Awareness and Uptake of Direct-to-Consumer Genetic Testing Among Cancer Cases, Their Relatives, and Controls: The Northwest Cancer Genetics Network

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Aims: To determine if awareness of, interest in, and use of direct-to-consumer (DTC) genetic testing is greater in a sample of high-risk individuals (cancer cases and their relatives), compared to controls. **Methods:** Participants were recruited from the Northwest Cancer Genetics Network. A follow-up survey was mailed to participants to assess DTC genetic testing awareness, interest, and use. **Results:** One thousand two hundred sixty-seven participants responded to the survey. Forty-nine percent of respondents were aware of DTC genetic testing. Of those aware, 19% indicated interest in obtaining and <1% reported having used DTC genetic testing. Additional information supplied by respondents who reported use of DTC genetic tests indicated that 55% of these respondents likely engaged in clinical genetic testing, rather than DTC genetic testing. **Conclusion:** Awareness of DTC genetic testing was greater in our sample of high-risk individuals than in controls and population-based studies. Although interest in and use of these tests among cases in our sample were equivalent to other population-based studies, interest in testing was higher among relatives and people who self-referred for a registry focused on cancer than among cases and controls. Additionally, our results suggest that there may be some confusion about what constitutes DTC genetic testing.

Introduction

THE TRANSLATION OF single nucleotide polymorphism (SNP) technology into commercial products such as direct-to-consumer (DTC) genetic testing is a controversial issue among members of the genetics and ethics communities. As the name suggests, DTC genetic tests are purchased by the consumer directly from the genetic testing company, without involving a health care provider either to order a test or to interpret the results. Often, these tests report risk for multifactorial diseases, such as cancer or diabetes, using data from SNP analysis and proprietary algorithms to calculate risk. The clinical validity and utility of these tests is questionable (Hunter *et al.*, 2008; Eng and Sharp, 2010). There is concern that inappropriate interpretation of disease risk by the consumer could lead to physical and psychological harm and that many primary care providers are unprepared to discuss and interpret the results of DTC genetic tests (Hunter *et al.*, 2008; McGuire and Burke, 2008; Powell *et al.*, 2011).

The size of the DTC genetic testing market is difficult to estimate because most DTC genetic testing companies are not publicly held (Wright and Gregory-Jones, 2010). To assess this market, Goddard *et al.* (2006) conducted a representative

survey in three states asking about awareness and use of DTC genetic tests. They found that 14% of the population were aware of DTC genetic tests, and less than 1% had used this type of test. Kolor *et al.* (2009) using the 2008 HealthStyles national survey, found similar prevalence of awareness (22%) and uptake (0.3%) of DTC genetic testing. Given that many of these tests are marketed and accessed online, one might expect that awareness and use of DTC genetic tests would be higher among social networkers. McGuire *et al.* (2009) found that Facebook users indeed reported higher awareness of DTC genetic testing than was found in national surveys, yet reported use was still fairly low (47% and 6%, respectively). Additionally, the Multiplex Initiative was conducted among a sample of members of the Henry Ford Health System in Detroit, Michigan (Kaphingst *et al.*, 2010). Study participants were offered a multiplex genetic test—similar to those offered through DTC genetic testing companies—that tested for the risk alleles of 15 genetic markers previously associated with eight common chronic diseases. Only 11% of participants chose to receive multiplex testing. These studies indicate interest in and uptake of DTC genetic tests is low among the general population, but it is likely that interest and use will vary among different subgroups, particularly as awareness of

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the importance of family health history and genetic contributions to disease risk increases.

However, prior studies have not evaluated awareness, interest or use of DTC testing among different segments of the population, particularly among those individuals with cancer or their first-degree relatives. One recent study assessed interest in (but not awareness or use of) genetic testing for modest changes in breast cancer risk among women with a personal and/or family history of breast cancer, finding that three-quarters of these women were interested in testing (Graves *et al.*, 2011). The DTC testing companies 23andMe and Navigenics offer testing for common variants associated with different types of cancer, including breast, colon, prostate, and melanoma (23andMe, 2011; Navigenics, 2011). Furthermore, 23andMe offers carrier testing for three specific *BRCA1* and *BRCA2* mutations found primarily among those of Ashkenazi Jewish descent (23andMe, 2011). Because of ease of access and the relatively low cost for DTC testing that frequently includes variants associated with cancers, we hypothesize that people with a personal or family history of cancer may be more aware, more interested, and have higher use of these tests than the general population.

Materials and Methods

The Northwest Cancer Genetics Network (NWCGN), funded by the National Cancer Institute (NCI), is a registry of individuals (subjects with cancer, their family members, and controls) who contributed information about individual and family history of cancer and other health conditions, tobacco use, and sociodemographic information (Anton-Culver *et al.*, 2003). The purpose of the NWCGN is to collect and maintain data from a large group of participants to support collaborative investigations on the genetic basis of cancer susceptibility. It was one of the eight original sites contributing to the Cancer Genetics Network (CGN), established by the NCI in 1998 as a nationwide network of centers to specialize in the study of inherited predisposition to cancer. The site for the NWCGN is at the University of Washington.

