

Additional findings amongst relatives pursuing oncology multigene panel cascade testing

Sarah Siddiqui, MS, CGC¹, Kelly Fulk, MS, CGC¹, Carrie Horton MS, CGC¹, Cassidy Carraway, BS¹

¹Ambry Genetics, Aliso Viejo, CA

ssiddiqui@ambrygen.com



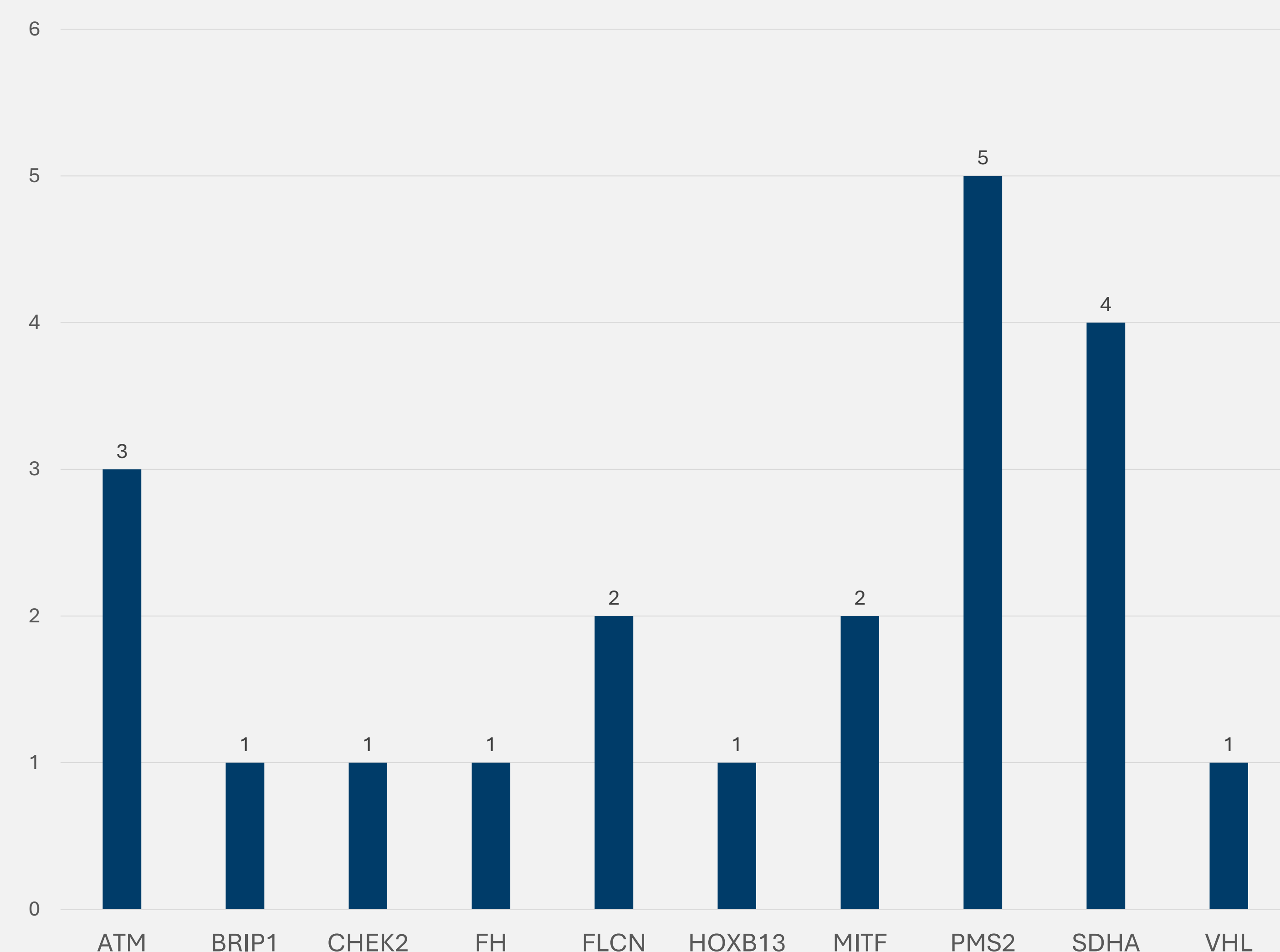
BACKGROUND & AIMS

- Historically, cascade testing often limited to site specific analysis (SSA)
- Studies investigating outcomes of cascade multigene panel testing (MGPT) as alternative are limited
- Identify additional familial pathogenic variants (AFPVs) and determine if unexpected
- Aid clinicians in determining when cascade MGPT may be more appropriate than SSA

