Age at Diagnosis May Trump Family History in Driving BRCA Testing in a Population of Breast Cancer Patients

Hetal S. Vig¹, Anne Marie McCarthy², Kaijun Liao², Mirar Bristol Demeter², Tracey Fredericks², and Katrina Armstrong²

Abstract

Background: Standard BRCA genetic testing criteria include young age of diagnosis, family history, and Jewish ancestry. The purpose of this study was to assess the effect of these criteria on BRCA test utilization in breast cancer patients.

Methods: Breast cancer patients aged 18 to 64 years living in Pennsylvania in 2007 completed a survey on family history of breast and ovarian cancer and BRCA testing (N=2,213). Multivariate logistic regression was used to estimate odds of BRCA testing by patient characteristics, and predicted probabilities of testing were calculated for several clinical scenarios.

Results: Young age at diagnosis (<50 years) was strongly associated with BRCA testing, with women diagnosed before age 50 years having nearly five times the odds of receiving BRCA testing compared to women diagnosed at age 50 or older (OR = 4.81; 95% CI, 3.85–6.00; P < 0.001). Despite a similar BRCA mutation prevalence estimate (8–10%), a young Jewish patient <50 years with no family history had markedly higher predicted probability of testing (63%) compared with an older, non-Jewish breast cancer patient with more than one first-degree relative (43%).

Conclusion: Age at diagnosis, Jewish ancestry, and both maternal and paternal family history are strongly predictive of BRCA testing. However, among women diagnosed at age 50 or older, family history may be an underused criterion that may benefit from targeted intervention.

Impact: Robust methods specific to ascertaining detailed family history, such as through electronic medical records, are needed to accurately identify patients for BRCA testing. Cancer Epidemiol Biomarkers Prev; 22(10); 1778–85. ©2013 AACR.
improvements in the risk assessment process, leading to an increased detection rate of BRCA carriers (and at risk family members) who can benefit from high-risk surveillance and risk-reducing strategies for BRCA-associated cancers. As different healthcare providers become more actively involved in risk assessment, their ability to accurately identify high-risk individuals will be dependent on fulfillment of specific family history criteria, in addition to ancestry and age at diagnosis (22, 23).

The aim of this study was to examine how known predictors of BRCA mutations based on clinical practice guidelines are associated with BRCA testing utilization. We conducted a retrospective cohort study of newly diagnosed breast cancer patients in the state of Pennsylvania to examine how age at diagnosis, individual family history, and Jewish ancestry predict BRCA testing. Furthermore, we aimed to determine the impact of specific family history characteristics including first-degree and second-degree relatives on both maternal and paternal sides including whether they carry equal weight in risk assessment.

Materials and Methods

Study design and participants
We recruited a retrospective cohort to examine utilization of BRCA testing among women diagnosed with invasive breast cancer. Study participants were identified through the Pennsylvania State Cancer Registry (PCR). The PCR has achieved NAACCR Gold certification for the accuracy and completeness of data. The institutional review board of the University of Pennsylvania and the PCR approved the study protocol. We identified women who were diagnosed with invasive breast cancer at age 18—64 in Pennsylvania between January 1 and December 31, 2007 (N = 4,920). Women meeting these criteria were mailed an introductory letter explaining the study purpose and procedures, followed by a second mailing with consent form, study questionnaire, a stamped, addressed return envelope, and an unconditional incentive of 5 dollars. Nonrespondents were sent 2 additional mailings. Women were excluded if they were deceased (N = 91), had invalid addresses (N = 594), or if found to be ineligible (reported not having cancer, not able to read/speak English N = 12). Of the 4,223 women eligible for the study, 2,259 women returned the questionnaire (53%). Of the 2,259 respondents, 2,213 women answered the BRCA testing question which resulted in the final analytic population of 2,213 (Table 1). There was no difference in mean age at diagnosis between respondents and nonrespondents. Women who responded were more likely to be White and had earlier stage at diagnosis compared to women who did not respond.

