J Genet Counsel (2011) 20:80–97
DOI 10.1007/s10897-010-9327-8

ORIGINAL RESEARCH

Can We Make Assumptions About the Psychosocial Impact of Living as a Carrier, Based on Studies Assessing the Effects of Carrier Testing?

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Received: 31 March 2010 / Accepted: 1 September 2010 / Published online: 29 September 2010

Abstract Receiving the results of genetic carrier testing may have an impact on the psychosocial health of the individual. Numerous studies have been conducted to assess the psychosocial effects of carrier status for a range of conditions. To systematically review research focused on the psychological and social impact of carrier testing on individuals in order to identify factors affecting the impact of carrier testing results, and discern areas where further research is needed. Twenty relevant papers meeting criteria for inclusion in this review were found. The main themes identified across these studies included: anxiety, guilt and stigmatization, effect on family relationships, effect on self image, active coping mechanisms and reproductive issues. Variables related to the psychosocial effect of carrier testing included whether the carrier has an affected child, mode of inheritance, genetic counseling, and life stage. A key finding concerns carriers who already have an affected child; they are more likely to experience guilt and self-blame, and change their reproductive plans compared to carriers without affected children. Additionally, some participants reported clinical features of the disorder for which they were being tested. Genetic counselors may erroneously assume that parents with affected children are aware of their own carrier status in the absence of testing, and they may offer inadequate support. Additionally, counselors should attempt to address patient misconceptions related to their health and carrier status.

Keywords Systematic review · Carrier testing · Genetic · Psychosocial · Genetic counseling

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Introduction

Variations in genetic material are inherent in all humans. While many of these variations do not change the protein product for which the gene codes, others may have a more deleterious effect (Adkison and Brown 2007). In autosomal or X linked recessive conditions, one normal copy of the gene is usually sufficient to ensure the protein product is not adversely affected; however if individuals are heterozygous, having one normal and one mutated copy of the gene, they are said to be a "carrier" of the condition. The offspring of carriers could be at risk of inheriting the disease. A woman carrying an X linked recessive condition, such as fragile X or Duchenne muscular dystrophy, could pass the condition to her children (usually her sons) but in the case of autosomal recessive conditions, such as cystic fibrosis or thalassaemia, both parents need to be carriers of the same disease for their children to be at risk. Fragile X does differ from most other X linked conditions because premutation carriers [individuals with 55 to 200 CGG repeats (Kronquist et al. 2008)] can be mildly affected by the condition, can present with late-onset

fragile X-associated tremor/ataxia syndrome (FXTAS) (Reis et al. 2008), and have an increased risk of premature ovarian failure (Hunter et al. 2008).

The term "carrier" is also used to describe individuals who have a balanced chromosome translocation. The translocation does not affect their own health, but their children could inherit an unbalanced form of the translocation that could have an adverse phenotypic effect (Meza-Espinoza et al. 2008).

Because of the potential reproductive implications of carrier status, individuals who are aware they could be carriers may wish to be certain of their own status. Carrier testing for a range of genetic diseases has been offered to individuals with a family history of the condition, or through community based screening programs in particular ethnic groups, for example community based screening for Tay Sachs disease in the Ashkenazi Jewish population conducted since the 1970's (Kaback et al. 1993). Population carrier testing has also been offered either regionally or nationally, for conditions including cystic fibrosis, thalassaemia and fragile X (Hartley et al. 1997; Kaufman et al. 2008; Metcalfe et al. 2008; Sangkitporn et al. 2004; Zlotogora et al. 2009).

Numerous studies have assessed the psychosocial impact of carrier testing and living as a carrier (Anido et al. 2005; Childs et al. 1976; Kenen and Schmidt 1978; McConkie-Rosell et al. 2001). As early as 1976, Childs et al. highlighted a number of emotional issues experienced by carriers including anxiety, self-stigmatization, and concern for offspring. Since then, other studies have assessed the impact of carrier testing in relation to a number of variables such as the particular condition (Anido et al. 2005), the mode of inheritance (James et al. 2006), the population being screened (Axworthy et al. 1996) and the impact of gender (Marteau et al. 1997). We conducted a systematic review to synthesize this body of knowledge. Carriers of fragile X were included in the review because a body of knowledge exists relating to the psychosocial effect of carrier testing on this group (Anido et al. 2007; Anido et al. 2005; McConkie-Rosell et al. 2000; McConkie-Rosell et al. 2001). Because female fragile X carriers can sometimes be affected by the condition, although in general more mildly, fragile X does differ from autosomal recessive and some other X linked conditions. However, because we were trying to ascertain similarities and differences across a range of different conditions, we felt it was relevant to include this group in the systematic review.

