Effects of genetic risk information on children's psychosocial wellbeing: A systematic review of the literature

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Purpose: As advances in research have made a growing number of genetic tests available, clinicians will increasingly be faced with making decisions about when offering genetic testing services to children is appropriate. A key factor in such decisions involves determining whether knowledge of genetic health risks might have an impact on children's psychosocial wellbeing. **Methods:** We conducted a systematic review of the literature using five online databases to identify studies that assessed the impact of communicating nondiagnostic carrier or presymptomatic genetic test results to children. **Results:** A total of 17 articles met the inclusion criteria for this review. These studies used a wide range of methodologies to explore carrier and predictive testing. Although there was little quantitative evidence that receiving genetic test results led to a significant impact on children's psychosocial wellbeing, it was found that methodological inconsistencies, small samples, and reliance on assessments most appropriate for psychopathology make any firm conclusions about the impact of genetic testing on children premature. **Conclusion:** Currently, there is insufficient evidence to inform a nuanced understanding of how children respond to genetic testing. This suggests a strong need for further research that uses rigorous approaches to address children's emotional states, self-perception, and social wellbeing. ***Genet Med* 2010:12(6):317–326.**

Key Words: *genetic testing, children, self-identity, psychosocial wellbeing, relationships, emotions, systematic review*

Since the inception of clinical genetic testing, health care professionals have been faced with the responsibility of determining when an individual is of an appropriate age to undergo testing. Although diagnostic genetic testing for childhood-onset conditions is standard practice, consensus has emerged among existing professional guidelines that children typically should not undergo predictive or carrier genetic testing unless there is a clear health benefit.[1,2] Nonetheless, this issue has continued to raise controversy, in part because parents and children often express interest in obtaining genetic testing.[3–7] Advances in knowledge about genetics will magnify this debate, given that new genetic tests could be applicable to the whole population and complement existing prenatal, newborn, and pediatric testing practices aimed at the primary prevention of adult-onset health conditions.[7–13]

The impact of offering genetic testing to children has been subject to considerable discussion among health practitioners, researchers, policy makers, and bioethicists,[6,7,14–20] although the majority of publications on the topic are not empirical.[18] Many have noted the possibility that genetic test results (e.g., knowledge of increased personal risks) might have a negative impact on children's psychosocial wellbeing[14,19,21,22] as measured by adverse emotional states, altered self-perception, or disrupted social relationships.[14,15,21–23] Countering these concerns is the perspective that testing may provide benefits such as relief from uncertainty, the opportunity to integrate risk status into an evolving self-concept, and improved social support through relationships with families and friends.[6,17,18,20] Such debates over the benefits and harms are common in the genetic testing literature and have given rise to empirical studies that aim to clarify the relevant social and ethical issues.[24–26]

Most suppositions about how genetic testing might influence children psychologically and interpersonally have originated in the context of carrier and predictive testing. The information conveyed by these tests may influence psychosocial outcomes through different causal pathways. In the case of carrier testing, genetic tests are conducted to inform an individual of their risk for having a child with a specific disease. Concerns have been raised that such knowledge could interfere with children's expectations for future parental roles, causing distress or negatively influencing self-concept.[1,27] In the case of predictive testing, where genetic tests indicate increased personal risk for a future disease state (e.g., adult-onset cancer), potential harms are that the test results might diminish a child's expectations of health and wellbeing, increase distress, or negatively alter life choices.[2,14,21] In both the cases, the impact of testing is likely to be complex. Developmental psychologists have noted the challenge of characterizing effects on children when multiple social and environmental factors influence each psychosocial outcome (i.e., the concept of equifinality) and identical genetic information could produce varied effects for different individuals (i.e., the concept of multifinality).[28]

In this report, we present a systematic review of the empirical literature to explore the evidence base regarding the impact of genetic testing on children's psychosocial wellbeing. Outcomes considered under the general overarching term "psychosocial wellbeing" include emotional states (e.g., anxiety and depression), self-perception (e.g., self-concept, self-image, and perceptions of personal health), and social wellbeing (e.g., familial and peer relationships). The review will focus on responses of participants between 8 and 18 years (henceforth referred to as "children") and includes empirical research where genetic information about health was communicated to children directly or via their parents. Also, we only consider studies on carrier

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and predictive testing scenarios and exclude research on diagnostic testing, where children were already experiencing serious symptoms of the condition.

The review is organized to accomplish three major objectives. First, we describe the characteristics of existing research evaluating the psychosocial impact of genetic testing on children. We then present findings in the literature addressing whether genetic testing has an impact in children's emotional states, self-perception, or social wellbeing. In conclusion, we discuss gaps in the literature and suggest directions for future research.

MATERIALS AND METHODS

Database search methodology

The search strategy used in this literature review was informed by the approach described by Heshka et al.[29] To obtain citations, we queried five databases: Web of Science, Scopus, PubMed, PsycInfo, and EMBASE. The search specified that a title, abstract, or keyword contain at least one term from each of the four search categories that are listed in Table 1: information source (e.g., "genetic testing" and "DNA testing"), age (e.g., "children" and "minors"), construct (e.g., "identity" and "anxiety"), and health domain (e.g., "health" and "condition"). All citations available in the databases as of January 21, 2009, were included.

Article selection

To be considered in the review, studies were required to: (1) be human subjects research published in peer reviewed journals in English, (2) convey genetic testing information based on actual, rather than hypothetical, genetic testing (studies using nongenetic biomarkers were excluded), (3) have at least half of the study sample be between the ages of 8 and 18 years at the time they received the genetic test result, (4) provide results to children who were not yet experiencing serious symptoms of the health condition, (5) include children's reports of subjective psychosocial wellbeing (specific outcomes of interest included but were not limited to worry, anxiety, depression, self-esteem, self-concept, self-image, perceptions of physical wellbeing, familial and peer relationships, and quality of life), and (6) not be a case study, review, or letter to the editor. Criteria for exclusion presented in Figure 1 were based on failure to meet one of these requirements.

The references and abstracts identified through the database search were entered into EndNote version 12 (Thomson Reuters, New York, NY), where duplicates across the different databases were removed. The lead author reviewed titles of articles based on the criteria described above, and then potentially relevant abstracts were evaluated for inclusion. In cases of uncertainty, a second author was consulted for an independent analysis. If the abstracts met the review criteria, full-text articles were retrieved and considered to confirm relevance. Reasons for exclusion were recorded and presented in Figure 1.

To identify additional articles not found in the initial search, we used cross-referencing techniques to explore the following: (1) references in relevant articles, (2) articles with similar references to relevant articles (Web of Science), (3) articles that referenced relevant articles (Scopus), and (4) other articles published by the first and last author of relevant articles (Scopus). These searches did not yield any additional articles that met our search criteria.