Table 1. Characteristics of the study population

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>Total N = 2,213</th>
<th>BRCA test (yes) N = 577, 26.1%</th>
<th>BRCA test (no) N = 1,636, 73.9%</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt;50*</td>
<td>793 (35.8)</td>
<td>353 (61.2)</td>
<td>440 (26.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age ≥ 50</td>
<td>1420 (64.2)</td>
<td>224 (38.8)</td>
<td>1196 (73.1)</td>
<td></td>
</tr>
<tr>
<td>Ancestry</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not Jewish</td>
<td>2041 (92.2)</td>
<td>507 (87.9)</td>
<td>1534 (93.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Jewish</td>
<td>134 (6.1)</td>
<td>61 (10.6)</td>
<td>73 (4.4)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td>0.341</td>
</tr>
<tr>
<td>Caucasian</td>
<td>2007 (90.7)</td>
<td>529 (91.7)</td>
<td>1478 (90.3)</td>
<td></td>
</tr>
<tr>
<td>Non-Caucasian</td>
<td>206 (9.3)</td>
<td>48 (8.3)</td>
<td>158 (9.7)</td>
<td></td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>1223 (55.3)</td>
<td>355 (61.5)</td>
<td>868 (53.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Not employed</td>
<td>990 (44.7)</td>
<td>222 (38.5)</td>
<td>788 (46.9)</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Married</td>
<td>1528 (69.0)</td>
<td>429 (74.3)</td>
<td>1099 (67.2)</td>
<td></td>
</tr>
<tr>
<td>Not married</td>
<td>685 (31.0)</td>
<td>148 (25.7)</td>
<td>537 (32.8)</td>
<td></td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
<td></td>
<td>0.000</td>
</tr>
<tr>
<td>Less than college</td>
<td>791 (35.7)</td>
<td>144 (25.0)</td>
<td>647 (39.6)</td>
<td></td>
</tr>
<tr>
<td>College and above</td>
<td>1422 (64.3)</td>
<td>433 (75.0)</td>
<td>989 (60.4)</td>
<td></td>
</tr>
<tr>
<td>Annual household income</td>
<td></td>
<td></td>
<td></td>
<td>0.000</td>
</tr>
<tr>
<td>&lt;30k</td>
<td>455 (20.6)</td>
<td>70 (12.1)</td>
<td>385 (23.5)</td>
<td></td>
</tr>
<tr>
<td>30–70k</td>
<td>759 (34.3)</td>
<td>191 (33.1)</td>
<td>568 (34.7)</td>
<td></td>
</tr>
<tr>
<td>&gt;70k</td>
<td>853 (38.5)</td>
<td>285 (49.4)</td>
<td>568 (34.7)</td>
<td></td>
</tr>
</tbody>
</table>

*Mean age of dx = 52.14 range (23–64 years).
Data collection
The study questionnaire elicited sociodemographic characteristics, detailed maternal and paternal family history of breast and ovarian cancer, and tumor characteristics. In addition, women were asked whether they underwent BRCA testing, and the approximate date of testing. Because of privacy concerns given the mailed questionnaire, we did not ask women to report the results of genetic testing. Participants’ responses were linked to age and stage at diagnosis of breast cancer from the cancer registry.

Statistical analysis
Age at diagnosis was categorized less than 50 years or greater than or equal to 50 years. Family history was categorized as: any (yes/no), first-degree relatives (FDR; none, mother only, sister/daughter only, and more than 1 FDR), and second-degree relatives (SDR; none, maternal, paternal, and both maternal and paternal).

Patient characteristics including age at diagnosis, Jewish ancestry, and family history were compared between patients who did and those that did not undergo BRCA testing. Differences in the characteristics of women who did and did not undergo BRCA testing were compared using Pearson $\chi^2$ tests. Multivariable logistic regression was conducted to estimate the odds of undergoing BRCA 1/2 testing by age at diagnosis, Jewish ancestry, race, employment status, marital status, education, annual household income, and family history of breast or ovarian cancer. These variables were selected because they were expected to influence genetic testing based on clinical experience and prior research studies. Model fit was assessed using the Hosmer–Lemeshow goodness-of-fit test. Next we conducted analyses among women with no first-degree relatives affected to better isolate the effects of maternal versus paternal family history among SDRs on BRCA testing utilization.