Specifically, the aim of this systematic review was to answer the following questions: (1) What are the factors affecting the impact of carrier testing results on individuals? (2) What is the methodological quality of the body of literature examining the psychosocial effects of carrier testing? (3) Can we make any assumptions about the psychosocial impact of living as a carrier, based on studies assessing the impact of carrier testing?

Methods

In conducting this systematic review the methods described by Pope et al. (2007) which involve using specific search parameters, defining inclusion and exclusion criteria, and undertaking quality appraisal of the studies that are included, were used as a guide. Due to the wide range of methods, conditions and samples in the studies reviewed, we did not conduct a meta-analysis of the data.

Search Methods

The following databases were searched: CINAHL, Embase, Ovid, Medline, PsychINFO, Pubmed and Web of Science, using the following search terms:

> carrier testing or carrier test* or carrier screening or genetic screening or population screening or cascade testing or heterozygote testing AND genetic or DNA or chromosome or autosomal recessive or recessive or X-linked AND depression or emotion or guilt or anxiety or worry or stress or blame or psychological or psychosocial or social or effect or impact or psychological impact or social impact or personal or carrier status or distress or relief or burden or coping or coping strategy or communication or coping behavior* or emotion* or stigma or self concept or attitude* or psychology or social adaptation or reproductive uncertainty or risk perception or genetic counselling or genetic counseling or carrier couples or family planning or prospective risk AND NOT children NOT cancer NOT prenatal NOT predictive.

Limits were set on publication dates (January 1990 to May 2010), language (English), and population (Human; Age: Adult.).

An author search and an ancestral search (reference search) were also carried out after relevant studies were identified. Keywords from relevant studies found this way were fed back into the search terms to ensure the search was thorough.

Inclusion and exclusion factors

Studies were included if they were:

- systematic reviews, literature reviews randomized controlled trials, quasi-experiments, observational studies, surveys or qualitative studies
- published between January 1990 to May 2010. We included studies published from 1990 onwards as around this time DNA carrier testing became feasible clinically for patients with a family history of recessive and X-linked conditions (Broide et al. 1993; Kerem et al. 1989). At the same time, studies that assessed the impact of the test on the patient began to appear in the literature
- focused on the psychological and social impact of the test result on the patient
- focused on either autosomal recessive and X linked conditions, or carriers of chromosomal changes such as translocations.

Studies were excluded if they were:

- about cancer, adult onset conditions or other dominantly inherited conditions, because the nature of the information derived from these tests will be different from receiving carrier information for recessive, X-linked or chromosomal conditions
- ones in which there was potential for participants to find out that they were homozygotes for a particular gene mutation where the age of onset of the disease was in adulthood (e.g., hemochromatosis)
- focused on pregnant women because their feelings may be influenced by worry for their offspring, and also because their decision to seek testing would be influenced by the immediate needs of a current pregnancy (Cheuvront et al. 1998)
- ones that included children or adolescents because it is likely that they will have very different psychosocial reactions and information needs than adults
- focused only on recall of information about risk
- focused only on motivation for taking/not taking the test.

Search Outcome

The literature search generated 1694 articles for consideration. Following exclusion based on title and abstract, the full text of 41 articles was retrieved. An ancestral and an author search identified 10 further studies. After reading the papers in full, 31 studies were excluded because they did not meet the inclusion criteria, leaving 20 relevant studies to be included in the systematic review. There were substantial differences in construct, design, measures, population and outcomes across the studies. In this section we cite one example of each particular design, measure or outcome studied. Table 1 contains a more detailed report of the characteristics of each study. Thirteen studies were quantitative, three were qualitative and four were mixed methods. Study designs comprised longitudinal studies (Bekker et al. 1994), randomised controlled trials (Callanan et al. 1999), and cross sectional studies (Dunn et al. 2008). Samples from different populations including the general population (Henneman et al. 2002), high risk groups (McConkie-Rosell et al. 2001) of Jewish decent (Marteau et al. 1992) and women only (Anido et al. 2005) were included. Sample size varied from eight participants (Anido et al. 2007) to 2220 participants (Honnor et al. 2000). Data collection methods varied from questionnaires (Bekker et al. 1994), to focus groups (Anido et al. 2005) and in-depth interviews (Williams and Schutte 1997). Various measures were used, including the Spielberger State-Trait Anxiety Inventory (STAI) (Spielberger et al. 1970), the Health Orientation Scale (HOS) (Wooldridge and Murray 1988) and the Tennessee Self Concept Scale (TSCS) (Fitts and Warren 1996). In two cases the same cohort of participants was involved in two studies, however because different findings were presented in the different papers, both studies were included in the review (Cheuvront et al. 1998; Newman et al. 2002).