Data extraction

Standardized forms were used to extract data from pertinent articles by two authors. The factors of interest were study

Table 1 Database search terms

Test 1: Information source	Test 2: Age	Test 3: Construct	Test 4: Health domain
Genetic test(s)(ing)	Child(s)(ren)(hood)	Identit(y)(ies)	Health(y)(iness)
Genetic disease(s)	Adolescen(t)(ts)(ce)	Self	Ill(ness)
Genetic disorder(s)	Teenage(r)(rs)	Cope(s)(d)(ing)	Disease(s)(d)
Genetic condition(s)	Young adult(s)	Adapt(s)(ed)(ing)(ation)	Disorder(s)
Molecular test(s)(ing)	Young people	Stigma(s)(ize)(ized)(izing)	Diagnos(e)(is)(ing)
Hereditary syndrome(s)	Boy(s)	Worr(y)(ied)(ies)	Disab(led)(ility)
Hereditary condition(s)	Girl(s)	Anxi(ety)(ous)(ties)	Syndrome(s)
Hereditary disease(s)	Student(s)	Harm(s)(ful)	Condition(s)
Predictive test(s)(ing)	Minors	Optimis(m)(tic)	Sick(ness)(nesses)
DNA test(s)(ing)		Happ(y)(iness)	
Susceptibility test(s)(ing)		Depress(ed)(ion)(ing)	
Carrier test(s)(ing)		Distress(ed)(ing)	
Genetic screen(s)(ing)		Attitud(e)(es)(inal)	
Diagnostic test(s)(ing)		Apprais(e)(es)(al)	
Family histor(y)(ies)		Relationship(s)	
		Quality-of-life	
		Quality of life	

Term endings contained in the parentheses were added to the root term.

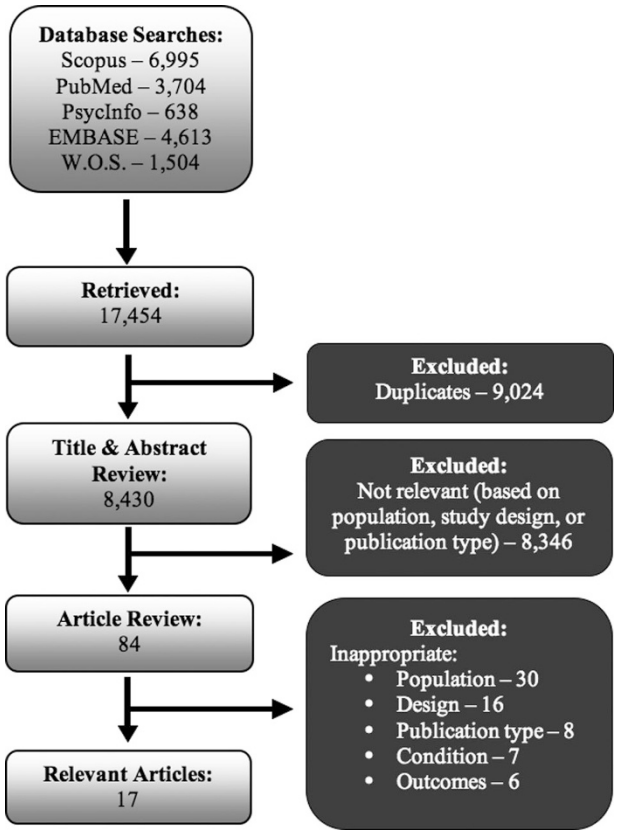

Fig. 1. The QUORUM flow diagram[75] presenting the inclusion and exclusion of publications identified in the literature review.

design, study characteristics, measurement methods, and outcomes with relevance to psychosocial wellbeing. The data and interpretations were reviewed for accuracy and consistency by all authors, and differences were resolved through discussion. Blinding was not used to hide authorship, journals, and institutions during the review.

RESULTS

Overview

This review will address the following questions: (1) what is the scope of the literature examining the impact of genetic testing on children's psychosocial wellbeing? and (2) does evidence suggest that genetic testing influences children's emotional states, self-perception, or social wellbeing? In brief, this review found that the current literature on genetic testing of children is still in a formative stage and, thus, cannot be synthesized into definitive conclusions about the impact of carrier and predictive testing on children's psychosocial wellbeing. Nonetheless, the overwhelming majority of the existing data did not suggest that genetic testing has a clinically significant effect on children's emotional states, self-perception, or social wellbeing. The findings of the review, along with specific results indicating potential harms and benefits, are described in greater detail in the following sections. In addition, studies that adopted stronger measurement and design strategies are discussed as illustrative examples.

Study Characteristics

In total, 8430 unique citations were retrieved using our intentionally broad database search strategy (see Fig. 1). When titles and abstracts were evaluated using our detailed article selection criteria (see Methods), only 84 of these citations were found to have potential relevance. When the full text of these candidate articles was evaluated, 17 articles from 12 separate studies published between 1977 and 2008 met all of the study selection criteria. Seven studies examined the implications of carrier testing in children (Table 2), and five studies explored the impact of offering predictive testing to children (Table 3). Moreover, these tables include information on the study location, condition addressed, study design, sample, age at testing, and length of time between testing and measurement of psychosocial wellbeing.

The constructs addressed, measurement tools used, and significance of impact of the test in each study are presented in Table 4. The 12 studies included international representation but were primarily conducted in countries with Caucasian populations. Also, the study samples included a relatively balanced representation of girls and boys. Most studies enrolled participants through clinical interactions with newly or previously tested members of at-risk families (with the exception of four studies that identified participants from screened high-school populations).

The majority of studies used a retrospective or cross-sectional design, with assessments occurring after the provision of the genetic test result. Exceptions to this were two prospective studies. Six of the 12 studies included at least one assessment averaging a year or less since testing, whereas 9 of 12 studies conducted at least one assessment averaging more than 1 year after testing. In addition, the majority of studies reported information and assessment designs that had the potential for differential attrition.

Most articles (10 studies) relied entirely on descriptive measurement strategies (based on face-to-face interviews or paper-and-pencil surveys) and did not conduct statistical significance testing on comparisons. The remaining seven articles used established scales that allowed comparison between participant groups or with population control groups. Three of these studies indicated that their measurement tools had acceptable reliability, and only one mentioned having conducted a power analysis to ensure that their study could detect important differences.

Children's understanding of the genetic test was assessed in the majority of studies (8 of 12). Although the studies ranged considerably in what knowledge was addressed, the most common question was whether the participants remembered their test result accurately (four studies). With respect to the communication of genetic test results, four studies sent letters directly to the children (three with a follow-up call to carriers), two studies informed the parent and/or child of the results in-person, and the remaining studies did not directly communicate test results because their study populations already knew their test status before enrollment.

