0.60–0.74)	1 (reference)
FH	33	28.3	1.16 (0.83–1.64)	1.78 (1.24–2.54)

Eating disorder is defined as one registration with ICD10 code F.50. Hazard ratio is derived from Cox regression (matched analysis).

[HR = 1.67 (95% CI: 1.18–2.35)] (*Table 1*). The corresponding incidence rates for women were 1.16 (95% CI: 0.83–1.64) for FH and 0.67 (95% CI: 0.60–0.74) for controls. Women with FH had a 78% higher risk of ED than controls [1.78 (95% CI: 1.24–2.54)].

In total, 29 individuals with FH and 343 controls had two or more registered ED events diagnosed from specialized health care, underlining the severity of the events. This resulted in an even stronger association between FH and EDs [HR = 1.71 (95% CI: 1.17–2.49)].

The results are worrying, and healthcare providers working with FH should consider the excess risk of EDs in this population, especially when dietary advice is given to young women. However, the results must be interpreted with caution due to methodological limitations. First, the study period was restricted to 10 years, so the participants could have been diagnosed with EDs both before and/or after this period. Second, we did not have information of ED subtypes. Third, the data were based on registrations within the specialized healthcare and not on individuals diagnosed by the primary healthcare service. Fourth, there might be a detection bias as individuals with FH are more in contact with health services and may have a greater chance of being diagnosed with a possible ED.

In conclusion, the present study suggests that individuals with FH have an excess risk of developing EDs compared with age- and sex-matched controls. The FH population possesses several triggering factors for EDs, including having a diet-treated chronic disorder. Although dietary counselling for FH is important and not very restrictive (mostly in line with national guidelines), the desire to comply with the dietary treatment to reduce the risk of premature disease may lead some patients to develop an unhealthy relationship with food. How this will impact treatment and later cardiovascular risk is, at present, unknown. Thus, more research is needed to explore the potential triggers of EDs in FH and the long-term consequences.

Authors' contributions

K.R., L.J.M., J.I., K.B.H., and K.S. contributed to the conception and design of the work. E.B.U., J.I., K.S., K.R., and L.J.M. contributed to the acquisition, analysis, or interpretation of data for the work. E.B.U. and K.S. drafted the manuscript. E.B.U., J.I., K.S., K.R., L.J.M., and K.B.H. critically revised the manuscript. All gave final approval and agreed to be accountable for all aspects of work, ensuring integrity and accuracy.

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Data availability

Anonymous and limited data can be made available on request. The data underlying this article will be shared upon reasonable request to the corresponding author.

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