METHODS

- Retrospective review to identify cascade family members (CFMs) of probands with PVs in *BRCA1/2*, *ATM*, *CHEK2*, *PALB2*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, or *EPCAM*
- CFM defined as relative who had testing (SSA, single gene, or MGPT) from 2018-2023, after the proband, that included the proband's impacted gene
- CFM testing of 8+ genes considered MGPT
- Personal and family history provided by ordering clinicians reviewed among individuals with an AFPV to evaluate testing criteria eligibility and management recommendations
- CFM personal and family history was reviewed for published testing criteria eligibility as well as core cancers (e.g. breast, ovarian) to track consistent phenotype in absence of testing criteria

FIGURE 2. GENES IN WHICH AFPVs IDENTIFIED WITHOUT CONSISTENT HISTORY



RESULTS

- 80 (74.07%) AFPVs consistent with reported personal/family history
 - 26 met published testing criteria (e.g. *BRCA1/2*)
 - 54 without gene-specific testing criteria (e.g. *CHEK2*)
- 28 (25.9%) AFPVs impacting medical management identified in individuals without suggestive history (Figure 2)
- 12 relatives had an AFPV within the same gene as proband

FIGURE 1.

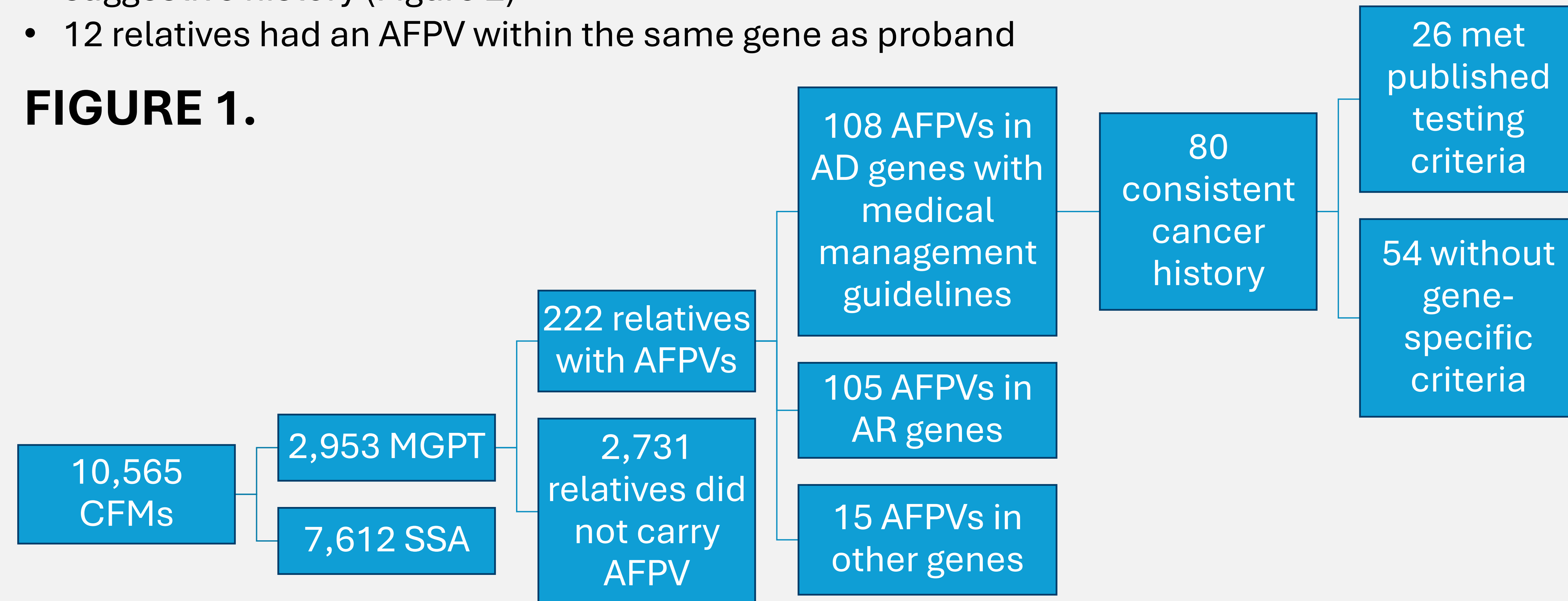
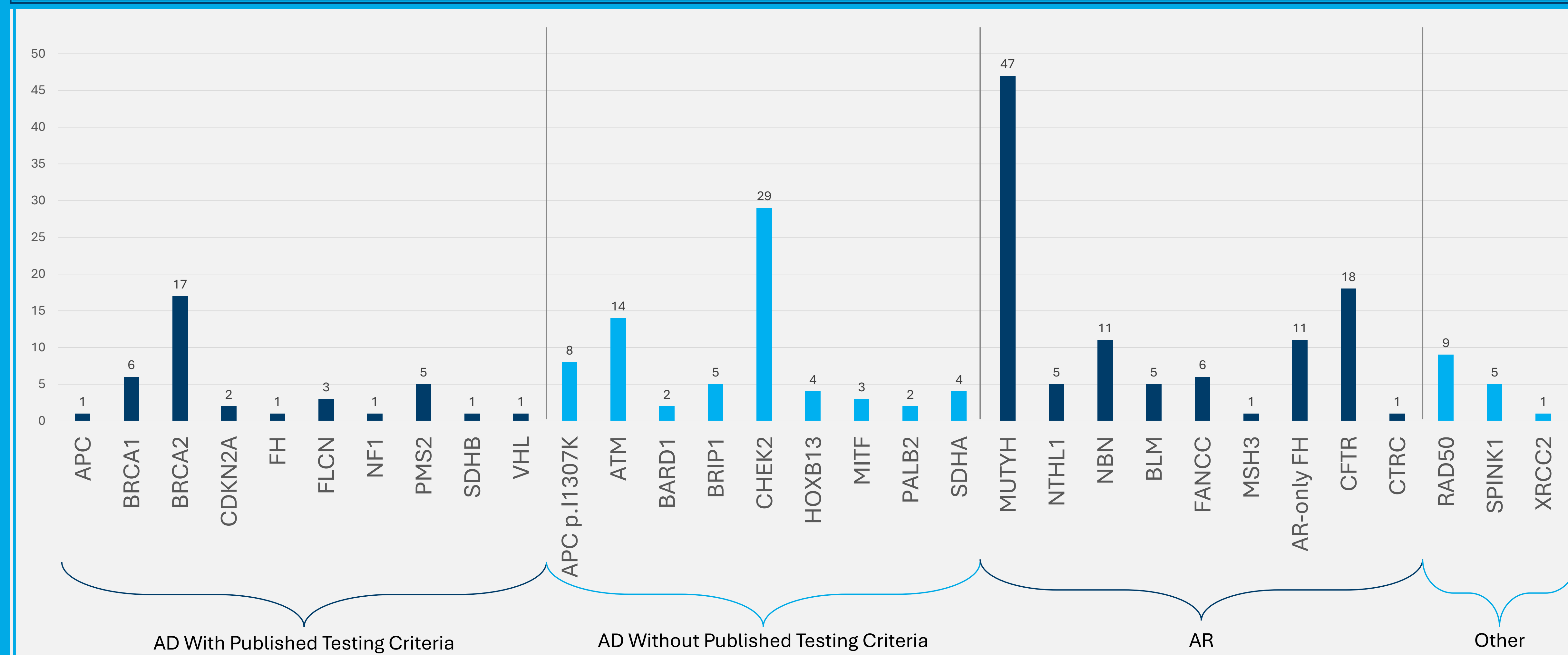


FIGURE 3. AFPVs BY GENE



TAKE HOME POINTS

- Cascade MGPT increases overall positive rate
- Comprehensive family history collection and pre-test counseling are critical
- 1 in 4 relatives had an AFPV, without suggestive history, impacting their medical management