Overall, the studies included in this review are heterogeneous and vary in quality. In addition to being conducted over a range of 30 years, there is relatively little overlap in study objectives, study populations, measurement tools, and carrier traits or health conditions addressed. Most studies were also limited by the small sample sizes, the potential for differential attrition, and the constraints of retrospective study designs. Finally, few quantitative studies had the proper design and power to detect significant differences in psychosocial wellbeing. Because of these concerns, the following sections will emphasize examples

Table 2 Reviewed articles examining children's response to carrier testing

Study	Country	Condition	Design	*N*	Age at testing (yr)	Time to assessment
McConkie-Rosell et al.[36]	USA	Fragile X syndrome	Cross-sectional, retrospective	53 (C = 20, NC = 18, AR = 15)	6–19	~4 yr
Barlow-Stewart et al.[35]	Australia	Tay-Sachs disease, cystic fibrosis	Retrospective	86 (C = 10, NC = 76)	15–18	3–6 yr
Järvinen et al.[32]	Finland	Duchenne muscular dystrophy, hemophilia	Cross-sectional, retrospective	46 (C = 7, NC = 17, Unsure = 22)[a]	5–17	8–12 yr
Järvinen et al.[34]	Finland	Aspartylglucosaminuria	Cross-sectional, retrospective	25 (C = 16, NC = 7, Unsure = 2)	5–18	10–24 yr
Järvinen et al.[33]	Finland	Duchenne muscular dystrophy, hemophilia	Cross-sectional, retrospective	46 (C = 7, NC = 17, Unsure = 22)[a]	5–17	8–12 yr
Järvinen et al.[39]	Finland	Duchenne muscular dystrophy, hemophilia	Cross-sectional, retrospective	46 (C = 7, NC = 17, Unsure = 22)[a]	5–17	8–12 yr
Mitchell et al.[31]	Canada	Cystic fibrosis	Retrospective	350 (C = 7, NC = 135, Control = 208)	15–17	1–2 wk
Zeesman et al.[37]	Canada	Tay-Sachs	Cross-sectional, retrospective	75 (C = 37, NC = 38)[b]	15–17	8 yr
Scriver et al.[38]	Canada	Beta thalassemia	Retrospective	139 (C = 43, NC = 96)	16–17	2 to 11 mo (average = 8 mo)
Clow and Scriver[30]	Canada	Tay-Sachs	Retrospective	90 (C = 45, NC = 45)[b]	15–17	6 wk to 17 mo (average = 8.25 mo)

[a,b]Studies that had overlapping populations.
C, carrier; NC, noncarrier; AR, at risk.

Table 3 Reviewed articles examining children's response to predictive testing

Study	Country	Condition	Design	*N*	Age at testing (yr)	Time to assessment
Meulenkamp et al.[45]	The Netherlands	Long QT syndrome, hypertrophic cardiomyopathy, familial hypercholesterolemia	Cross-sectional, retrospective	33 (Pos = 33)[a]	~8–18	~0.5 to >3 yr
Smets et al.[43]	The Netherlands	Long QT syndrome, hypertrophic cardiomyopathy, familial hypercholesterolemia	Cross-sectional, retrospective	35 (Pos = 35)[a]	~8–18	~0.5 to >3 yr
Duncan et al.[61]	Australia	Huntington disease, familial adenomatous polyposis	Cross-sectional, retrospective	18 (Pos = 7, Neg = 11)	10–25	~5 yr
Liljeström et al.[44]	Finland	Maturity-onset diabetes of the young, type 3	Cross-sectional	29 (Pos = 9, Neg = 20)	12–18	1 yr
Codori et al.[41]	USA	Familial adenomatous polyposis	Prospective	48 (Pos = 22, Neg = 26)[b]	5–17	0 wk, 3 mo, 12 mo, 23–55 mo
Michie et al.[42]	United Kingdom, Australia	Familial adenomatous polyposis				
Study 1			Cross-sectional	60 (Pos = 31, Neg = 29)[c]	10–16	~46 wk
Study 2			Prospective	31 (Pos = 16, Neg = 15)[c]	10–16	0 wk, 1–43 wk, 20–77 wk
Codori et al.[40]	USA	Familial adenomatous polyposis	Prospective	41 (Pos = 19, Neg = 22)[b]	6–16	0 wk, 3 mo

[a,b,c]Studies that had overlapping populations.
Pos, tested positive; Neg, tested negative.

Table 4 Concepts addressed, significance of impact, and measurement tools applied in reviewed studies

	Concepts Addressed													
	Emotion						Self				Social			
Study	Depression	Anxiety	Worry	Behavior problems	Satisfaction	Other/ qualitative	Self-image	Self-esteem	Physical self	Other/ qualitative	Parental relationship	Sibling relationship	Communication	Other/ qualitative
Carrier testing														
McConkie-Rosell et al.[36]						+√[a]	√[a]	+√[b]	√[a]	√[a,b]	√[b]	√[b]	√	+√
Barlow-Stewart et al.[35]					√	√							√	√
Järvinen et al.[32]										√	√			
Järvinen et al.[34]					√	√[c]			+√[c]		√			√[c]
Järvinen et al.[33]			√			√[c]			√[c]					√[c]
Järvinen et al.[39]					√									
Mitchell et al.[31]		√			√		√		√					√
Zeesman et al.[37]			√											
Scriver et al.[38]			√				√						√	√
Clow and Scriver[30]	√		√		√	√	√		√				√	√
Predictive testing														
Meulenkamp et al.[45]						√				√				√
Smets et al.[43]						√[d]	√[d]		√[d]		√[d]			√[d]
Duncan et al.[61]						√				√				√
Liljeström et al.[44]					√									
Codori et al.[41]	√[e,f]	√[g]		+	√[h]							√	√	
Michie et al.[42]	√[i]	√[j]	−,√	√[k]	√	−,√[l, m, n]		√[o]	√					
Codori et al.[40]	√[e,f]	√[g]		+√[h]							√			

√, addressed in study; +, beneficial clinically or statistically ($P < 0.5$) significant effect found; −, adverse clinically or statistically ($P < 0.5$) significant effect found.
[a]Tennessee Self-Concept Scale II was the measurement tool used.
[b]Fragile X Value Added Scale was the measurement tool used.
[c]RAND Health Survey 1 was the measurement tool used.
[d]Kidscreen was the measurement tool used.
[e]Children's Depression Inventory was the measurement tool used.
[f]Reynold's Adolescent Depression Scale was the measurement tool used.
[g]Revised Children's Manifest Anxiety Scale was the measurement tool used.
[h]Child Behavior Checklist was the measurement tool used.
[i]Hospital Anxiety and Depression Scale was the measurement tool used.
[j]Spielberger State Trait Anxiety Inventory was the measurement tool used.
[k]Rutter Child Behavior Scale was the measurement tool used.
[l]Impact of Events Scale was the measurement tool used.
[m]Life Orientation Test was the measurement tool used.
[n]Health Orientation Scale was the measurement tool used.
[o]Rosenberg Self-Esteem Scale was the measurement tool used.

and data from studies with stronger designs that are not fully representative of the range of quality in the existing literature.