We formulated clinically relevant scenarios and calculated the corresponding predicted probability for testing for an individual with a given set of characteristics. We compared the predicted probabilities of testing by age, family history, and Jewish ancestry, assuming a woman was college educated, married, employed, and had income $>$70,000.

Results
Demographic characteristics of the study population by BRCA testing status are listed in Table 1. The mean age at diagnosis was 52 years (range 23–64 years). Most women had early stage, localized disease (64.7%). Over 90% of respondents were White, over 64% reported some form of college education, and 38% reported annual household income greater than $70,000. Ninety percent of participants reported having health insurance. In total, 26.1% of patients reported that they underwent BRCA genetic testing. Of the 2,213 respondents, 36% had a young age at diagnosis ($<$50 years).

Women who had undergone BRCA testing had higher education and household income, were more likely to have any family history (as well as a maternal or paternal family history of breast/ovarian cancer), more likely to be employed, married, and of Ashkenazi Jewish ancestry ($P<0.001$). Tumor characteristics, including stage at diagnosis and ER/PR status did not differ by BRCA testing status.

Half of the population (50%) had some family history of breast or ovarian cancer (Table 2). As expected, women who reported BRCA testing (vs. no BRCA testing) were significantly more likely to have any family history, an affected FDR, or an affected SDR ($P<0.001$). Among

<table>
<thead>
<tr>
<th>Family history</th>
<th>BRCA test (yes)</th>
<th>BRCA test (no)</th>
<th>P-value$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$N =$ 577</td>
<td>$N =$ 1,636</td>
<td></td>
</tr>
<tr>
<td>Any family history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1106 (50.0)</td>
<td>379 (56.7)</td>
<td>727 (44.4)</td>
</tr>
<tr>
<td>No</td>
<td>1107 (50.0)</td>
<td>198 (34.3)</td>
<td>909 (55.6)</td>
</tr>
<tr>
<td>FDR categories</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1630 (73.7)</td>
<td>342 (59.3)</td>
<td>1288 (78.7)</td>
</tr>
<tr>
<td>Mother only</td>
<td>340 (15.4)</td>
<td>148 (25.7)</td>
<td>192 (11.7)</td>
</tr>
<tr>
<td>Sister/daughter only</td>
<td>180 (8.1)</td>
<td>55 (9.5)</td>
<td>125 (7.6)</td>
</tr>
<tr>
<td>More than 1 FDR</td>
<td>63 (2.9)</td>
<td>32 (5.6)</td>
<td>31 (1.9)</td>
</tr>
<tr>
<td>SDR categories</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1326 (59.9)</td>
<td>283 (49.1)</td>
<td>143 (63.8)</td>
</tr>
<tr>
<td>Maternal</td>
<td>428 (19.3)</td>
<td>133 (23.1)</td>
<td>195 (18.0)</td>
</tr>
<tr>
<td>Paternal</td>
<td>356 (16.1)</td>
<td>118 (20.5)</td>
<td>238 (14.6)</td>
</tr>
<tr>
<td>Both maternal and paternal</td>
<td>103 (4.7)</td>
<td>43 (7.5)</td>
<td>60 (3.7)</td>
</tr>
</tbody>
</table>

$^a$Pearson $\chi^2$ test.
women who received BRCA testing, 41% had one or more affected FDRs and 51% had one or more affected second-degree relatives, compared with 21% with affected FDRs and 36% with affected SDRs among women who did not receive BRCA testing.