For the parent NWCGN study, cases were recruited via population-based cancer registries and direct referral from health care providers throughout Western Washington. Controls were randomly selected, within the 5-year age and

gender strata, from English-speaking male and female residents of the 3-county study area, and included individuals with cancer to allow for comparisons with a population-based control sample. Some participants self-referred to the registry in response to community awareness and education efforts and included both people with and without cancer. The NWCGN also enrolled first-degree relatives of cases and those who self-referred to the registry. All participants completed core data questionnaires at baseline and have been sent follow-up questionnaires since study entry. The questionnaires cover a variety of topics, including basic demographic information, personal medical history, family medical history, and awareness and use of genetic testing. The NWCGN is the only CGN site to ask questions about DTC genetic tests, and it served as the source of subjects for this study.

From 2008 to 2009, all active NWCGN participants ($n=3719$) were mailed a follow-up survey that included questions about awareness, intention, and actual use of DTC genetic tests (Table 1). These questions, derived from state-added questions on Michigan's Behavioral Risk Factor Surveillance System survey in 2009, were pilot-tested by the Michigan Department of Community Health.

Individuals who responded to any of these questions were considered eligible for the present study. Participants who responded "yes" to Question 3 and/or "already had genetic testing" to Question 5 were considered to have had DTC genetic testing. Interest in genetic testing was defined as answering "considering having genetic testing," "probably will have genetic testing," or "definitely will have genetic testing" to Question 5.

For the present study of DTC genetic testing, participants were categorized into four groups based on their referral method and cancer status. Those categorized as "Cases" were recruited through a health professional or a cancer registry and had cancer at the time they were recruited to the NWCGN study. The most frequent cancers reported at the NWCGN study baseline were melanoma (34%), thyroid (16%), breast (12%), skin (12%), and prostate (9%). "Relatives" were the first-degree family members of those identified as having had cancer at recruitment, but who themselves had not had cancer at the time they were recruited to the NWCGN study. The "Controls" category was made up of study participants who had not had cancer at the time of recruitment to the NWCGN

TABLE 1. DIRECT-TO-CONSUMER GENETIC TESTING SURVEY QUESTIONS

Question no.	Question text	Measures
1	"Private companies now offer genetic tests that assess a person's genetic makeup for a variety of potential health risks. These tests are being marketed (advertised and sold) directly to the public by several different private companies (e.g., 23andMe, deCODEme, Navigenics). Have you heard or read about these genetic tests from private companies that assess a person's genetic makeup for health risks?"	Awareness
2	"From which of the following sources did you hear or read anything about these genetic tests: newspaper, health professional, friend, magazine, internet, TV or radio, family member, other, not sure?"	Awareness
3	"Have you ever had one or more of these genetic tests?"	Use
4	"Did you discuss the results of this test (or these tests) with your healthcare provider?"	Use
5	"At the present time, which of the following statements best describe your feelings about these types of genetic tests? (Not considering or thought about having genetic testing, considering having genetic testing, probably will have genetic testing, definitely will have genetic testing, already had genetic testing)."	Interest, use

and were not a first-degree relative of a case. Although the parent study included people with cancer at baseline among the population-based controls, in the present study, we excluded people who had a personal history of cancer at recruitment from the "Control" category to clarify interpretation of results. Finally, the "Self-referral" category was composed of both individuals with and without cancer at recruitment (39% and 61%, respectively). Because those who self-referred to the NWCGN may be more interested in genetics than those who were actively recruited, we chose to keep "Self-referral" as a separate category rather than incorporate these participants into "Cases" and "Controls."

Family history of cancer was assessed as the number of cancer cases reported normalized by the number of family members reported. This ratio was then categorized into four groups based on the percent of family members reported to have had cancer, where the highest category was individuals reporting cancer in 25% or more of relatives (roughly the highest quartile) and the lowest category was individuals who reported no family history of cancer.

This study was approved by the University of Washington Human Subjects Division, and all subjects provided informed consent to participate.

Means and proportions were calculated for continuous and categorical variables, respectively. Analysis of variance was used to compare means, and the chi-squared test was used to compare categorical variables across categories of participant type. Logistic regression analysis was used to calculate odds ratios (OR). All analyses were conducted using the STATA 8 statistical software package.