Impact on emotional states

Carrier testing

Studies using single questions to assess children's perceptions of emotional harm,[30] anxiety,[31] or influence on their lives[32] found no indication of an acute impact on children's affect. Multi-item scales examining emotional wellbeing,[33,34] concern,[35] and emotional impact[36] similarly did not observe significant differences in emotional states between carriers and noncarriers.

This general lack of effect was found in a well-designed study by McConkie-Rosell et al.,[36] which investigated the influence of communicating carrier status for fragile X syndrome to girls aged 14–25 years ($N = 53$). The investigators used the fragile X Visual-Analog Scale, a measurement tool designed specifically for the study. Overall, girls who were carriers ($n = 20$) did not report significant changes in emotional responses (e.g., being upset, scared, relieved, angry, or happy) on learning their test results compared with when they learned that they were at risk, nor did the average ranking for any negative emotion exceed intermediate levels. Additional structured interviews with the girls supported the finding that the test results generally did not increase carriers' distress levels. This neutral impact is notable because fragile X carriers have a higher chance (~25–50%) of having an affected child than is expected with most carrier tests. However, because the girls in the study knew they were at risk before testing, experiencing testing may not have significantly increased their concern over preexisting levels.

Several studies lend support to the possibility that carrier status may increase negative emotions. Indeed, between 20% and 70% of carriers expressed some level of worry, which was considerably higher than for noncarriers (2–10%).[30,33,37,38] However, the importance of this finding is unclear because the questionnaires used by these studies were not sensitive enough to distinguish between worry experienced as a modest concern and clinically significant levels of worry that interfered with wellbeing (e.g., "If you were a carrier or your test result was uncertain, are you worried about it?" Answers were: yes, slightly, uncertain, indifferent, or no.[33]).

Some studies also suggested that carrier testing may have emotional benefits for children, particularly when test results indicated that a child was not a carrier. Two studies that returned carrier test results for Tay-Sachs disease[30,37] and fragile X syndrome[36] found that noncarriers had a positive emotional response on learning their result and that these responses were sustained over time. Also, in the context of fragile X carrier testing, some evidence from interviews suggested that girls who were carriers had better emotional coping after testing than untested girls who knew they were at risk.[36]

Finally, retrospective reports indicated that most children were generally content with their overall experience of having undergone carrier testing. High proportions of tested children answered affirmatively when a single item question was used to ask whether they were satisfied with testing (90–100%),[30,31,34] completely satisfied with testing (76%),[39] either satisfied or very satisfied (91%),[35] would be tested again (85–100%),[34,39] and would recommend testing to a friend (76–89%).[31,34,39] However, these measures could be subject to social desirability bias or, given the retrospective designs, optimistic recall bias.

Predictive testing

In the context of predictive genetic testing, most studies found no statistically or clinically significant differences in depression,[40–42] anxiety,[40–42] general psychological wellbeing,[43] dispositional optimism,[42] or behavioral problems and competence[40–42] when comparing those with positive and negative test outcomes. However, the survey assessments used were generally intended for serious psychopathology and, thus, may not be sensitive to subtle nonclinical shifts in emotional wellbeing.

Illustrative of these studies is a prospective study by Codori et al.[40,41] evaluating the impact of testing for familial adenomatous polyposis (FAP) among children aged 5–17 years. Information about the test and disclosure of the results were communicated to participants by a medical geneticist. The investigators assessed depression, anxiety, and behavioral states at four time points (before testing, and then 3 months, 1 year, and about 3 years after testing) using well-established measures. No clinically significant negative outcomes were observed among the children at any time point, regardless of the test result that they received. However, it is worth noting that the relatively small sample size ($n = 48$) may have affected the ability of the study to detect significant effects.

Only one study, conducted by Michie et al.,[42] provided support for concerns about emotional harm as a result of predictive testing for FAP among children aged 10–16 years ($N = 60$). Although most measures suggested no clinically significant impact and supported the conclusions of Codori et al. (described above), children who had high-risk test results for FAP reported worse scores than those who received negative results for worry (3.1 vs. 0.7 on a scale of 0–6) and perceived threat (32.6 vs. 16.4 on a scale of 11–55). These findings were statistically significant, but their interpretation is ambiguous, given the lack of an established cutoff for clinical significance. It is also worth noting that children receiving positive results reported somewhat worse scores for depression, anxiety, and likelihood of clinically relevant anxiety at follow-up than those who received negative results, although none of these differences were clinically or statistically significant.

As in the context of carrier testing, some studies suggested that children experience positive emotions as a result of predictive testing. Prospective assessments (before testing, then 8 weeks and 8 months after testing) by Michie et al.[42] showed that children who tested negative for FAP ($n = 15$) seemed to benefit from statistically significant drops in worry, anxiety, perceived threat, and situational distress after learning their test result. Moreover, longitudinal results found that children who tested positive for FAP ($n = 16$) had nonsignificant improvements for some emotional states over time.[42] However, as mentioned above, these differences are in some cases difficult to interpret with respect to clinical significance. Finally, two studies found that children reported relatively high levels of satisfaction with testing.[42,44]

Impact on self-perception

Carrier testing

Results of studies on carrier testing generally suggest no significant effect of carrier testing on children's self-image,[30,31,38] self-concept,[36] or self-evaluations of physical wellbeing.[33,34,36] For example, in the study by McConkie-Rosell et al. that explored self-concept among girls tested for fragile X carrier status, girls' responses on the Tennessee Self-concept Scale II were within the normal range for all groups, and there were no significant differences between the carriers ($n = 20$,

mean score 56.60), noncarriers ($n = 18$, mean score 52.17), or those at-risk ($n = 15$, mean score 53.33; 82 items, $\alpha = 0.73$).[36] Furthermore, no significant differences were found between the three groups for any of the nine subscales (physical, moral, personal, family, social, academic/work, identity, satisfaction, and behavioral states). Responses to a question asking "has knowing your carrier status affected the way you feel about yourself?" showed the most positive feelings from noncarriers, whereas carriers had marginally positive feelings and at-risk participants reported no effect. Although girl's responses in structured interviews were complex and varied, there was little indication of major shifts in self-perception. However, it is worth noting that the time lag between testing and assessment, approximately 4 years on average, may have diminished the ability of this study to detect significant effects.

