FALLING SHORT OF GUIDELINES: UPTAKE OF FAMILY CASCADE TESTING IN INHERITED ARRHYTHMIAS



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BACKGROUND

Individuals with a pathogenic variant for an inherited arrhythmia require regular cardiac screening and possible life-saving interventions. Due to this, major professional societies unanimously recommend cascade genetic testing of family members when a pathogenic variant has been identified in an index case (AHA, ACC, HRS, EHRA, APHRS, PACES, AEPC, CCS, CHRS). Recent studies investigating the uptake of cascade genetic testing in small populations (≦75 index) with inherited cardiac diseases have found that 40-66% of families pursued testing (Christian *et al.* 2017; Restrepo-Cordoba *et al.* 2017; Burns *et al.* 2015; van der Roest *et al.* 2009).

OBJECTIVE

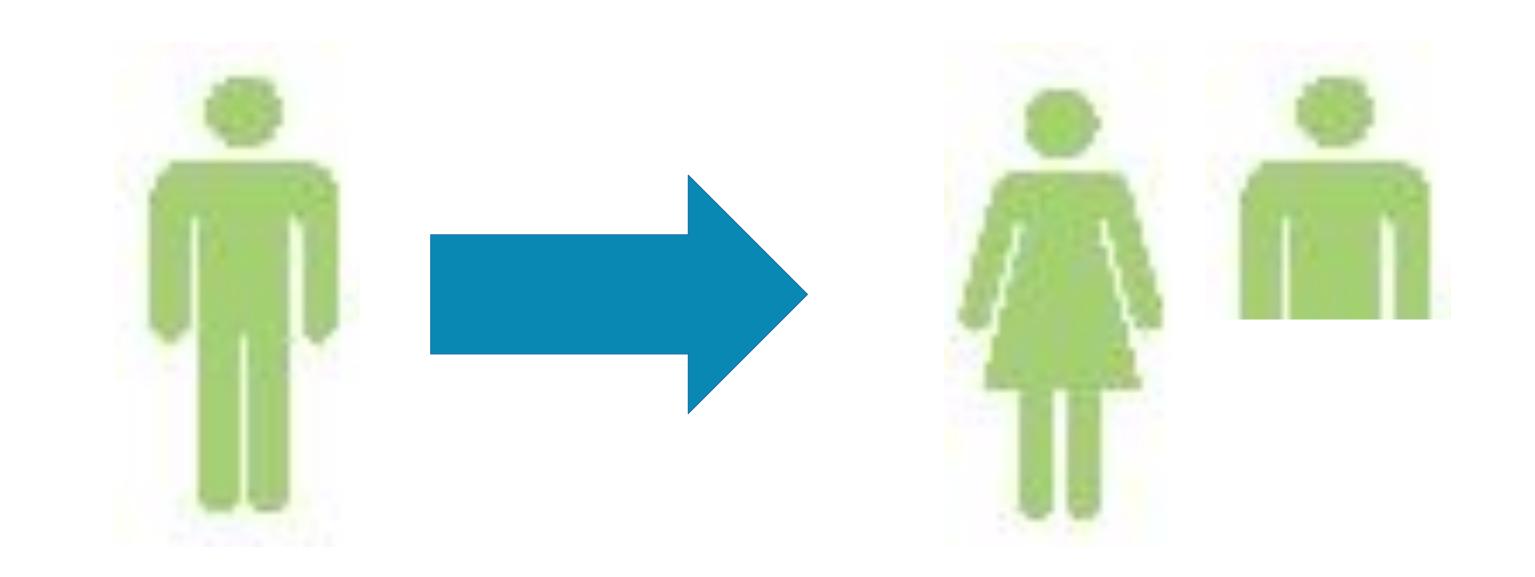
We aim to elucidate the uptake of cascade genetic testing for inherited arrhythmias in a broad population referred for arrhythmia genetic testing and compare it to the guidelines for universal family testing.

