Understanding and Impact of Negative Direct-to-Consumer BRCA Test Results: A Pilot Study

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Abstract

Many people pursue direct-to-consumer (DTC) DNA testing to learn about health risks. While DTC testing for breast cancer genes BRCA1 and BRCA2 may provide vital information to those testing positive, it is unclear whether individuals testing negative understand the implications of these results. Furthermore, it is unknown how such findings may influence future cancer risk management. Sixty-nine individuals who underwent BRCA testing through the DTC service, 23andMe, completed a survey designed to assess their understanding of a negative result and how this result may impact cancer risk management. Respondents were recruited via social media sources Reddit and Facebook. All participants tested negative for the three BRCA variants analyzed by 23andMe: BRCA1 185delAG, BRCA1 5382insC, and BRCA2 6174delT. Six questions assessed understanding of the limitations of the testing. Results indicated that 77.1% of respondents answered five or more questions correctly, confirming participants adequately understood testing limitations. While 92% of participants reported their results would not alter the frequency of their cancer screenings, analysis of variance indicated that lower understanding of testing limitations was associated with less clarity about how to proceed with cancer risk management, F (2, 93) = 5.98, p < .05. Analyses were conducted to identify factors contributing to overall understanding scores. Significant correlates of understanding were age and education level. Participants perceived risk played a role in both their understanding and future cancer risk management, F (2, 93) = 5.98, p < .05.

Methods

- 55-question fixed-choice survey
- Distributed via social media
- Inclusion criteria:
  - Consent to survey
  - 18 years of age
  - Chose to view BRCA report
- Tested BRCA1/2 negative
- Recruitment though Reddit and Facebook

Results

- Participant Understanding:
  - Six questions asked to gauge participant’s understanding of the limitations of DTC BRCA testing:
    - What do you understand about the testing?
    - Are BRCA1 and BRCA2 the only known cancer susceptibility genes?
    - Could you still be at risk for having a mutation in your BRCA1 or BRCA2 genes after testing negative through 23andMe?
    - Could you still be at risk for having a mutation in a different cancer susceptibility gene after testing negative through 23andMe?
    - Could anyone in your family still be at risk for having a mutation in their BRCA1 or BRCA2 genes after you test negative through 23andMe?
    - Can a person’s ethnicity influence how likely they are to be a BRCA1/2 carrier?
  - Answers were dichotomously scored and an additive metric was applied.
  - Scores displayed in Table 2:
    - Average score = 5.1/6 ± 1.4
    - Adequate understanding of the limitations of DTC BRCA testing
    - Cancer Risk Management:
      - Assessed by a single item
      - Participants asked how negative BRCA results would alter cancer screenings
        - 91.7% reported they would not change cancer screenings based on negative results
        - 4.2% planned to increase vigilance
        - 4.2% were unsure
      - No participants reported decreasing cancer screenings

Demographics

- Table 1: Demographic Information
  - Total = 69
  - Understanding Score = 5.1 ± 1.4
  - % = 3.1%

Explanatory Analyses

- Identify factors predictive of participants’ understanding:
  - Age and education level were significantly correlated:
    - Individuals under the age of 40 (n=76) scored significantly better than individuals over the age of 40 (n=20)
      - F (1, 94) = 6.390, p < .05
    - A significantly positive correlation was seen between participant’s education levels and understanding.
      - r = .215, p < .05
  - Recruitment source, gender, and ethnicity were not indicative of understanding.
  - Perceived risk, understanding and preventative behavior:
    - Risk score calculated
    - Respondents asked to gauge their risk to develop cancer based on:
      - BRCA results
      - Family history
      - Personal habits
    - Significant positive correlation between perceived risk and understanding
    - Individuals who reported more vigilant cancer screening perceived themselves to be at higher risk
    - Interaction not significant (possibly due to small sample size)

Discussion

- First Degree Relatives (FDR)
  - FDR diagnosed with BRCA related cancer (n=30) perceived their overall risk to be higher than those without an affected FDR (n=66)
    - F (1, 94) = 6.715, p < .05
  - Individuals with an affected relative had a better understanding of the limitations of DTCGT
    - F (1, 94) = 5.471, p < .05
- Raw Data Analysis
  - 58.8% analyzed their raw data through a secondary source
  - No significant difference noted in understanding between those who analyzed their raw data and those who did not

Research Aims

- Determine participant’s understanding of a negative 23andMe BRCA test result
- Examine whether participants use negative results to impact cancer risk management

Introduction

- Direct-to-consumer genetic testing (DTCGT) allows consumers access to their genetic information outside of the healthcare world.
- 23andMe was the first DTCGT company to receive FDA approval to analyze breast cancer genes BRCA1 and BRCA2.
- Pathogenic variants in the BRCA genes cause Hereditary Breast and Ovarian Cancer Syndrome (HBOC) which drastically increases an individual’s lifetime risk of cancer (breast, ovarian, prostate, pancreatic, and melanoma) over that of the general population.
- Limitations to DTC BRCA testing:
  - Only three Ashkenazi Jewish founder mutations analyzed:
    - BRCA1 185delAG
    - BRCA1 5382insC
    - BRCA2 6174delT
  - Common in the Ashkenazi Jewish population but rare in the general population.
  - >1000 disease causing variants in the BRCA genes have been identified.
  - Only BRCA1 genes are examined:
    - Dozens of other cancer predisposition genes have been identified.
  - Speculations that consumers do not understand the limitations of DTC BRCA testing and may feel falsely reassured by a negative result have been made.

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Discussion

- Majority of individuals in this population:
  - Understood limitations of DTC BRCA testing
  - Would not use results to alter cancer screenings
  - Promising that individuals in this population were not falsely reassured of personal cancer risk due to negative results
  - Individuals who were unsure how their results would alter screenings had a lesser understanding of the testing.
  - This is concerning as it implies that DTCGT may influence how some individuals proceed with cancer risk management.

- Limitations:
  - Demographic data is not publicly available from 23andMe
  - It is not clear what individuals are currently doing for their cancer risk management
  - Recruitment method may be biased:
    - Subreddits and Facebook groups dedicated to 23andMe, genetics and genomics were utilized
  - 23andMe was the only DTC company examined