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Review

Measurement of psychological factors associated with genetic testing for hereditary breast, ovarian and colon cancers*

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Abstract

Despite numerous individual studies of psychological factors (depression, anxiety, distress) related to genetic testing for inherited cancer syndromes (CGT), there has been no systematic review of the psychological factors are measured among individuals at increased risk for hereditary breast, ovarian, or colon cancer. Our review provides an analysis of psychological factors in studies of CGT and discusses the instruments most commonly used to measure them. We performed a literature search using three major OVID databases from 1993 to January 2003. In the 19 studies that met our inclusion criteria, the most commonly assessed psychological factors were distress, anxiety, and depression. These factors were most often measured by the impact of event scale (IES), the state-trait anxiety inventory (STAI), and the Centers for Epidemiologic Studies and Depression scale (CES-D), respectively. Our results show deficits in the existing body of literature on psychological factors associated with CGT including limited documentation of psychometrics and variability in instrumentation.

Introduction

Recent advances in molecular genetics have led to DNA-based blood tests that can identify deleterious germline mutations transmitted in an autosomal dominant fashion, placing an individual at increased risk for developing hereditary forms of breast, ovarian, or colon cancer. An estimated 5–10% of all cases of breast, ovarian, and colon cancer can be attributed to known germline mutations. The majority of hereditary breast and ovarian cancers (HBOC) are associated with mutations in *BRCA1* and *BRCA2* tumor suppressor genes [1, 2]. Carriers have a 55–85% lifetime risk of developing breast cancer and 15–60% for developing ovarian cancer [3, 4]. The most common form of hereditary colon cancer, hereditary nonpolyposis colon cancer (HNPCC), is related to mutations in the DNA mismatch repair genes such as *hMLH1*, *hMSH2*, *hMSH6*, *hPMS1*, and *hPMS2* [5]. There are also less common forms of hereditary colon cancer known as familial adenomatous polyposis (FAP) and attenuated familial adenomatous poplyposis (AFAP) resulting from a mutation in the APC gene. Those with an HNPCC related mutation have a 70–82% lifetime risk for developing colon cancer and for those with a mutation in the APC gene, the risk of colon cancer is nearly 100% [5, 6].

Due to the increased incidence of cancers associated with these mutations, the psychological impact and outcomes of testing among high risk individuals and their biologic families have been the focus of intense

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study. On a practical level, research in this area has been and continues to be strongly influenced by the National Human Genome Research Institute (NHGRI) Cancer Genetics Studies Consortium core set of questionnaires developed by 12 multidisciplinary teams [7] as well as the publication of a model protocol for evaluating behavioral and psychosocial effects of *BRCA1* testing in the Journal of the National Cancer Institute [8]. Both sets of questionnaires included measures related to distress, anxiety, and depression.

The psychological research to date has provided an opportunity to learn valuable information related to the psychological aspects of cancer genetic testing (CGT) among these research cohorts and kindreds. Current evidence suggests that adverse psychological consequences of CGT are uncommon [9–11]. However, a recent review of the behavioral science literature concerning prenatal, carrier, and predictive testing by Lerman et al. [11] suggested that certain subgroups of individuals with specific psychological traits, including higher levels of intrusive thoughts, depression, and distress, may be at increased risk for negative outcomes associated with CGT.

For example, in a study of women with a personal history of cancer and their first-degree relatives awaiting BRCA mutation test results, women identified as high monitors on the Miller behavioral style scale at baseline interview experienced more anxiety on the State Anxiety subscale of the state trait anxiety inventory (STAI) than low monitors [12]. Another study examined distress in women diagnosed with breast cancer in the year prior to undergoing genetic counseling and testing. Compared with women who were diagnosed prior to a year, women more recently diagnosed with cancer had higher levels of cancer-related distress as measured on the impact of events scale (IES) [13]. In addition to face-to-face genetic counseling, clinical psychological assessment, and patient-provider communication, self-report instruments can be an important tool to identify subgroups at risk for psychological distress at many points in the CGT process.