Predictive testing

Two studies on predictive testing among children did not support either positive or negative influences on self-esteem,[42] self-perception,[43] or health-related wellbeing.[42,43] As an illustration of these findings, Michie et al.[42] used the well-established Rosenberg Self-Esteem Scale (10 items, $\alpha = 0.77$) to assess children's response to genetic testing for FAP. Both the cross-sectional ($n = 60$) and prospective ($n = 31$, follow-ups at about 8 weeks and 33 weeks) results indicated that tested children had self-esteem measures in the normal range regardless of the test result (30.4 for those testing negative and 32.4 for those testing positive, on a scale of 10–40). Furthermore, children's perceptions of their physical wellbeing may not have changed dramatically in response to testing because when asked "in general, how would you describe your current health," almost all children ranked their health as good or excellent (26 of 29 who tested negative; 30 of 31 who tested positive).

Impact on social wellbeing

Carrier testing

Among the studies that asked children whether knowledge of their carrier status resulted in altered social relationships, most found little indication of an impact. Generally, carriers did not see testing as having influenced their relationships with parents,[32,34,36] siblings,[36] or extended family.[36] Tested children also did not express difficulty communicating with their family about their results.[30,35,36,38] For example, the study by McConkie-Rosell et al.[36] on fragile X syndrome testing among girls assessed their relationships with parents, siblings, and extended family (e.g., "How has knowing your carrier status affected your relationship with your siblings?"). No significant differences were found between carriers ($n = 20$), noncarriers ($n = 18$), and untested at-risk girls ($n = 15$).

Modest evidence of a negative impact on children's social wellbeing was found in two domains; future relationships and parental roles. Four studies[30,31,35,38] conducted in high-schools found that most students (65–100%), particularly carriers, would want to know the carrier status of a future partner. In some cases (17%), noncarrier students said they would use carrier status as a criterion for partner selection, even when there was a vanishingly small chance of having an affected child.[31] Interviews conducted by McConkie-Rosell et al.[36] also suggested that fragile X syndrome carrier and at-risk girls have heightened concern about future parental roles and frequently mentioned barriers to parenthood (such as difficulties with finding a partner and having an affected child).

Indications that carrier testing has a positive impact on children's social relationships were found in a single study conducted by McConkie-Rosell et al.[36] Comparisons between girls who had been tested for fragile X syndrome carrier status ($n = 38$) and girls who were untested but known to be at risk ($n = 15$) found that testing was significantly associated with more positive evaluations of relationships with friends after learning their status. Interviews also suggested that testing correlated with much greater willingness to communicate with and receive support from friends and the belief that the testing experience had a positive impact on their family. Furthermore, half of the noncarriers expressed relief during interviews that they no longer had to worry about how their potential carrier status might impact their future roles as parents.

Predictive testing

Neither of the two studies examining social relationships in the context of predictive genetic testing suggested a strong positive or negative impact. The first study, conducted among children who had all tested positive for cardiovascular disease risk ($n = 35$, 8–18 years), found no significant impact on parental and peer relationships using established quantitative measures, and this finding was largely supported in semistructured interviews.[43,45] Another study conducted by Codori et al.[40,41] (discussed previously) asked whether the response of tested children was influenced by the risk status of other family members. Although no clinically significant impact was observed for depression, anxiety, and behavioral problems, affected children with a sibling who tested positive had a higher likelihood of depression that was statistically significant. The status of siblings also appeared to influence children's behavior and anxiety levels. In addition, it is worth noting that children with affected fathers tended to have better depression, anxiety, and behavioral problem profiles than children with affected mothers, although this was not a significant finding at most time points.

DISCUSSION

Our systematic review of the literature identified 17 published articles that met the inclusion criteria. The clearest conclusion of this review is that the evidence base is sparse and lacking in replication to an extent where it can only provide a relatively superficial picture of the psychosocial impact of genetic testing on children. Comparisons across studies were hindered by the wide variability in carrier traits and health conditions addressed (see Table 2 and 3) and the many different approaches used (Table 4). Virtually, all quantitative studies were susceptible to differential attrition, had limited power to identify significant effects because of small sample sizes, and used measurement tools better suited to studying the psychosocial impact of major traumatic events. Finally, the near universal use of retrospective study designs limits insight into the causation of psychologic effects and raises questions about whether children would be able to accurately recall the details of their testing experience.[46] Because of these concerns, we acknowledge the precursory nature of the findings in this review and repeat previous calls for further research that clarifies the psychosocial impact of genetic testing on children in a rigorous manner.[17,18,47,48]

Despite these limitations, a preponderance of the early evidence suggests that children who received genetic test results, whether indicative of increased risk or not, did not experience significant changes in psychosocial wellbeing.[30,31,33,34,36,38,40–43,45] However, it is plausible that this lack of impact was because of methodological weaknesses in quantitative studies rather than an absence of responses among children. The most adverse

findings were relatively high levels of worry about the test among those at risk and some indication that testing might influence children's perspectives on future partner selection and parental roles.[30,31,37,38,42] Beneficial influences also were observed, including high reported satisfaction among tested children and positive emotional responses among children who tested negative.[30,31,34,36,37,39,42]

Implications for future research

Although this review suggests that a majority of publications do not indicate a substantial impact of genetic testing on children's psychosocial wellbeing, most position statements recommend against the testing of children.[1,2] This difference is likely because of the serious limitations of the current evidence and a tendency of health care organizations to take a precautionary stance with respect to potential harms,[49] particularly when children are involved.

We suggest four areas for consideration in future research that will assist these organizations in developing evidence-based practice guidelines (see Table 5). Specifically, we recommend that studies: (1) consider new genomic tests assessing risk for common health conditions, (2) use prospective study designs, (3) include sensitive and appropriate psychosocial assessments, and (4) examine the web of social relationships.