Quality Appraisal

Each study was assessed using a quality appraisal tool developed by Kmet et al. (2004). The Kmet scale enables assessment of both qualitative and quantitative studies. This tool has proven internal validity and provides a systematic, reproducible and quantitative means of simultaneously assessing the quality of research encompassing a broad range of study designs. Using this tool, the first author scored each paper based on quality criteria including the description of the research question, appropriateness of design, justification of sampling strategy, appropriate data collection and analysis and estimates of variance (for quantitative studies) to produce a score phrased as a percentage. Five papers across the range of scores were selected and a blind appraisal was made by the second author to verify the results. The papers were ranked in the same order by both appraisers.

All 20 papers scored greater than 60% on the Kmet scale (range between 63% to 95%; median 81%) and therefore none were excluded on the basis of quality (Kmet et al. do not provide a 'cut-scale' at which studies

Table 1 Summary of studies

Reference	Purpose of study	Study design	Sample and size	Data collection	Method of analysis	Results
Anido et al. 2007	To explore the attitudes towards FX mutation carrier testing from women identified from the general population.	Qualitative. In-depth interviews.	Eight women from the general population, of reproductive-age, who had been identified as FX carriers. Aged 21–44.	Semi-structured qualitative in-depth interviews. Seven were conducted in person, one by phone. Topic guide consisted of twenty eight questions covering topics including testing experience, premature ovarian failure, affect of information on relationships and family planning.	Interpretative phenomenological analysis. Tapes transcribed. Recurring primary patterns in data noted. After independent analysis, team members compared their assessment to discuss clarification and development of themes.	Women were wholly unprepared for positive carrier results. For many carriers the information was not relevant at this stage of their lives in terms of family planning and personal relationships.Many expressed the information could be relevant in the future. For majority, providing information to family was not problematic. Providing information to partners depended on seriousness of relationship. Resulting information came as a surprise but for most women was put quickly out of mind.
Anido et al. 2005	To identify issues related to carrier testing and population screening for premutation carrier women.	Qualitative. Focus groups.	General population and women from families with FX from Atlanta, aged 28-50. Forty focus group participants. Ten women per focus group.	Focus groups were audio and video recorded. Questions included: How would you describe your first reaction to getting results? Did your test result cause you to take any action or make decisions about your life plans? Did your result make you feel anything new about yourself?	Thematic analysis. Tapes transcribed. Primary patterns noted and classified into themes. Data analyzed independently then findings compared. Themes then compared to existing literature to determine novel findings.	Nearly all carries from FX families reported some sort of guilt experience. Reactions of relief expressed equally strongly—relief for carriers in terms of finding diagnosis, and relief for non-carriers. Anxiety dissipated either immediately or over a few months. Carrier status led to reconsideration of life plans. 'Grandmother guilt' experienced by several carriers. Timing of carrier testing with respect to a woman's life stage and views on abortion dictates whether the information on carrier status will be seen as beneficialor detrimental.
Bekker et al. 1994	To evaluate the short term effects of population based screening for carriers of CF.	Longitudinal, study. Self completed postal questionnaire completed at three time points.	Adults between 18–45 years registered with a general practitioner in Inner London. Five thousand five hundred and twenty-nine adults approached (5529). Nine hundred and fifty seven (957) patients tested (637 females 320 males) Full data received from 427 with negative results and 14 carriers.	Questionnaires at three time points: before testing, upon receiving results, three months later. STAI used to assess anxiety. Six interviews with carriers six months after receiving test results.	MANOVA Univariate analysis. No information on how interview data were analyzed.	Receipt of results had no effect on perceptions of health. Those who received a positive result were significantly more anxious upon receipt but by three months this anxiety had dissipated. Main problem of population carrier screening would be false reassurance as opposed to anxiety.
Callanan et al. 1999	To identify risk perceptions, psychological status and reproductive plans of carrier by non carrier couples.	Randomized controlled trial comparing home education and testing with clinic education and testing.	CF carrier testing offered to 120 partners of previously identified carriers of individuals with CF. Fifty seven partners were tested Participants: 18+ years, not pregnant, living in study inclusion area (N. Carolina). Participants randomly assigned to either clinic or home screening.	Survey during interval between partners' testing and receiving results six months later. STAI used to measure anxiety and personality trait. Positive and negative affect measured using PANAS.	Paired comparison t test. Descriptive statistics used to summarize data.	Both relatives and their partners showed slightly higher anxiety scores while waiting for partners test results, although within 'normal' anxiety range. No significant differences between the relative and partner at either time point. Both showed decrease in anxiety score six months after completion of testing. Eighty-nine percent of relatives reported no change in reproductive plans.
Cheuvront et al. 1998 (same cohort as Newman et al. 2002)	To look at psychosocial and knowledge outcomes of two different approaches to CF gene pre-test education and carrier testing.	Randomized controlled trial comparing home education and testing with clinic education and testing. Secondary analysis comparing carriers and Non-carriers.	Two hundred and ninety-nine accept ed offer of free education and testing, aged 18+ years (majority between 26–45 years). Participants were relatives of people with CF living in N. Carolina. Participants randomly assigned into two groups before being contacted; those assigned to the clinic (91) and those assigned to education and testing at home (208).	Participants completed a baseline telephone interview, and completed a questionnaire at two time points: while waiting for their test results and immediately after learning their test results. STAI used to measure anxiety.	Data analyzed using SUDAAN software for clustered samples. Value of $p<0.05$ was considered significant.	No significant differences in positive or negative affect or anxiety while waiting for results or after results were known as a result of where person had been educated and tested. Nostatistically significant differences on any of the outcome measures based oncarrier status (anxiety, positive and negative effectand satisfaction with education and testing arrangements)

