Title: Prevalence of BRCA1/2-Negative, Unaffected Women Requiring Adjunctive Breast MRI Screening

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Objectives
The American Cancer Society (ACS) guidelines for breast screening recommend magnetic resonance imaging (MRI) as adjunct to mammography for individuals with a 20% or greater lifetime risk of breast cancer based on risk models that account for family history. Previous studies to identify the prevalence of individuals who would benefit from breast MRI based on family history have not included assessment of genetic BRCA1/2 status. This study aims to assess the proportion of women that may qualify for additional imaging and risk reduction in a cohort of BRCA1/2-negative women without a personal history of BRCA-related cancer.

Methods
All female patient samples reported by Myriad Genetic Laboratories, Inc. that underwent full BRCA1 &2 sequencing (Comprehensive BRACAnalysis®) or Ashkenazi Jewish founder mutation analysis with reflexive Comprehensive BRACAnalysis® were ascertained. Individuals with a personal history of breast or ovarian carcinoma, without a family history of breast cancer in a first- or second-degree relative, a Deleterious BRCA1/2 result, or a Variant of Uncertain Significance - Suspected Deleterious BRCA1/2 result were excluded. Family history of breast cancer and age at diagnosis in first- and second-degree relatives were ascertained from test requisitions completed by each ordering provider at the time of sample submission. Ascertainment of lifetime breast cancer risks of 20% or greater were calculated based on the breast cancer risk prediction tables published by Claus et al (1994).

Results
We identified 23,658 unaffected women that had testing for Comprehensive BRACAnalysis®. Of these women, 7599, or 32.1%, had a calculated lifetime risk of breast cancer greater than 20% based on the Claus tables.

Conclusions
In this large case series, nearly one-third of unaffected women with a negative BRCA1&2 sequencing result but a positive family history of breast cancer qualified for adjunctive MRI screening per ACS guidelines, initiating radiographic breast screening at age 30 (per NCCN 2013 guidelines) and breast cancer risk reduction counseling. These results present a significant opportunity to optimize the medical management of this common high-risk patient type by increasing appropriate MRI screening referrals.