Results of logistic regression of predictors for BRCA testing in the overall sample are shown in Table 3. After adjusting for demographics and socioeconomic factors including college education, employment, and marital status, young age at diagnosis (<50 years) was strongly associated with BRCA testing, with women diagnosed before age 50 years having nearly 5 times the odds of receiving BRCA testing compared to women diagnosed at age 50 or older (OR = 4.81; 95% CI, 3.85–6.00; P < 0.001). Family history was another strong predictor of BRCA testing but resulted in a lower odds of BRCA testing compared to young age at diagnosis, with the exception of women with 2 FDRs having 6 times the odds (OR = 5.97; 95% CI, 3.42–10.43; P < 0.001) of having undergone BRCA testing. FDR categories including mother alone affected (OR = 3.10; 95% CI, 2.36–4.08; P < 0.001) and sister or daughter affected (OR = 2.83; 95% CI, 1.94–4.13; P < 0.001) were also associated with BRCA testing. Having affected SDRs was also associated with BRCA testing, although the association for SDRs was weaker than FDRs. Second-degree family history associated on the maternal and paternal sides were both significantly associated with BRCA testing, although the odds ratio for paternal relatives (OR = 1.81; 95% CI, 1.37–2.41; P < 0.001) was greater than that of maternal relatives (OR = 1.37; 95% CI, 1.04–1.79; P = 0.024). Women with both maternal and paternal SDRs had the highest odds of testing (OR = 2.03; 95% CI, 1.28–3.23; P = 0.003) compared to women with no affected SDRs.

In addition, college education (OR = 1.52; 95% CI, 1.19–1.95; P = 0.001), annual household income of greater than $70,000 (OR = 2.20; 95% CI, 1.52–3.18; P < 0.001), and Jewish ancestry (OR = 1.59; 95% CI, 1.20–2.09; P = 0.001) were also strongly associated with BRCA testing, although less so than age and family history. We assessed model fit using the Hosmer–Lemeshow goodness-of-fit test which indicated adequate model fit (P = 0.300).

To further examine the effect of maternal versus paternal family history of breast and ovarian cancer, we repeated the analysis among women with no affected FDRs, because paternal relatives are by definition second degree (Table 4). Women with affected paternal SDRs had 2 times the odds of having undergone BRCA testing (OR = 2.14; 95% CI, 1.52–3.03; P = 0.001), whereas women with maternal SDRs had 1.3 times the odds of BRCA testing compared to women with no family history (OR = 1.30; 95% CI, 0.91–1.87; P = 0.151), and this difference between the effect of maternal and paternal SDRs was statistically significant (P = 0.024). The effect of having both maternal and paternal family history was stronger than either maternal or paternal family history alone (OR = 2.57; 95% CI, 1.47–4.51; P = 0.001). The Hosmer–Lemeshow goodness-of-fit test indicated adequate model fit (P = 0.734).

Next, we used the logistic regression model to estimate the predicted probabilities of BRCA testing for several clinical scenarios based on age at diagnosis, family history of breast or ovarian cancer, and Jewish ancestry (Table 5).
For illustration, we assumed women to be college educated, married, employed, and have income >$70,000 when predicting probabilities to estimate the highest potential testing rate. The probability would be lower for those with lower income, lower education, unmarried, and unemployed status. In this analysis, Jewish women with any family history with age at diagnosis less than 50 had the highest predicted probability of BRCA testing (82%). Interestingly, young Jewish women with no family history had similar probability of testing as young non-Jewish women with a family history (63% for both groups, respectively). In general, Jewish ancestry when combined with other patient characteristics such as a young age at diagnosis significantly elevated the predicted probability for testing in many subgroups (63% in Jewish women with young age at diagnosis vs. 39% in non-Jewish women, 26% with older age at diagnosis compared to 12% in non-Jewish women).

The strong effect of age at diagnosis on BRCA testing is illustrated in the predicted probabilities. The likelihood of BRCA testing was below 50% in all cases for women 50 years or older at diagnosis, even among those with more than 1 FDR affected. For example, a young Jewish patient <50 years with no family history had markedly higher predicted probability of testing (63%) compared with an older, non-Jewish breast cancer patient with more than 1 FDR (43%).