A number of studies have examined psychological factors related to CGT [14–27]. However, no systematic review has been conducted of the specific self-report instruments used to measure psychological factors among individuals at increased risk for hereditary breast, ovarian, and colon cancer. We defined psychological factors as depression, anxiety, or distress related to CGT that were assessed using a self-report instrument. Our rationale for selecting these three psychological factors was that they are the most commonly reported outcomes in reviews of genetic counseling and testing [9, 11]. The purpose of this paper is to: (1) review the instruments most commonly used to measure depression, anxiety, and distress and summarize the reported psychometric properties; (2) discuss current limitations associated with the use of existing instruments; (3) and suggest directions for future research.

Methods

Search strategy

We modeled our search strategy after previous reviews that examined the psychological issues related to predictive genetic testing [9, 28]. We began with a literature search using three major OVID databases including Medline, PsychInfo, and CINAHL from January 1993 (before the first genes for HBOC and HNPCC were cloned) to January 2003. We searched the databases using combinations of key words (complete list is available in Appendix 1) for the following categories: cancer types and syndromes (i.e., breast, ovarian, colon, HNPCC, or Lynch syndrome); genetics (i.e., *BRCA1*, *BRCA2*, or mutation); CGT (i.e., mutation testing or CGT); and psychological factors (i.e., anxiety, depression, or distress). In addition to the above strategy used in previous reviews [9, 28], we also: (1) reviewed reference lists cited in identified papers for titles that included combinations of our key words and (2) solicited the names of experts who have published in the area of psychological factors and CGT from colleagues and then searched by author name in the three databases. While Broadstock et al. [9] also searched additional databases in their review, their validation strategy comparing their findings to that of a previous review of risk assessment found that all articles identified in the previous review were identified in the Medline database alone [9]. Using the same validation strategy, when we compared our results to that of Broadstock, we identified all of the same articles (although some were not included in the current review due to different study inclusion criteria).

Inclusion criteria

CGT studies were included in this review if they: (1) were published in a peer-reviewed journal in English; (2) utilized adult samples; and (3) used self-report instruments to measure psychological factors (depression, anxiety, or distress). Studies assessing only intention to undergo testing were excluded. Prior studies have shown that while intention to obtain CGT was high [29–32], actual uptake of CGT was low [25, 33]. In addition we excluded studies with 'mixed samples' that included both individuals at increased risk for hereditary cancer and other adult-onset hereditary conditions such as Huntington's disease (HD). Our rationale was that the course of distress and how it may be measured for a disorder such as HD for which no medical interventions are available might be different from that of hereditary cancer [34]. Because of our focus on quantitative measurement of psychological factors through self-report instruments, we excluded qualitative studies and case reports from our review.

Psychological factors in studies of CGT

Our key word searches in OVID yielded 283 articles from the Medline, PsychInfo, and CINAHL databases. Sixteen ($n = 16$) studies met the inclusion criteria, and, author and reference list searches yielded three additional studies. This resulted in a total of 19 studies for our review, 15 related to HBOC and 4 to HNPCC. Table 1 includes the study citation, description of the study sample, primary outcome variable, psychological factors measured in each study, instruments used, and estimates of internal consistency reliability for the 19 studies.

All studies in our review were published after 1996, with 68% ($n = 13$) published in the years between 2000 and 2003. Samples ranged in size from 21 to 290, with 10 of the studies (53%) having 100 or more participants. With the exception of one study of high-risk African American women [35], all studies were conducted with primarily Caucasian participants. Fifty-three percent ($n = 10$) of the studies included both affected and unaffected participants, 26% ($n = 5$) included only affected participants, and 21% ($n = 4$) only unaffected participants. Sixty-eight percent ($n = 13$) of the studies were conducted in the United States, and the remainder in Europe, Canada, and Australia. Over half of the studies (63%; $n = 12$) examined psychological factors *resulting from* CGT post-test disclosure, 32% ($n = 6$) focused on psychological factors that *predicted participation in* CGT, and 5% ($n = 1$) on both.