Results

A total of 1267 participants in the NWCGN responded to the survey (34% response rate). The average age of respondents was 62.4 years. Sixty-four percent of respondents were women. Most respondents had at least some college education; only 14% reported attaining a high school diploma or less (Table 2). Forty-nine percent of respondents reported awareness of DTC genetic tests. Of those, 19% reported interest in using a DTC genetic test and 0.9% reported having used a DTC genetic test. There were significant differences in awareness, interest, and use of DTC genetic tests by partici-

pant type (Table 3). Additionally, those who self-referred to the NWCGN were five times more likely to report a family history of cancer compared to controls (OR: 5.45 [2.46–12.05], $p < 0.001$). Cases were not more likely to report a family history of cancer compared to controls ($p = 0.15$).

DTC awareness

Participants recruited to the study as cancer cases were 60% more likely to be aware of DTC genetic testing compared to controls (OR: 1.57 [1.03–2.39], $p = 0.04$). Regardless of personal cancer history, those who self-referred to the study were three times more likely to be aware of DTC genetic testing compared to controls (OR: 3.04 [1.93–4.79], $p < 0.001$). Relatives were no more likely to be aware of DTC genetic testing than controls ($p = 0.12$). However, regardless of participant type, those whose reported family history of cancer was in the highest quartile were 70% more likely to be aware of DTC genetic testing than those who reported no family history of cancer (OR: 1.67 [1.05–2.67], $p = 0.03$, adjusted for participant type). Adjusting for family history did not attenuate the association of self-referring to the study and DTC awareness.

Educational attainment also predicted awareness of DTC testing. Those whose highest educational attainment was a 4-year college or graduate/professional degree were 60% and 80% more likely, respectively, to be aware of DTC genetic testing compared to those who achieved a high school diploma or lower (ORs: 1.62 [1.12–2.36], $p = 0.01$; 1.82 [1.25–2.65], $p = 0.002$). Women were also 40% more likely to be aware of DTC genetic testing compared to men (OR: 1.43 [1.13–1.81], $p = 0.003$).

DTC interest

Among those aware of DTC genetic testing, participant type (i.e., case, control, relative, and self-referral) was not associated with interest in obtaining DTC genetic testing. However, participants who reported a family history of cancer in 25% or more of their relatives reported interest in DTC genetic testing nearly three times greater than those who reported no family history of cancer (OR: 2.84 [1.08–7.48], $p = 0.04$). Women were 75% more likely to be interested in DTC genetic testing compared to men (OR: 1.75 [1.10–2.77], $p = 0.02$). Educational attainment was associated with interest

TABLE 2. DEMOGRAPHIC INFORMATION BY AWARENESS OF, INTEREST IN, AND USE OF DIRECT-TO-CONSUMER GENETIC TESTING

	All	DTC awareness	DTC interest	Had DTC
Mean age (SD)	62.4 (13.3)	61.8 (13.0)	54.7 (13.9)	58.1 (13.4)
Female, % (n/N)	64 (812/1267)	68 (422/620)	77 (93/121)	82 (9/11)
Education, % (n/N)				
≤ High school	14 (176/1256)	11 (68/618)	5 (7/128)	18 (2/11)
College, 1–3 years	31 (393/1256)	30 (184/618)	45 (57/128)	55 (6/11)
College, 4 or more years	28 (351/1256)	29 (182/618)	26 (33/128)	18 (2/11)
Graduate/professional school	27 (336/1256)	30 (184/618)	24 (31/128)	9 (1/11)
Family history of cancer, % (n/N)				
No family history	8 (105/1267)	6 (40/620)	4 (5/128)	9 (1/11)
Family history <10% of family members	19 (238/1267)	15 (90/620)	9 (12/128)	18 (2/11)
Family history between 10% and 25% family members	41 (523/1267)	42 (259/620)	39 (50/128)	27 (3/11)
Family history >25% of family members	32 (401/1267)	37 (231/620)	48 (61/128)	45 (5/11)

DTC, direct-to-consumer; SD, standard deviation.

TABLE 3. KNOWLEDGE OF, INTEREST IN, AND UPTAKE OF DIRECT-TO-CONSUMER GENETIC TESTING BY PARTICIPANT TYPE

	Self-referral N=332 % (n/N)	Cases N=654 % (n/N)	Relatives N=168 % (n/N)	Controls N =113 % (n/N)	p-Value
Heard of DTC genetic testing	63 (208/331)	47 (304/649)	46 (78/168)	36 (41/113)	<0.001
Interested in having DTC genetic testing	25 (52/205)	15 (43/295)	27 (20/75)	17 (7/41)	0.009
Had DTC genetic testing	3 (7/208)	1 (4/304)	—	—	—

in DTC testing. Only 5% of respondents who expressed interest in DTC genetic testing had a high school diploma or lower (Table 2). Those whose highest educational attainment was 1–3 years of college were nearly four times more likely to be interested in obtaining DTC genetic testing compared to those who had completed high school or lower (OR: 3.65 [1.57–8.49], $p=0.003$). However, those who had completed college or graduate/professional school were not more likely to be interested in obtaining DTC genetic testing compared to those who had completed high school or lower.