METHODS

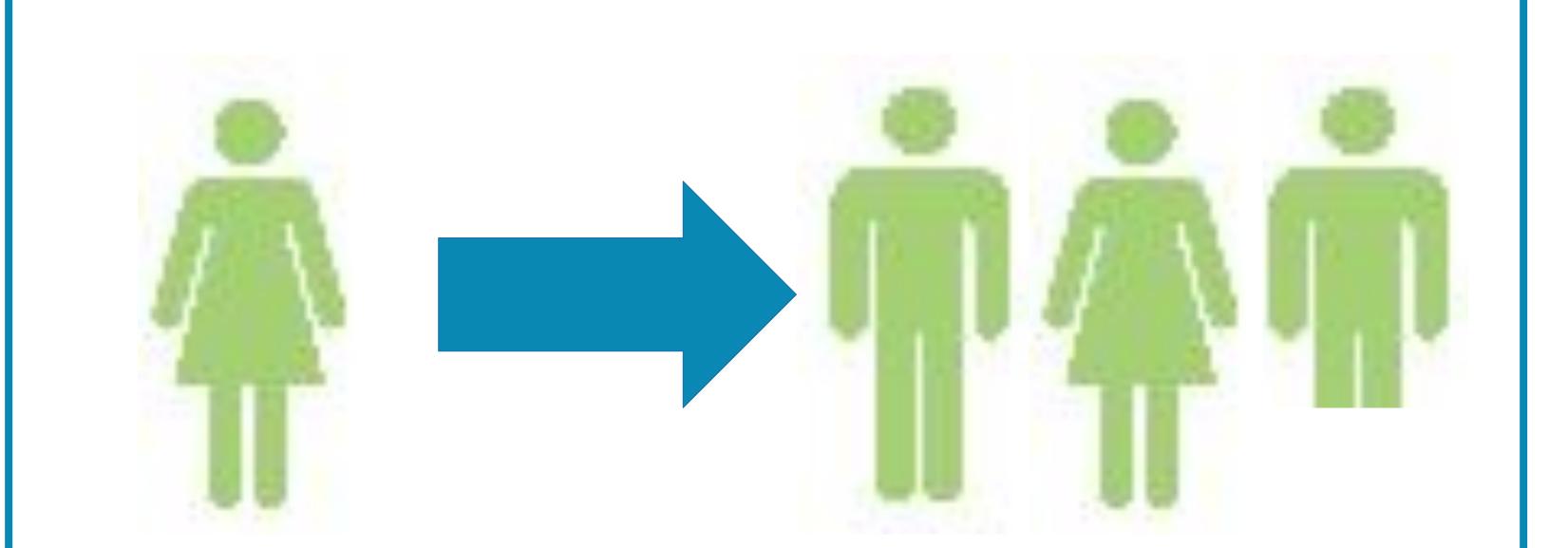
The total number of positive (pathogenic or likely pathogenic) arrhythmia-causing gene test results for index cases were compiled, along with all family member test results linked to each index case.

RESULTS

- We identified 682 index individuals with a positive test result in an arrhythmia-causing gene. Family members of 374 (54.8%) of these individuals requested testing for the familial variant from our laboratory.
- Among these 374 families, 1,030 individuals pursued testing, with 472 (45.8%) having inherited the familial variant.
- Family variant testing was more widely used (63.1% [171/271]) when the index individual was younger than 18 years compared to 49.4% (203/411) when 18 years or older.
- For every positive index case, an average of 1.51 family members pursued cascade testing.