Instruments commonly used to measure psychological factors in CGT

As shown in Table 2, out of 19 studies, the 3 most frequently measured psychological factors were distress ($n = 13$), anxiety ($n = 7$), and depression ($n = 7$). Although multiple instruments were used, these factors were most often assessed using the IES, the STAI, and the Center for Epidemiological Studies Depression Scale (CES-D), respectively. The total IES was used in 53% ($n = 10$) and the Intrusion subscale was used in 16% ($n = 3$) of the studies to assess general distress, cancer- or breast cancer-specific distress, or testing-related distress. The total STAI was used in 32% ($n = 6$) of studies as an indicator of general anxiety, general psychological distress and general emotional distress. One study used only the state anxiety scale of the STAI. The CES-D was used to measure distress, depression, and depressive symptomatology in 42% ($n = 7$) of the studies in our review. The next sections provide a more detailed discussion of each of these instruments.

Distress – the impact of event scale (IES)

The IES [36] was developed in 1979 to assess the subjective impact of a specific event on an individual. Based on qualitative information obtained from in-depth evaluation and psychotherapy interviews, the scale focused on two major responses to stressful events: intrusion and avoidance. In this self-administered scale, respondents are asked to indicate how frequently a set of 15 statements occurred during the past 7 days with a 4-point response scale (0 = 'not at all', 1 = 'rarely', 3 = 'sometimes', 5 = 'often'). The IES allows for the calculation of an overall score ranging from 0 to 75, an intrusion subscale score ranging from 0 to 35, and an avoidance subscale score ranging from 0 to 40. An overall score of 40 or greater is considered to be indicative of a significant stress response. The two subscales include 7 items to measure intrusion and 8 to measure avoidance. Intrusion is characterized by repetitive thoughts, mental images, disturbing dreams, and repetitive behavior. An example of an item on the intrusion subscale is 'I thought about it (i.e., CGT) when I didn't mean to.' Avoidance is associated with denial of consequences from an event, blunting feelings, and emotional numbness related to an event. An example of an item on the avoidance subscale is, 'I tried to remove it (i.e., CGT) from my memory' [36].

The IES was initially standardized with 66 adults who sought psychotherapy at an outpatient clinic as a result of reactions to a serious life event and then later standardized with medical student populations. The overall internal consistency reliability for the initial sample was adequate for the total scale (0.86), the intrusion subscale (0.78), and the avoidance subscale (0.82) [36]. Since then, the IES has been used in a variety of situations that may invoke a stress response such as death of a loved one, drug addiction, war, and medical illness [37, 38]. A review of the IES among women at increased risk for HBOC found the IES to be a valid and reliable instrument for the measurement of breast cancer-related distress in this population [38].

Thirteen studies from our sample of 19 studies included the IES to measure emotional state specific to breast cancer risk, genetic testing-related distress, psychological distress, or breast cancer-specific distress. While most used the entire IES, three studies used only the intrusion scale. Nine ($n = 9$) studies from our sample of 19 provided reliability coefficients. These studies reported acceptable reliability estimates, ranging from a Cronbach's alpha (α) of 0.79–0.92 for the total IES and 0.84–0.89 for the intrusion subscale.

Anxiety – state trait anxiety inventory (STAI)

The STAI is based on the work of Cattell and Spielberger [39] that suggests personality *states* are transient and occur when a particular situation arises. In contrast, personality *traits* are more permanent dispositions developed during childhood. State anxiety is an emotional reaction expressed at a point in time with a certain level of intensity and includes subjective feelings of tension, apprehension, nervousness, and worry. Trait anxiety refers to the relatively stable individual characteristic of anxiety proneness that exists

Table 1. Summary of instruments, use, and reliability estimates for HBOC & HNPCC cancer genetic testing.