Forecasts of advances in genetic technology suggest a future in which the current paradigm of genetic testing (where single variants for rare disorders are detected) will be broadened to genomic testing (where many variants are tested simultaneously to indicate risk for multiple common diseases in the absence of a known family history[7,17]). Such testing could enable primary prevention to be targeted to the young and healthy by motivating decreases in tobacco use, poor diet, and physical inactivity, all of which are habits established in early childhood.[7,50,51]

The consequences of offering such genomic testing to children may be substantially different from the single-gene testing approaches considered in this review. The results of genomic tests are likely to span multiple health conditions, contain considerable ambiguity, and suggest a range of behavioral modifications. Although the observed lack of effects on global psychosocial traits found in this review may generalize to genomic testing, such extrapolation is currently speculative. Therefore, we believe that forward-looking research that addresses genomic testing among children is both appropriate and necessary before implementation. This need is emphasized by the fact that several commercial genetics companies already offer direct-to-consumer genomic testing services for children, which provide information about disease risks, physical traits, psychological characteristics, and ancestry.[52] Specific research domains that might be particularly helpful in policy development include the following: characterizing how children understand complex genetic risk information, studying the impact of high-risk test results on health behavior change in the context of the family, and clarifying how genomic information influences components of children's psychosocial wellbeing.

A second area for consideration is the need for study designs that can assess how psychosocial conditions change prospectively over time. It is essential to establish a temporal order that helps clarify whether observed changes in psychosocial constructs could be causally attributed to genetic testing. This may be especially important among high-risk families. If children suspect that they are at increased risk, negative emotional effects may exist before testing. Even in studies where children are not expected to have a strong family history of disease, current evidence suggests that children's psychosocial response may change over time and, therefore, should be addressed with multiple follow-ups.[36,37,42] Of note, it may be most effective to include at least one assessment within the first 3 months after testing, given that this is the timeframe where adults are most affected by genetic test results (e.g., short-term changes in stress or distress).[29,53–58]

A third area for consideration is the need for appropriate assessments. The measurement tools that were used by the quantitative studies in this review mainly assessed changes in global psychosocial constructs associated with pathology (e.g., depression, anxiety, and disrupted self-concept). These tools consistently failed to detect substantial differences between those at higher genetic risk and comparison groups, a finding which seems to be in line with other health research among children. For example, children with existing genetic conditions or stigmatized physical conditions, such as sickle cell anemia[59] or obesity,[60] seem to have only modest changes in measures of global psychosocial wellbeing. Furthermore, a lack of sustained global psychosocial impact also has been repeatedly observed among adults tested for a wide range of genetic conditions.[29,53–58]

Some evidence in this review suggests that genetic testing is more likely to produce subtle effects on children that might initially be explored most effectively using mixed methods approaches. For example, studies using structured interviews revealed the complex ways that children interpret test results (e.g., genetic identity and complex social impacts), many of which were not addressed by global quantitative measures.[36,45,61,62] Also, quantitative research tools that included

Table 5 Recommendations for future research

Recommendation 1: Investigate genomic testing for common health conditions
Address response to testing when there is no known family history of a disease
Examine how children respond to information about multiple variants, risk levels, and diseases
Recommendation 2: Use study designs that can detect change over time
Prospective study designs control for pre-existing distress among children from high-risk families
Conduct at least one follow-up assessment within 3 months of receiving test results
Recommendation 3: Develop sensitive and appropriate assessments
Use qualitative approaches to identify a range of psychosocial responses in different testing contexts
Focus on strategies that would be capable of detecting subtle, rather than global, influences on psychosocial constructs
Use theoretical models to inform expectations of cognitive and emotional coping
Recommendation 4: Consider web of social relationships
Examine how the test status of other family members effect children's testing experience
Use approaches that integrate data from family and peer networks in addition to children's individual responses
Include diverse populations and varied social contexts for test delivery

questions specifically about the testing experience (e.g., "How has knowing your carrier status affected the way you feel about yourself"[36]) rather than a global feeling were more likely to observe significant differences between children with positive or negative test outcomes. Taken together, this suggests that qualitative and test-specific quantitative measurement approaches should be considered when appropriate to the study goals. Specific areas in need of research include development of measurement tools that can detect subtle changes in children's wellbeing and analysis that clarifies whether such shifts are of a sufficient magnitude as to warrant concern in a clinical context.

Studies could also be improved by using existing theoretical models to develop hypotheses about children's response to genetic information about health.[62–72] Including less extensively studied concepts such as benefit finding,[63–65] hoped for and feared possible selves,[66,67] adaptive coping,[63,68] resilience traits,[69] and communal coping responses[70] may lead to a richer understanding of children's testing experienced. Furthermore, research that examines the translational potential of genomic or genetic testing of children (e.g., studies assessing methods for communicating test results, approaches for the use of testing in clinical settings, and influences of testing on health or health behavior outcomes) should be considered alongside psychosocial effects so as to make possible a balanced risk/benefit analysis before the test implementation.[71]

Finally, future research should address the fact that children seem to understand genetic test results within a web of social influences. This review suggests that carrier and predictive genetic testing, particularly in the presence of a family history of disease, is intermeshed with family and peer relationships.[36,40,41,61] Fully exploring these influences will involve addressing the roles that relevant individuals play in relationships (emotional support, care giving, leadership, health advice, etc.),[72] and also their test status, their gender, and their connection to the tested individual.[40,41] Other factors, such as the environment where children receive test information (e.g., home, clinic, school, and religious institution) and their racial and ethnic background[73,74] are also likely to play a role in the type, relevance, and influence of different social networks. Finally, given the role that parents play in forming children's health beliefs and behaviors, a more detailed understanding of parental responses to their children's genetic test results will be essential.

In considering these suggested directions for future research, it is important to note that the approach taken in this systematic literature review is limited in several ways. First, the review was restricted to peer reviewed articles in journals published in English, and therefore it is plausible that it excluded relevant findings presented in other publication types and languages. Perhaps more importantly, the review focused exclusively on the response of tested children who were not experiencing serious disease symptoms. As such, some research that is broadly relevant to understanding the impact of genetic testing on children was not addressed. In particular, assessments of children's wellbeing that relied exclusively on parental or clinician reports were not reviewed. Also absent from this review are studies that examined responses to genetic testing for childhood-onset conditions and explorations of the attitudes toward testing of untested children.

CONCLUSIONS

Current research on carrier and predictive genetic testing among children provides little evidence of a significant negative or positive impact on an array of indicators of psychosocial wellbeing. However, the methodological approaches used in quantitative studies might have been inadequate to detect important effects on children's emotions, self-perception, and social wellbeing. Furthermore, the existing literature on single-gene traits may not generalize well to children's response to future uses of genomic testing because the clarity, specificity, and implications of these approaches are substantially different. In light of these considerations, additional research is needed to gain a more accurate understanding of when offering genetic information to children can achieve health benefits.