DTC use

Among those aware of DTC genetic testing, 11 participants reported having had DTC genetic testing. Of those, 63% were self-referrals and 36% were cases. Ten of the 11 participants reported a family history of cancer; half of the participants reporting family histories of cancer had cancer in 25% or more of relatives. All but one of those reporting DTC use also reported having had cancer at baseline. The person who did not report cancer at baseline reported a family history of cancer. These participants were younger than the overall sample and mostly female (Table 2).

Survey questions 3 and 5 assessed the DTC use (Table 1). Answers to these questions were discordant (i.e., participant marked no to Question 3, but yes to Question 5 or vice versa) among 6 of the 11 participants (55%). Five of the 6 participants with discordant answers reported that they had heard about DTC genetic testing from their health care provider. By contrast, the participants who were concordant reported hearing about DTC genetic testing from various media sources and friends. Also, several of the discordant participants wrote additional information about their genetic test in the margins of the survey. One participant reported that she was tested for a Mendelian disorder that was not included on any DTC panel at the time of the survey. Another said that the testing was done on tumor tissue, and yet another said she was tested by her rheumatologist. These responses indicate that discordant participants likely misunderstood what DTC genetic tests were, perhaps confusing them with traditional clinical genetic tests.

Discussion

Awareness of DTC genetic testing was higher among this highly educated sample of individuals with cancer, their relatives, controls, and self-referrals compared to awareness in national studies (49% vs. 14% or 22%) (Goddard *et al.*, 2006; Kolor *et al.*, 2009). Whether they had a history of cancer or not, those who self-referred into the NWCGN study were more aware of DTC testing than were other participant types. This finding suggests that those who are highly motivated and

interested in research are also aware of DTC genetic testing. NWCGN participants recruited as cancer cases were also more aware of DTC genetic testing compared to controls. Additionally, participants with the strongest family histories of cancer were more aware of DTC genetic testing compared to those without a family history of cancer, even after adjusting for participant type. Higher educational attainment was also associated with awareness of DTC genetic testing, echoing findings of the Multiplex Initiative (Kaphingst *et al.*, 2010).

Although awareness of DTC genetic testing was higher in the NWCGN compared to other studies, in contrast to Graves and colleagues' study of women at high risk for breast cancer in which 77% expressed definite interest in genetic testing for modest changes in breast cancer risk, only 19% of NWCGN participants who were aware of DTC genetic testing were also interested in obtaining testing (Graves *et al.*, 2011). The interest in testing in the NWCGN sample is similar to the findings from the Multiplex Initiative, in which 11% of study participants ultimately decided to undergo multiplex genetic testing (Kaphingst *et al.*, 2010). Additionally, although study participants who were recruited as cancer cases and participants who self-referred to the study were more aware of DTC genetic testing, neither they nor relatives of the cancer cases were more interested in obtaining testing compared to controls. However, having a family history of cancer in 25% or more of relatives was strongly associated with interest in DTC genetic testing. These findings suggest that having a family history *per se* does not drive interest in DTC genetic testing, but rather the strength of the family history motivates DTC genetic testing interest.

Less than 1% of our study sample reported having had a DTC genetic test, which is very similar to findings from national surveys (Goddard *et al.*, 2006; Kolor *et al.*, 2009). However, over half of these participants gave discordant answers to questions assessing DTC use. These participants also reported hearing about DTC testing through their health care provider (instead of through a DTC medium) and gave specifics about the kind of test they received that are characteristic of clinical genetic tests rather than DTC tests. Taken together, this evidence suggests that these participants were confused about what DTC genetic testing is and likely did not engage in DTC testing. If this is true, our DTC use prevalence estimate is inflated by about 50%; the prevalence of DTC awareness and interest are also likely overestimated. Furthermore, DTC use, interest, and awareness prevalence estimates assessed by population-based surveys may be similarly overestimated, due to a possible conflation of DTC and clinical genetic testing in the general population.

Demographically, our sample is highly educated, which limits the generalization of our results, even to other

individuals with cancer and their relatives. Further, all data were self-reported, thus our data could be affected by recall bias.

Further studies are needed to assess the prevalence of DTC genetic testing awareness, interest, and use in DTC testing among individuals with a positive family history of disease. Additionally, our finding that more than half of our participants who reported DTC genetic testing appeared to confuse DTC testing with traditional clinical genetic testing points to a need for additional clarification of true testing modality on future surveys assessing DTC awareness, interest, and use. Additional questions on the health care provider's involvement in testing and specimen tested (i.e., blood versus buccal swab), for example, may help elucidate whether a participant reporting DTC testing likely received testing through this modality.

Author Disclosure Statement

No competing financial interests exist.

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