Authors and year	Sample	Primary outcome variable(s)	Psychological variable(s)	Instrument used	Psychometric properties[a]
Aktan-Collan et al. [51]	• N = 271 men and women • Cancer status = unaffected • Cancer = HNPCC • Research cohort in Finland	Psychological consequences 1 month and 12 months after genetic testing for HBOC result disclosure	General anxiety	STAI	CA[b] 1 month, 1 year ≥ 0.90
Biesecker et al. [18]	• N = 172 men and women • Cancer status = affected & unaffected • Cancer = HBOC • Research cohort in US	Participation in genetic testing for HBOC	Depressive symptomatology	CES-D	CA = 0.79
Bonadona et al. [19]	• N = 56 men and women • Cancer status = affected • Cancer = HBOC or HNPCC • Research cohort in France	Psychological consequences 1 month after genetic testing for HBOC result disclosure	Anxiety	HADS	NR
			Depression	HADS	NR
Broadstock et al. [20]	• N = 21 women • Cancer status = unaffected • Cancer = HBOC • Research cohort in the UK	Short and long term psychological consequences of waiting for the results of genetic testing for HBOC	General emotional state	GHQ	CA baseline = 0.93
				STAI	CA baseline = 0.90
			Emotional state specific to breast cancer risk	Lerman breast cancer worries scale	CA baseline = 0.70
				IES	CA baseline = 0.92
Croyle et al. [21]	• N = 60 women • Cancer status = affected and unaffected • Cancer = HBOC • Research kindred of US Caucasians	Psychological responses to genetic testing for HBOC	General psychological distress	STAI	CA baseline = 0.94
			Test-related distress	IES	CA 1 week follow-up = 0.95 CA 1 week follow-up = 0.88
Dorval et al. [23]	• N = 65 men and women • Cancer status = affected and unaffected • Cancer = HBOC and Li–Fraumeni syndrome • Research cohort of US Caucasian adults	Agreement between anticipated and actual emotional states 6 months post genetic testing for HBOC and Li–Fraumeni result disclosure	General emotional distress	BSI	NR
Esplen et al. [15]	• N = 50 men and women • Cancer status = affected and unaffected • Cancer = HNPCC • Research cohort of US (n = 7) and Canadian (n = 43) primarily Caucasians	Motivation and psychosocial impact of genetic testing for HNPC	Anxiety	STAI	NR
			Depressive symptoms	CES-D	NR
			Distress associated with genetic testing	IES	NR

Friedman et al. [56]	• N = 199 men and women • Cancer status = affected and unaffected • Cancer = HBOC • Research cohort of US Ashknenzim	Psychological impact 1 and 6 month post genetic testing for HBOC result disclosure	General psychological distress Cancer-specific distress	POMS-SF IES	CA = 0.89 CA = 0.89
Lerman et al. [25]	• N = 192 US men and women • Cancer status = affected and unaffected • Cancer = HBOC • Research cohort of US Caucasians	Emotional outcomes 1 month post genetic testing for HBOC result disclosure	Depression symptoms	CES-D	CA = 0.91
Lerman et al. [26]	• N = 149 men and women • Cancer status = affected and unaffected • Cancer = HBOC • Research cohort of US Caucasians	Participation in genetic testing for HBOC	General distress Breast cancer specific distress	CES-D IES	CA = 0.91 CA = 0.84
Lerman et al. [16]	• N = 139 men and women • Cancer status = affected and unaffected • Cancer = HNPCC • Research cohort of US primarily Caucasians	Participation in genetic testing for HNPCC	Psychological distress	CES-D	CA = 0.86
Lodder et al. [27]	• N = 63 women • Cancer status = unaffected • Cancer = HBOC • Research cohort in Netherlands	Course of distress one year after genetic testing for HBOC result disclosure	Cancer-related distress	IES	CA = 0.82
Meiser et al. [57]	• N = 90 women • Cancer status = unaffected • Cancer = HBOC • Research cohort in Australia	Psychological impact of genetic testing for HBOC	Distress of being at risk for developing breast cancer State anxiety depression	IES STAI-State BDI	NR NR NR
Schwartz et al. [54]	• N = 290 women • Cancer status = affected • Cancer = HBOC • Research cohort of US primarily Caucasians	Participation in genetic testing for HBOC	Cancer-specific distress	IES	0.84
Schwartz et al. [55]	• N = 279 women • Cancer Status = affected and unaffected • Cancer = HBOC • Research cohort of US primarily Caucasians	Distress related to genetic testing for HBOC	Cancer-specific distress General distress	IES HSCL-25	CA = 0.89 CA = 0.88

Table 1. Continued.