A positive relationship was seen with respect to the number and degree of relation of relatives, with a predicted probability of 79% for individuals with more than 1 FDR and 66% for individuals with one affected FDR among women with young age at diagnosis. Women with paternal SDRs had slightly higher predicted probability (54%) of undergoing testing than patients with maternal SDRs (47%), and the additive effect of maternal and paternal SDRs was slightly greater than paternal SDRs alone (57% vs. 54%).

Discussion

To our knowledge, this is among the first population-based studies to examine which aspects of BRCA testing criteria, including detailed family history (both first-degree and second-degree relatives in maternal and paternal lineages), are most predictive of testing utilization in breast cancer patients. Overall, we found that young age at diagnosis, family history of breast and ovarian cancer, Jewish ancestry, higher education, and higher income were predictive of BRCA utilization in a cohort of women diagnosed with breast cancer before age 65 recruited from the PA cancer registry.

The patterns of BRCA utilization observed largely reflected evidence-based clinical guidelines for genetic testing, suggesting that BRCA testing is, for the most part, being applied appropriately. Women with a combination of high-risk factors including: Jewish ancestry, young age at diagnosis, and family history had the highest probability of undergoing BRCA testing, consistent with their high risk for a BRCA mutation (16, 17). However, age of diagnosis seemed to have the strongest overall effect in BRCA testing utilization. Young age at diagnosis did lower the threshold for BRCA testing and may have had an effect on the ascertainment of family history which has been supported in other studies (24). In non-Jewish women diagnosed at age 50 or older, testing utilization was markedly lower, even among women with significant family history.

Myriad II is a set of mutation prevalence tables categorized by ethnicity, age of onset of breast cancer, and family history of breast and ovarian cancer based on empiric clinical testing from Myriad Genetic Laboratories (18). In our study, despite the elevated chance for a BRCA mutation in older women with a significant family history (~8.0% by Myriad prevalence tables) compared to women diagnosed less than age 50 with no family history (4.7% based on Myriad prevalence tables), the predicted
probability for testing was similar (43% vs. 39%, respectively). Furthermore, despite similar Myriad prevalence scores (8–10%), a young Jewish patient <50 years with no family history had markedly higher predicted probability of testing (63%) compared with an older, non-Jewish breast cancer patient with more than 1 FDR (43%). This finding may be due to the fact that age and ancestry are easy to identify, while ascertaining detailed family history can be more complicated, requiring additional time from the clinician.

Maternal first-degree relatives were significantly associated with BRCA testing. With the maternal family history, the mother is informative and is likely a main predictor for BRCA uptake, which was supported by this study as well. Among patients with no affected FDRs, paternal SDRs were more predictive of genetic testing than maternal SDRs. Each paternal female relative, as opposed to maternal second-degree relatives, becomes more crucial to the assessment because the father is uninformative. It has been shown that in single cases of early onset breast cancer, the limited family structure (seen more in paternal family history) weighs more heavily in predicting a BRCA mutation, and subsequently more crucial to the risk assessment process (25). In the cited study, BRCA mutations were detected in 13.7% participants with limited family structure versus 5.2% with informative family structure. Paternal second-degree relatives were a particularly strong predictor of BRCA testing among those without affected FDRs in this study, highlighting the importance of paternal lineage in the risk assessment process in individuals with no affected maternal first-degree relatives.

Accurate identification of high-risk candidates based on family history for BRCA testing is largely dependent on 2 factors: reporting of the family history and the clinical assessment of the reported family history. Although this is not the focus of this study, it has been suggested in the literature that there may be a bias in reporting of family history such that paternal family history is underreported compared to maternal family history (26–28). On a population basis, women should have equal numbers of maternal and paternal extended relatives affected with breast cancer (not including the mother; ref. 28). In our study, paternal SDRs and maternal SDRs were both reported similarly (19.3% having maternal SDRs and 16.1% having paternal SDRs). Equivalent reporting of family history in this study may be a function of formal genetic counseling.