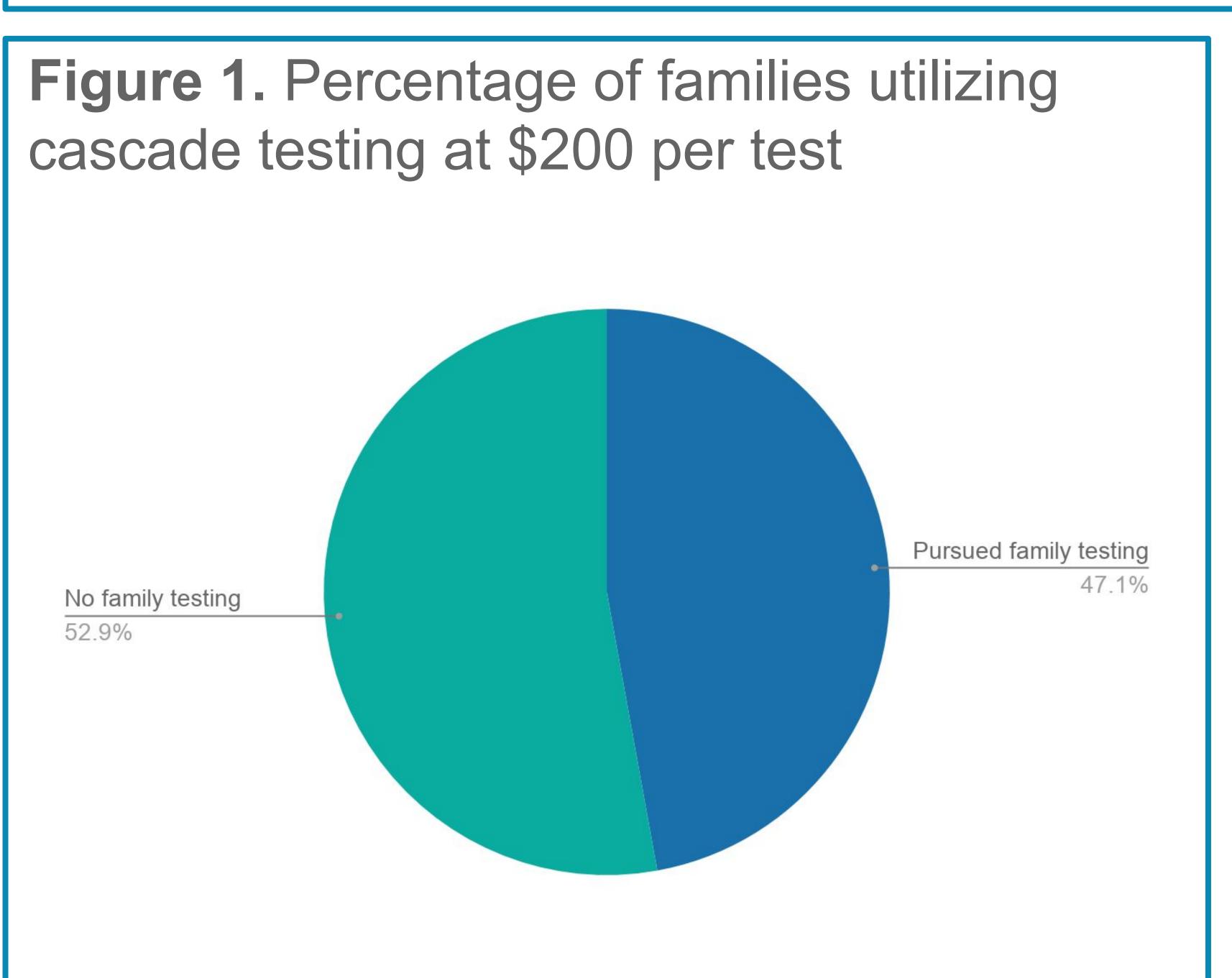


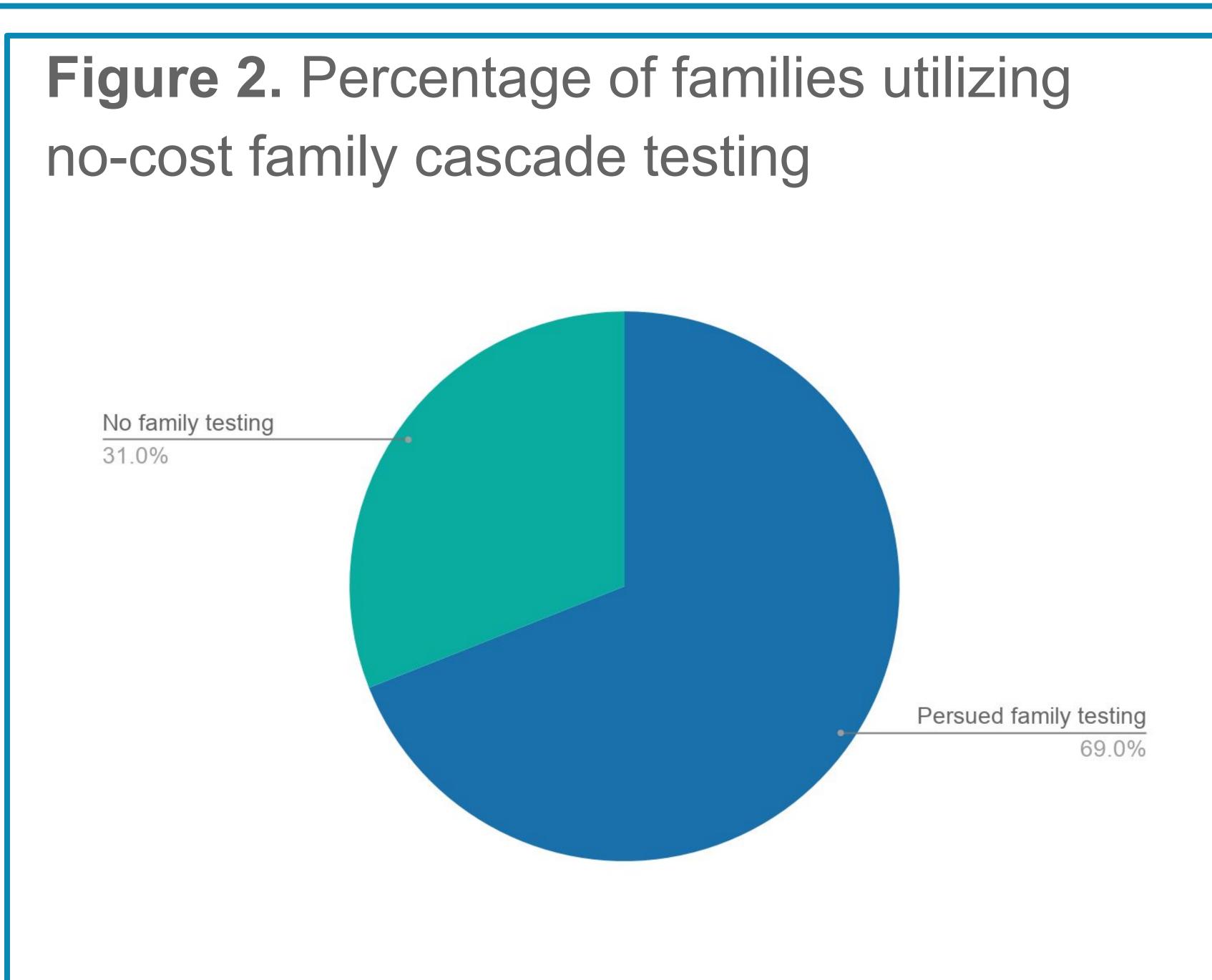
• In families that utilized cascade testing, an average of 2.76 family members were tested.



RESULTS

Family members were more likely to utilize cascade testing when it was offered at no additional cost: 47.1% (206/437) of index cases had family members utilize testing at a cost of \$200 versus 69.0% (169/245) when cascade testing was offered at no additional cost.





CONCLUSIONS

- In our large cohort of individuals with a positive genetic test for arrhythmia, the uptake of familial cascade testing is above the reported range when the cost barrier is removed.
- However, this does not nearly approach the recommendation for all family members to benefit from cascade testing
 and illustrates the need for access to specialists via telemedicine, online data sharing platforms for families, and other
 tools supporting cascade testing.
- Additionally, it is important to establish the genetic diagnosis in an index individual in order to allow for the increasing uptake of cascade testing.