Authors and year	Sample	Primary outcome variable(s)	Psychological variable(s)	Instrument used	Psychometric properties[a]
Tercyak et al. [12]	• N = 107 women • Cancer Status = affected and unaffected • Cancer = HBOC • Research cohort of US primarily Caucasians	Anxiety during pre and post disclosure period	Anxiety	STAI	CA at times 1, 2, 3 ≥ 0.90
Thompson et al. [35]	• N = 79 women • Cancer Status = unaffected • Cancer = HBOC • Research cohort of US African Americans	Participation in genetic testing	Breast cancer-specific distress	IES	CA = 0.90
Thompson et al. [17]	• N = 200 men and women • Cancer Status = affected • Cancer = HNPCC • Research Cohort of US primarily Caucasians	Psychosocial and behavioral impact of genetic testing for HNPCC	Depression	CES-D	CA = 0.91
			Anxiety	STAI	CA (for state scale) = 0.94 CA (for trait scale) = 0.92
Wood et al. [13]	• N = 35 women • Cancer Status = affected • Cancer = HBOC • Research cohort of US primarily Caucasians	Psychological impact of genetic testing for HBOC	Severity of anxiety and depressive symptoms past month	HSCL-25	CA = 0.93
			Cancer specific distress and genetic testing specific distress	IES	NR

STAI – state trait anxiety inventory; CES-D – Center for Epidemiologic Studies for Depression; HADS – hospital anxiety depression scale; GHQ – general health questionaire; IES – impact of events scale; BSI – brief symptom inventory; POMS-SF – profile of mood states-short form; HSCL-25 Hopkins symptom checklist-25.

[a]NR – did not provide estimates of reliability.

[b]CA – Cronbach's alpha (α).

Table 2. Psychosocial factors assessed and instruments used to measure.

Psychosocial factor	Instrument	Time frame of instrument	Psychosocial factor as specified by author
Distress	BSI	Past 1 week	General emotional distress [23]
	CES-D	Past 1 week	General distress [26] Psychological distress [16, 56]
	GHQ	Past few weeks	General emotional state [20]
	HSCL-25	Past 1 week	General distress [52]
	IES – intrusion subscale	Past 1 week	Breast cancer specific distress [16, 27, 54]
	IES – total	Past 1 week	Breast cancer specific distress [13, 20, 26, 35, 55–57] Test-related distress [13, 15, 21]
	Lerman breast cancer worry scale	Past 1 month	Emotional state specific to breast cancer risk [20]
	POMS-SF	Past 1 week	General psychological distress [56]
	STAI	Present moment (State anxiety) Generally feel (Trait anxiety)	General psychological distress [21] General emotional state [20]
Anxiety	HADS	Past 1 week	General anxiety [19, 27]
	HSCL-25	Past 1 week	Severity of anxiety [13]
	SCL-90	Past 1 week	Anxiety [27]
	STAI – state subscale	Present moment (State anxiety)	State anxiety [57]
	STAI – total	Present moment (State anxiety Generally feel (Trait anxiety)	General anxiety [12, 15, 17, 51]
Depression	BDI	Past 1 week	Depression [57]
	CES-D	Past 1 week	Depressive symptomatology [15, 18, 25] Depression [17]
	HADS	Past 1 week	Depression [19]
	HSCL-25	Past 1 week	Severity of depressive symptoms [13]

BSI – brief symptom inventory; CES-D – Center for Epidemiologic Studies Depression scale; GHQ – general health questionnaire; HSCL-25 – Hopkins symptom checklist-25; IES – impact of events scale; POMS-SF – profile of mood states-short form; STAI – state trait anxiety inventory; HADS – hospital anxiety and depression scale; SCL-90 – symptom checklist; BDI – Beck's depression inventory.

across situations. The two types of anxiety are related; in general, the stronger the level of trait anxiety the more likely that an individual will exhibit higher levels of state anxiety in a threatening situation [39, 40]. The original STAI (form X) was developed for use in 1970 with extensive revisions to the STAI resulting in the development of STAI (form Y), published in 1983. Form Y was the version of STAI used in all of the studies in this review [39].