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REFERENCES

1. Borry P, Fryns JP, Schotsmans P, Dierickx K. Carrier testing in minors: a systematic review of guidelines and position papers. *Eur J Hum Genet* 2006;14:133–138.
2. Borry P, Stultiens L, Nys H, Cassiman JJ, Dierickx K. Presymptomatic and predictive genetic testing in minors: a systematic review of guidelines and position papers. *Clin Genet* 2006;70:374–381.
3. Peshkin BN, DeMarco TA, Garber JE, et al. Brief assessment of parents' attitudes toward testing minor children for hereditary breast/ovarian cancer genes: development and validation of the Pediatric BRCA1/2 Testing Attitudes Scale (P-TAS). *J Pediatr Psychol* 2009;34:627–638.
4. Borry P, Fryns JP, Schotsmans P, Dierickx K. Attitudes towards carrier testing in minors: a systematic review. *Genet Couns* 2005;16:341–352.
5. Borry P, Stultiens L, Nys H, Dierickx K. Attitudes towards predictive genetic testing in minors for familial breast cancer: a systematic review. *Crit Rev Oncol Hematol* 2007;64:173–181.
6. Parker M. Genetic testing in children and young people. *Fam Cancer* 2010;9:15–18.
7. Haga SB, Terry SF. Ensuring the safe use of genomic medicine in children. *Clin Pediatr (Phila)* 2009;48:703–708.
8. Bottinger EP. Foundations, promises and uncertainties of personalized medicine. *Mt Sinai J Med* 2007;74:15–21.
9. The President's Council on Bioethics. The changing moral focus of newborn screening: an ethical analysis by the President's Council on Bioethics. Washington, DC: The President's Council on Bioethics, December 2008.
10. Alexander D, van Dyck PC. A vision of the future of newborn screening. *Pediatrics* 2006;117(5 Pt 2):S350–S354.
11. Segal ME, Sankar P, Reed DR. Research issues in genetic testing of adolescents for obesity. *Nutri Rev* 2004;62:307–320.
12. Robertson JA. The $1000 genome: ethical and legal issues in whole genome sequencing of individuals. *Am J Bioeth* 2003;3:W–IF1.
13. Almond B. Genetic profiling of newborns: ethical and social issues. *Nat Rev Genet* 2006;7:67–71.
14. Fanos JH. Developmental tasks of childhood and adolescence: Implications for genetic testing. *Am J Med Genet* 1997;71:22–28.
15. Malpas PJ. Why tell asymptomatic children of the risk of an adult-onset disease in the family but not test them for it? *J Med Ethics* 2006;32:639–642.
16. Malpas PJ. Predictive genetic testing of children for adult-onset diseases and psychological harm. *J Med Ethics* 2008;34:275–278.
17. Wilfond B, Ross LF. From genetics to genomics: ethics, policy, and parental decision-making. *J Pediatr Psychol* 2009;34:639–647.
18. Duncan RE, Delatycki MB. Predictive genetic testing in young people for adult-onset conditions: where is the empirical evidence? *Clin Genet* 2006; 69:8–16.
19. Richards FH. Maturity of judgement in decision making for predictive testing for nontreatable adult-onset neurogenetic conditions: a case against predictive testing of minors. *Clin Genet* 2006;70:396–401.
20. Rhodes R. Why test children for adult-onset genetic diseases? *Mt Sinai J Med* 2006;73:609–616.
21. Wertz DC, Fanos JH, Reilly PR. Genetic testing for children and adolescents: who decides?. *JAMA* 1994;272:875–881.
22. Lessick M, Faux S. Implications of genetic testing of children and adolescents. *Holist Nurs Pract* 1998;12:38–46.
23. Tercyak KP, Streisand R, Peshkin BN, Lerman C. Psychosocial impact of predictive testing for illness on children and families: challenges for a new millennium. *J Clin Psychol Med Sett* 2000;7:55–68.
24. Task Force on Genetic Testing. Promoting safe and effective genetic testing in the United States. Final Report of the Task Force on Genetic Testing. Washington, DC: NIH-DOE, 1997.