Interestingly, cumulative effect of maternal and paternal second-degree relatives was seen to be more strongly associated with BRCA utilization than having only maternal or paternal relatives affected. In clinical genetics practice, each side of the family is assessed independently when assessing the probability of a mutation. Therefore, it is unclear the reason behind the stronger association with both maternal and paternal SDRs. Patients may inaccurately perceive their risk of having a mutation as higher than what it is when they have affected relatives on both sides of the family, and this inflated risk perception could be driving BRCA testing. If these women are of higher socioeconomic status, they may choose to undergo genetic testing despite lack of insurance coverage. Biallelic mutations can also occur in specific ethnic groups, such as Ashkenazi Jews, which may partially explain this association, but it does not seem that Jewish ancestry was overrepresented in patients with both maternal and paternal family history. In addition, it is possible that some genetic tests in this cohort were ordered by nongenetics professionals who may not be aware of the need to evaluate maternal and paternal lineages separately. Although family history is a known risk factor, patient and provider risk perceptions remain variable and do not necessarily reflect standard criteria in unaffected patients (21). Studies have also documented different risk assessment practices among genetics versus nongenetics providers (29–32). Although Myriad Genetics, the sole proprietor of BRCA 1/2 testing, began direct to physician and direct to consumer marketing in select pilot cities prior to 2007 (33), this did not include Pennsylvania. This cohort may precede the effects of massive marketing efforts of Myriad (34) and most patients who received genetic testing were still likely being referred to a genetics professional for BRCA genetic testing in accordance with NCCN guidelines. Further analysis is needed to understand why women with both maternal and paternal family history were more likely to undergo BRCA testing than women with family history in only one lineage.

The association of education with BRCA testing is not surprising because those with better understanding of how these results can impact risk for future cancers, have a greater desire to be proactive and notify at risk family members, especially children (20, 35). Although almost all of the patients did have some insurance, their extent for coverage for BRCA testing remains unknown. There are likely less economic barriers in educated women, who may be able to pay for genetic testing if insurance coverage was suboptimal.

The main strength of our study is the population-based design with recruitment from the PCR, which provided a large sample of women with cancer diagnosed before age 65. Furthermore, this study elicited detailed family history data among breast cancer patients recruited from the cancer registry. Many prior studies of genetic testing have relied on small convenience samples recruited from genetic testing clinics (9, 11, 15, 36, 37).

Several limitations of the data should be considered. First, the response rate to the questionnaire was modest, and minority women and women with later stage disease were underrepresented. Second, we relied on self-report of BRCA testing as well as family history; however, we did not see evidence of significant underreporting of paternal versus maternal family history. A possible bias may be that women with a family history were more likely to
participate in the survey. Also, patients who underwent genetic counseling are likely more familiar with both their maternal and paternal family history which may have resulted in an overestimate of the associations between family history and BRCA utilization. In addition, as we did not have the results of the genetic testing due to privacy concerns, we cannot calculate the exact positive predictive value of each study variable for risk of BRCA mutation, but the predictors of early onset breast cancer, family history of breast or ovarian cancer, and Ashkenazi Jewish ancestry are present in standard criteria because of their overall high predictive value consistent with Myriad prevalence data. Future studies will be needed to assess the positive predictive value of each study variable with respect to BRCA mutation status to ascertain whether observed rates of testing are adequate on a population level.

Early onset breast cancer, Jewish ancestry, family history, education, and income were strongly associated with BRCA test utilization. Our results suggest that family history may be an underused tool, particularly among breast cancer patients older than age 50 at diagnosis. Methods to assess detailed family history that can easily be integrated into routine clinical care, such as through electronic medical records and validated patient referral tools, are needed.

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

Authors’ Contributions
Conception and design: H. Vig, A.M. McCarthy, K. Armstrong
Development of methodology: H. Vig, M.B. Demeter, K. Armstrong
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): K. Liao, M.B. Demeter, T. Fredericks, K. Armstrong
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): H. Vig, A.M. McCarthy, K. Liao, M.B. Demeter, K. Armstrong
Writing, review, and/or revision of the manuscript: H. Vig, A.M. McCarthy, M.B. Demeter, T. Fredericks, K. Armstrong
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): H. Vig, M.B. Demeter, T. Fredericks
Study supervision: M.B. Demeter

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