The STAI is a self-report instrument that uses 20 statements to evaluate how a person feels at that moment, such as 'I feel worried.' Respondents are asked to indicate how they feel on a 4-point scale (1 = 'not at all', 2 = 'somewhat', 3 = 'moderately so', 4 = 'very much so'). An additional 20 statements (the 'trait' measure) assess how an individual generally feels; for example, 'I wish I could be as happy as others seem to be.' Respondents rate all 40 items on a 4-point scale (1 = 'almost never', 2 = 'sometimes', 3 = 'often', 4 = 'almost always'). After reversing positively worded items, the responses for each scale are summed to provide an overall score ranging from 20 to 80. The manual that accompanies this instrument provides normative values for a variety of age, gender, and socioeconomic subgroups [39].

This STAI has been widely used in research settings over the past two decades. It is written on a 6th grade reading level and has been used with a variety of populations including: high school and college students, working adults, military personnel, and psychiatric, psychosomatic, medical, surgical, and dental patients. The STAI has acceptable internal consistency reliability estimates ranging from an α of 0.86–0.96 [39].

In our review, this scale was used in seven studies to measure anxiety and distress among women participating in *BRCA1* and *BRCA2* mutation testing. Of the five studies that provided reliability estimates, all had high levels of internal consistency ranging from an α of 0.90–0.94.

Depression – Center for Epidemiological Studies Depression Scale (CES-D)

The CES-D [41] was developed to screen for depression in the general population. It is primarily focused on affective components of depression, such as depressed

mood and feelings of helplessness, and includes items from other scales assessing depression, such as Beck's depression inventory [42] and Zung's self-rating depression scale [43].

The 20-item, self-report depression scale can be either self- or interviewer-administered. The questions are asked in the context of the way respondents might have felt or behaved in the last seven days, such as, 'During the past week, I was bothered by things that usually don't bother me' and 'During the past week my sleep was restless.' Both positively and negatively worded items use a 4-point response scale (0 = 'rarely or none of the time i.e., less than 1 day'; 1 = 'some or a little of the time i.e., 1–2 days; 2 = 'occasionally or a moderate amount of the time i.e., 3–4 days'; 3 = 'most or all of the time i.e., 5–7 days'). Responses are summed to provide an overall score ranging from 0 to 60, with scores of 16 or more considered indicative of depression. Norms for samples representing a range of demographic differences (race, income, occupation etc), were published after CES-D was administered as part of the 1974–1975 Health and Nutrition Examination Survey [44]. This scale has been widely used in community and clinical populations with reliability estimates at acceptable levels ranging from 0.76 to 0.91. Shorter forms have also been shown to have high levels of agreement and reliability when compared to the full version [45, 46].

In our review, the full 20-item scale was used in seven separate studies to measure what authors termed depressive symptoms, depression, general distress, or psychological distress among women participating in *BRCA1* and *BRCA2* mutation testing. In all of the studies the CES-D was given as a self-administered questionnaire. Of the six of the studies that provided Cronbach's alpha reliability estimates all were adequate and ranged from 0.79 to 0.91.

Discussion

Our review found that psychological factors were used as both predictors and outcomes of CGT. The majority of studies focused on testing for HBOC cancer and a few studies were related to HNPCC testing. There were no FAP/AFAP related studies in our review. Because genetic testing is the most cost effective way of diagnosing FAP/AFAP, and avoids having young children undergo invasive screening procedures such as sigmoidoscopy or colonoscopy [47], those tested for FAP are likely to be children and therefore not included in our review which was limited to adult only samples. The most commonly measured psychological factors were distress, anxiety, and depression. These were most often measured by the IES, STAI, and CES-D, respectively. Studies reporting the use of these instruments, as well as other instruments identified in Tables 1 and 2, reported acceptable internal consistency reliability when it was reported. In contrast, some studies have reported no relevant psychometric data while others reports are limited to internal consistency reliability. Additionally, the variability in instrumentation across studies makes direct comparisons of psychological variables difficult, particularly for anxiety and depression.

Limited documentation of psychometrics

Twenty one percent of the studies ($n = 4$) in our review did not provide reliability estimates of any of the instruments used and 5% ($n = 1$) failed to provide reliability estimates for some of the instruments used. This may be of less concern for instruments in which reliability has previously been demonstrated among individuals at increased genetic risk for cancer, such as the IES [38]. However, even with instruments that have previously established reliability, the estimates are generally based on a fairly homogenous population of Caucasian women of higher socioeconomic status participating in research protocols. As CGT moves further into mainstream clinical practice, consistently assessing reliability will be one important way to determine whether these instruments are equally salient to diverse racial/ethnic groups, men, those of lower socioeconomic status, and community populations.

