National Hospital of the Faroe Islands

AALBORG UNIVERSITY

# The Faroe Islands – a possible founder population with a very high prevalence of familial hypercholesterolemia

Sanna á Borg[1], Christian Sørensen Bork[2], Michael René Skjelbo Nielsen[3], Rudi Kollslíð[1],Erik Berg Schmidt[2,4], Søren Lundbye-Christensen[5], Albert Marni Joensen[2]

[1]Department of Medicine, National Hospital of the Faroe Islands, [2]Department of Cardiology, Aalborg University Hospital, Denmark, [3]Heart Clinic of Northern Jutland, Denmark, [4]Department of Clinical Medicine, Aalborg University, Denmark, [5]Unit of Clinical Biostatistics, Aalborg University Hospital, Denmark

## Aim

The population of the Faroe Islands has been significantly influenced by genetic drift and is considered the genetically most homogenous population in the North Atlantic Region. The aim of this study was to investigate the prevalence of familial hypercholesterolemia (FH) in the Faroe Islands.

## Methods

We used an electronic nationwide database that included all low-density lipoprotein cholesterol (LDL-C) measurements in the Faroe Islands between January 2006 and September 2020. We estimated the prevalence of FH according to the Make Early Diagnosis Prevent Early Death (MEDPED) criteria, which is based on age-specific LDL-C cut-offs, and performed a partial estimation by the Dutch Lipid Clinic Network (DLCN) score.

**Dutch Lipid Clinic Network diagnostic criteria for FH**

| | Points |
|---|---|
| **1. Family history** | |
| First-degree relative with known premature (men: <55 years; women: <60 years) coronary or vascular disease, OR first-degree relative with known LDL-C above the 95th percentile | 1 |
| First-degree relative with tendinous xanthomata and/or arcus cornealis, OR children <18 years of age with LDL-C above the 95th percentile | 2 |
| **2. Clinical history** | |
| Patient with premature (men: <55 years; women: <60 years) coronary artery disease | 2 |
| Patient with premature (men: <55 years; women: <60 years) cerebral or peripheral vascular disease | 1 |
| **3. Physical examination** | |
| Tendinous xanthomata | 6 |
| Arcus cornealis before age 45 years | 4 |
| **4. LDL-C levels** | |
| LDL-C ≥ 8.5 mmol/L | 8 |
| LDL-C 6.5–8.4 mmol/L | 5 |
| LDL-C 5.0–6.4 mmol/L | 3 |
| LDL-C 4.0–4.9 mmol/L | 1 |
| **5. DNA analysis** | |
| Functional mutation in the LDLR, apoB or PCSK9 gene | 8 |
| **Definite FH (>8 points)** | **Probable FH (6–8 points)** | **Possible FH (3–5 points)** |

**Prevalence of FH according to the MEDPED criteria and a partial DLCN score based on LDL-C levels**

| | Individuals meeting the criteria (n) | Total number of individuals (n) | Period prevalence (95% CI) | |
|---|---|---|---|---|
| **MEDPED** | | | | |
| LDL-C | 216 | 30,711 | 0.70 % (0.62; 0.80 %) | 1:142 |
| **DLCN** | | | | |
| Possible FH | 3,823 | 30,711 | 12.45 % (12.08; 12.82 %) | 1:8 |
| Probable FH | 10 | 30,711 | 0.03 % (0.02; 0.06 %) | 1:3071 |

Abbreviations: DLCN, Dutch Lipid Clinic Network; MEDPED, Make Early Diagnosis to Prevent Early Deaths.
We defined possible DLCN as LDL-C ≥5 mmol/L, while probable DLCN was defined as LDL-C ≥8.5 mmol/L.

## Results

We identified 186,305 LDL-C measurements among 30,711 individuals including 15,730 men and 14,981 women. A total of 216 subjects fulfilled the criteria of definite FH corresponding to a prevalence of 0.70% (95% CI 0.62 – 0.80%) according to the MEDPED diagnostic criteria.

According to the DLCN score, a total of 3,823 subjects had possible FH, and 10 subjects fulfilled the criteria of probable FH corresponding to a prevalence of 12.4% (95% ci 12.1 – 12.8%) and 0.03% (95% CI 0.02 – 0.06%), respectively.

## Conclusion

The Faroe Islands might represent a founder population with a prevalence of possible FH as high as 1:8. Further studies investigating the genetic and clinical characteristics of FH in the Faroe Islands are warranted.

**MedPed Diagnostic criteria for FH**

| Age (years) | FH is diagnosed if LDL-cholesterol exceeds these cutpoints in mmol/L | | | |
|---|---|---|---|---|
| | First degree relative with FH | Second degree relative with FH | Third degree relative with FH | General population |
| **< 20** | 4.0 | 4.3 | 4.4 | 5.2 |
| **20-29** | 4.4 | 4.7 | 4.8 | 5.7 |
| **30-39** | 4.9 | 5.2 | 5.5 | 6.2 |
| **≥ 40** | 5.3 | 5.6 | 5.8 | 6.8 |

Funding: Research Counsil Faroe Islands, National Hospital of the Faroe Islands, Amgen