**TESTING COHORT**

*Time* *period*: 2007 – 2015

*Cohort*: eMERGE phase I and II

*Sample*: 100 individuals (n=58 cases and 42 controls)

**Defining cases and controls:**

* A case status for familial hypercholesterolemia was assigned if the total score was >=6 points in individuals identified as a case for primary hypercholesterolemia
* A control status for familial hypercholesterolemia was assigned if the score was =<2 points in individuals identified as a case for primary hypercholesterolemia.

**Statistics**:

The positive predictive value (PPV) for being a case was determined as number of cases identified by the phenotyping algorithm and confirmed by review divided by the total number of cases identified by the algorithm.

The negative predictive value (NPV) for being a control was defined as number of true negatives in the numerator with total number of controls classified by the algorithm in the denominator.

Gold standard: manual chart review by an expert cardiologist-lipidologist initially blinded to a case-control status.

A subset of an algorithm-defined “unknowns” was included in the case group.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | |  |  | | --- | --- | | Sensitivity | 98.3% | | Specificity | 100% | | PPV | 100% | | NPV | 97.7% | |

**Diagnostic accuracy of the individual components of the Mayo SEARCH algorithm v2.0 for ascertaining clinical criteria for FH (eMERGE cohort):**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variable | Sensitivity | Specificity | PPV | NPV |
| Xanthomas (n=100) | 100 | 100 | 100 | 100 |
| Family history of ASCVD (n=100) | 98.4 | 100 | 100 | 97.3 |
| Family history of hypercholesterolemia (n=100) | 100 | 100 | 100 | 100 |
| Premature CHD (n=100) | 93.8 | 100 | 100 | 98.8 |
| Premature CVD/PAD (n=100) | 97.1 | 100 | 100 | 98.4 |

CHD=coronary heart disease; CVD=cerebrovascular disease; PAD=peripheral arterial disease

**Diagnostic accuracy of the individual components of the Mayo SEARCH algorithm v1.0 for ascertaining FH criteria (ECH cohort):**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variable | Sensitivity | Specificity | PPV | NPV |
| Xanthomas (v3.0; n=60) | 89 | 82 | 80 | 90 |
| Corneal arcus ≤45 y (v2.0; n=40) | 100 | 100 | 100 | 100 |
| Family history of ASCVD (v2.0; n=120) | 100 | 71 | 60 | 100 |
| Family history of hypercholesterolemia  (v1.0; n=20) | 83 | 69 | 56 | 90 |
| Premature CHD (v2.0; n=40) | 100 | 83 | 80 | 100 |
| Premature CVD (v 2.0; n=40) | 100 | 77 | 70 | 100 |
| Premature PAD (v2.0; n=40) | 100 | 77 | 70 | 100 |