Similarly, there was inadequate discussion in all of the articles in our review about validity. The issue of what self-report psychological instruments actually measure in the samples included in the studies and the clinical utility of the information they generate is an ongoing source of concern. In a review of 17 depression-rating scales by Snaith [48], they found extensive variability in the aspects of depression measured by depression self-report instruments. Some focus on patient cognition, others on somatic symptoms, and still others on behavior. Despite such substantive differences, these instruments are generally assumed to be equivalent in their assessment of depression and are often used interchangeably. Instrument selection may be arbitrary or based on tradition, rather than to suit the unique needs of a given study population. For example, the CES-D, which primarily focuses on depressed mood and anhedonia, was frequently used in studies included in our review to measure depression and distress. Yet, none of the identified studies provide a rationale for selecting a measure that focuses on these two aspects of depression among individuals at increased risk for hereditary cancer.

An example of the importance of considering validity of the psychological instruments used among individuals at increased risk of hereditary cancer was demonstrated in a study by Coyne et al. [49]. The study included 196 women with either a personal or family history indicative of HBOC syndrome were mailed a questionnaire prior to receiving their *BRCA1/2* test results. The goal of the study was to validate the interpretation of cancer-specific distress scores commonly used to assess psychological distress among women at increased risk of hereditary cancer. This was done by comparing women's ratings on multiple sources of cancer-related distress

(i.e., stress of testing, threat of positive finding) and by using standardized measures of more validated measures of general distress and functioning (i.e., Hopkins symptom checklist-25 (HSCL-25), SF-36). This study found that ratings of specific aspects of cancer-related distress (i.e., stress of testing, threat of positive finding) were not related to women's levels of general psychological distress or emotional and social functioning. The study concluded that despite the popularity of cancer specific distress measures, the clinical utility of findings generated from those instruments might be limited.

Variability of instrumentation

As shown in Table 2, another issue is the variety of instruments used to measure the same psychological variable. Eight different instruments were used to measure distress, including the brief symptom inventory (BSI), CES-D, general health questionnaire (GHQ), Hopkins symptom checklist-25 (HSCL-25, intrusion avoidance scale (IES), Lerman breast cancer worry scale, profile of mood states-short form (POMS-SF), and state trait anxiety inventory (STAI). The questionnaires ask the respondents to consider different time frames, ranging from the 'present time' to 'the past month.' Recent studies have shown that the level of distress related to CGT may vary depending on the time period during which distress is assessed [9, 11, 21]. Thus, when multiple instruments are used to assess the same psychological factor or when different time frames are involved, this variability in instrumentation makes comparisons across studies difficult.

Across studies, the same instrument was often used to measure different variables. For example we found that the STAI was used as both a measure of general psychological distress [21] and anxiety [12, 17, 50, 51]. Because this instrument was designed to be a measure of anxiety, it is not appropriate to use this measure to draw general conclusions about the impact of CGT on overall psychological distress or emotional state. If one found the STAI score in their sample to be high, but used the instrument as a measure of anxiety, then their recommendations for intervention may be more targeted and potentially more effective than those based on using the STAI as a measure of general psychological distress.

Variability in instrumentation may become less of an issue in future studies as researchers develop instruments to measure psychosocial reactions specific to genetic testing for hereditary cancer risk. The multidimensional impact of cancer risk assessment (MICRA) developed by Cella et al. is a new instrument that holds promise for measuring previously understudied psychosocial factors related to CGT. It includes 25-items in 3 subscales that measure distress, uncertainty, and positive experience related to genetic testing for hereditary cancer risk. A recent report shows that in initial studies, each scale has acceptable levels of reliability (ranging from 0.75 to 0.86) and was able to differentiate participants who were positive for a BRCA mutation from those who were BRCA negative, panel negative, or true negative [52].