25. Borry P, Schotsmans P, Dierickx K. Empirical research in bioethical journals. A quantitative analysis. *J Med Ethics* 2006;32:240–245.
26. Kon AA. The role of empirical research in bioethics. *Am J Bioeth* 2009;9:59–65.
27. McConkie-Rosell A, Devellis BM. Threat to parental role: a possible mechanism of altered self-concept related to carrier knowledge. *J Genet Couns* 2000;9:285–302.
28. Cicchetti D, Rogosch F. Equifinality and multifinality in developmental psychology. *Dev Psychopathol* 1996;8:597–600.
29. Heshka JT, Palleschi C, Howley H, Wilson B, Wells PS. A systematic review of perceived risks, psychological and behavioral impacts of genetic testing. *Genet Med* 2008;10:19–32.
30. Clow CL, Scriver CR. Knowledge about and attitudes toward genetic screening among high school students: the Tay Sachs experience. *Pediatrics* 1977;59:86–91.
31. Mitchell J, Scriver CR, Clow CL, Kaplan F. What young people think and do when the option for cystic fibrosis carrier testing is available. *J Med Genet* 1993;30:538–542.
32. Järvinen O, Lehesjoki AE, Lindlöf M, Uutela A, Kääriäinen H. Carrier testing of children for two X-linked diseases: a retrospective study of comprehension of the test results and social and psychological significance of the testing. *Pediatrics* 2000;106:1460–1465.
33. Järvinen O, Aalto AM, Lehesjoki AE, et al. Carrier testing of children for two X linked diseases in a family based setting: a retrospective long term psychosocial evaluation. *J Med Genet* 1999;36:615–620.
34. Järvinen O, Hietala M, Aalto AM, et al. A retrospective study of long-term psychosocial consequences and satisfaction after carrier testing in childhood in an autosomal recessive disease: aspartylglucosaminuria. *Clin Genet* 2000;58:447–454.
35. Barlow-Stewart K, Burnett L, Proos A, et al. A genetic screening programme for Tay-Sachs disease and cystic fibrosis for Australian Jewish high school students. *J Med Genet* 2003;40:e45.
36. McConkie-Rosell A, Spiridigliozzi GA, Melvin E, Dawson DV, Lachiewicz AM. Living with genetic risk: effect on adolescent self-concept. *Am J Med Genet C Semin Med Genet* 2008;148:56–69.
37. Zeesman S, Clow CL, Cartier L, Scriver CR. A private view of heterozygosity: eight-year follow-up study on carriers of the Tay-Sachs gene detected by high school screening in Montreal. *Am J Med Genet* 1984;18:769–778.
38. Scriver CR, Bardanis M, Cartier L. β-Thalassemia disease prevention: genetic medicine applied. *Am J Hum Genet* 1984;36:1024–1038.
39. Järvinen O, Lehesjoki AE, Lindlöf M, Uutela A, Kääriäinen H. Carrier testing of children for two X-linked diseases: a retrospective evaluation of experience and satisfaction of subjects and their mothers. *Genet Test* 1999;3:347–355.
40. Codori AM, Petersen GM, Boyd PA, Brandt J, Giardiello FM. Genetic testing for cancer in children: short-term psychological effect. *Arch Pediatri Adolesc Med* 1996;150:1131–1138.
41. Codori AM, Zawacki KL, Petersen GM, et al. Genetic testing for hereditary colorectal cancer in children: long-term psychological effects. *Am J Med Genet A* 2003;116A:117–128.
42. Michie S, Bobrow M, Marteau TM. Predictive genetic testing in children and adults: a study of emotional impact. *J Med Genet* 2001;38:519–526.
43. Smets EMA, Stam MMH, Meulenkamp TM, et al. Health-related quality of life of children with a positive carrier status for inherited cardiovascular diseases. *Am J Med Genet A* 2008;146:700–707.
44. Liljeström B, Tuomi T, Isomaa B, Sarelin L, Aktan-Collan K, Kääriäinen H. Adolescents at risk for MODY3 diabetes prefer genetic testing before adulthood. *Diabetes Care* 2007;30:1571–1573.
45. Meulenkamp TM, Tibben A, Mollema ED, et al. Predictive genetic testing for cardiovascular diseases: impact on carrier children. *Am J Med Genet A* 2008;146A:3136–3146.
46. Hardt J, Rutter M. Validity of adult retrospective reports of adverse childhood experiences: review of the evidence. *J Child Psychol Psychiatry* 2004;45:260–273.
47. Marteau TM. The genetic testing of children. *J Med Genet* 1994;31:743.
48. Duncan RE. Predictive genetic testing in young people: when is it appropriate? *J Paediatr Child Health* 2004;40:593–595.
49. Caulfield T. Direct-to-consumer genetics and health policy: a worst-case scenario? *Am J Bioeth* 2009;9:48–50.
50. Centers for Disease Control and Prevention. Improving the health of adolescents and young adults: a Guide for States and Communities. Atlanta, GA: CDC, 2004.
51. Tercyak KP, Tyc VL. Opportunities and challenges in the prevention and control of cancer and other chronic diseases: children's diet and nutrition and weight and physical activity. *J Pediatr Psychol* 2006;31:750–763.
52. Borry P, Howard HC, Senecal K, Avard D. Health-related direct-to-consumer genetic testing: a review of companies' policies with regard to genetic testing in minors. *Fam Cancer* 2010;9:51–59.
53. Meiser B, Gleeson MA, Tucker KM. Psychological impact of genetic testing for adult-onset disorders. An update for clinicians. *Med J Aust* 2000;172:126–129.
54. Meiser B, Dunn S. Psychological impact of genetic testing for Huntington's disease: an update of the literature. *J Neurol Neurosurg Psychiatry* 2000;69:574–578.
55. Meiser B, Dunn S. Psychological effect of genetic testing for Huntington's disease: an update of the literature. *West J Med* 2001;174:336–340.
56. Butow PN, Lobb EA, Meiser B, Barratt A, Tucker KM. Psychological outcomes and risk perception after genetic testing and counselling in breast cancer: a systematic review. *Med J Aust* 2003;178:77–81.
57. Meiser B. Psychological impact of genetic testing for cancer susceptibility: an update of the literature. *Psychooncology* 2005;14:1060–1074.
58. Meiser B, Tucker K, Friedlander M, et al. Genetic counselling and testing for inherited gene mutations in newly diagnosed patients with breast cancer: a review of the existing literature and a proposed research agenda. *Breast Cancer Res* 2008;10:216.
59. Midence K, Fuggle P, Davies SC. Psychosocial aspects of sickle cell disease (SCD) in childhood and adolescence: a review. *Br J Clin Psychol* 1993;32(Pt 3):271–280.
60. Wardle J, Cooke L. The impact of obesity on psychological well-being. *Best Pract Res Clin Endocrinol Metab* 2005;19:421–440.
61. Duncan RE, Gillam L, Savulescu J, Williamson R, Rogers JG, Delatycki MB. "You're one of us now": Young people describe their experiences of predictive genetic testing for Huntington disease (HD) and familial adenomatous polyposis (FAP). *Am J Med Genet C Semin Med Genet* 2008;148:47–55.
62. Bernhardt BA. The role of qualitative research in medical genetics: listening to the voices of our patients. *Am J Med Genet A* 2008;146A:3132–3135.
63. Phipps S. Adaptive style in children with cancer: implications for a positive psychology approach. *J Pediatr Psychol* 2007;32:1055–1066.
64. Currier JM, Hermes S, Phipps S. Children's response to serious illness: perceptions of benefit and burden in a pediatric cancer population. *J Pediatr Psychol* 2009;34:1129–1134.
65. Helgeson VS, Reynolds KA, Tomich PL. A meta-analytic review of benefit finding and growth. *J Consult Clin Psychol* 2006;74:797–816.
66. Hoyle RH, Sherrill MR. Future orientation in the self-system: possible selves, self-regulation, and behavior. *J Pers* 2006;74:1673–1696.
67. Black ME, Stein KF, Loveland-Cherry CJ. Older women and mammography screening behavior: do possible selves contribute? *Health Educ Behav* 2001;28:200–216.
68. Gooding HC, Organista K, Burack J, Biesecker BB. Genetic susceptibility testing from a stress and coping perspective. *Soc Sci Med* 2006;62:1880–1890.
69. Campbell-Sills L, Cohan SL, Stein MB. Relationship of resilience to personality, coping, and psychiatric symptoms in young adults. *Behav Res Ther* 2006;44:585–599.
70. Koehly LM, Peters JA, Kuhn N, et al. Sisters in hereditary breast and ovarian cancer families: communal coping, social integration, and psychological well-being. *Psychooncology* 2008;17:812–821.
71. Scheuner MT, Sieverding P, Shekelle PG. Delivery of genomic medicine for common chronic adult diseases: a systematic review. *JAMA* 2008;299:1320–1334.
72. Koehly LM, Peterson SK, Watts BG, Kempf KK, Vernon SW, Gritz ER. A social network analysis of communication about hereditary nonpolyposis colorectal cancer genetic testing and family functioning. *Cancer Epidemiol Biomarkers Prev* 2003;12:304–313.
73. Ford ME, Tilley BC, McDonald PE. Social support among African-American adults with diabetes. Part 1: theoretical framework. *J Natl Med Assoc* 1998;90:361–365.
74. Ford ME, Tilley BC, McDonald PE. Social support among African-American adults with diabetes. Part 2: a review. *J Natl Med Assoc* 1998;90:425–432.
75. Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. Quality of Reporting of Meta-analyses. *Lancet* 1999;354:1896–1900.