Recommendations

Given the relatively rare nature of hereditary cancers, some level of uniformity and comparability across research studies may be an important next step in making definitive conclusions about the psychological impact of CGT. Thus, it is imperative that researchers provide information about the psychometric properties of the instruments used to measure psychological states. This report should extend beyond reporting internal consistency reliability. Validity of instruments should be addressed by providing a rationale for the selection of study instruments. This may be accomplished by developing a standard set of reporting criteria similar to the guidelines developed by CONSORT group for reports of randomized controlled trials [53]. With regard to variability in instrumentation, one approach may be to have a basic set of instruments to assess key psychological issues related to hereditary cancers. While this was initially done through the membership of the NHGRI Cancer Genetics Studies Consortium over a decade ago [7], it is time to apply what researchers have learned toward developing an updated set of core instruments. Given the increasing number of investigators conducting research in the area of psychosocial and behavioral issues related to CGT, one strategy is to develop a working group with representatives from key organizations with membership conducting psychosocial research in this area. One such example of collaboration across professional organizations is the shared membership directory of the American Society of Preventive Oncology Behavioral Oncology Working Group and the Society of Behavioral Medicine Cancer Special Interest Group used to promote contact and collaboration between behavioral oncology researchers (http://www.scgcorp.com/sbmasposig/). An expanded version of this type of group may be suitable for establishing both a basic set of instruments and a standard method of reporting psychometric properties for psychological studies related to genetic testing.

Study limitations

This study is among the first to focus on the measurements used to determine psychological outcomes associated with genetic testing. However, there are some limitations to the present review. First, while there are 19 individual studies included in this review, approximately one fourth of the papers included in the review are likely to stem from a common research protocol and databases that represent the same measures and subjects [12, 25, 26, 54, 55]. Therefore, one set of researchers was highly influential in determining the overall frequency with which a certain measure is used and limits conclusions about the true popularity of certain instruments.

Second, it is possible that studies in our review assessed psychometrics without reporting it. Thus, we may have underestimated the frequency with which such analyses were completed. Finally, almost all of the studies in our review came from research cohorts or kindreds that were primarily comprised of Caucasian women or participants of high socioeconomic status. This limits the generalizability of our findings to a primary care or community based setting that is more likely to include a variety of racial/ethnic and socioeconomic groups.

Conclusions

To date, cancer genetic counseling and testing has often been provided in settings devoted to clinical research and care by specialists in hereditary cancer. It is very likely that in these research settings more attention is given to all psychological issues associated with CGT than will be received in general clinical practice and community settings. Before CGT moves into mainstream clinical practice, it is very important to understand the full psychological impact of testing.

As molecular genetics and diagnosis in cancer continue to advance, CGT may expand to cover other cancer sites. Interpretation of test results may become even more complex as the ability to detect multiple gene influences on cancer risk is developed. It is increasingly important to understand the impact genetic risk information will have on the psychological well being of individuals who are provided with such information. Self-report instruments are one way to understand this impact. However, unless we address current limitations of psychometrics and variability in instrumentation, the information we gain from these instruments may limit our ability to precisely identify and improve the psychological outcomes associated with CGT.

Appendix 1. key word search terms

Cancer types
Neoplastic syndromes
Ovarian/breast/colorectal neoplasm
Cancer
Breast/ovarian/colon/colorectal cancer
Hereditary nonpolyposis colon cancer
HNPCC
Lynch syndrome
Familial adenomatous polyposis coli
Adenomatous polyposis coli
FAP
Hereditary breast ovarian cancer
HBOC
Familial cancer syndrome

Genetics
Genetic predisposition to disease
Breast cancer susceptibility
BRCA1
BRCA2
BRCA 1 2
hMLH1
hMSH2
APC gene

Cancer genetic testing
Genetic tests
Susceptibility tests
Genetic predictive testing
Cancer genetic testing
Mutation testing
APC genetic testing
HNPCC genetic testing
BRCA 1 genetic testing
BRCA 2 genetic testing

Psychosocial factors
Psychological
Psychosocial
Behavioral
Emotion
Distress
Anxiety
Depression
Stress
Social support
Optimism
Pessimism
Fear
Fatalism

Author search
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