Dunn et al. 2008	A descriptive study which aims to report adult carriers' and their husbands/partners' experiences of carrier diagnosis for hemophilia A and B	Cross sectional study. Self completed postal questionnaire.	Carriers registered on the Katharine Dormandy Hemophilia Centre database at the Royal Free, London. Two hundred and thirty-five carriers identified aged 18–65 and sent introductory letter. Sixty-six carriers responded. Median age 42. 76% were in a relationship and 78% of their husbands/partners completed the questionnaire.	Questionnaire influenced by Systematic Theory. Included yes/no, multiple choice, example scenario, ranking and open ended questions.	Most of the data analysis was descriptive; where appropriate a Student's t-test or a Mantel-Haenszel chi-squared test was used and a value of $p<0.05$ was considered statistically significant.	Carriership was considered an issue by both groups at two key points: 34% once their relationship had become serious and 39% once their son had been diagnosed with hemophila. Thirty-eight percent of carriers said the timing of the test had a negative effect on them. Reasons cited were: sense of shock and grief, concern about having children, feeling blamed by their partner and a prolonged sense of guilt. Where timing was seen as positive (22%) it was because of feeling completely accepted by their husband/ partner despite the diagnosis. Forty-two percent reported a negative effect on the husband/partner, 13% reported a postive effect. Carriers' perception of the effect on their husband ranged from his appreciation at knowing early to anxiety and anger. Self-assessments of both carriers and husbands/partner showed the effects had mostly been negative orneutral.
Fanos and Johnson 1995b	To explore levels of understanding and feelings about carrier status and genetics of CF in affected families.	Mixed methods study. Qualitativeinterviews and questionnaire to measure anxiety and depression, and knowledge of CF.	Eighty four individuals interviewed including 54 adult CF siblings and 30 spouses. Of the 54 interviewed siblings, 45 five had been tested and nine had not at the time of the interview. Participants ranged in age from 18-55 years. Twenty-six were male siblings and 28 female siblings. They were recruited through the Genetics Division at Children's Hospital, Oakland, US.	Semi-structured, face to face interviews including: What was your reaction to the results? Were they what you had expected or different? Scales were developed for various categories capturing important aspects of family functioning and psychosocial adaptation. Questionnaires included anxiety and depression scales from Hopkins checklist.	Inter-rater reliability obtained for interview codes. Hypotheses analyze using X^2 procedure. Relationship between guilt and sibling resentment explored through a Pearson's correlation.	Fifty-three percent (53%) of CF siblings assumed they were carriers before testing and were neither upset nor surprised by positive results. Those with a negative result were relieved. For those that did not assume they were carriers, a positive result did not come as a shock as they knew there was a strong possibility they were. Identified carriers and non-carriers were equally likely to have moderate or severe anxiety around their child's health.
Gordon et al. 2003	An assessment of CF knowledge and emotional consequences of CF population testing 18 months after screening was offered. (results of initial screening and 3–6 month follow-up reported in Honnor et al. 2000)	Cross sectional study. Self completed postal questionnaire survey.	English speaking individuals aged 18–50 years who presented (for visits unrelated to pregnancy) to either Family Planning Clinic or one of 20 GP practices in Perth, Western Australia. Three hundred and fifty-three (59.5%) responded to questionnaire.	Eighteen months after testing follow-up questionnaires were sent to a consecutive sample. Questionnaire contained the HOS.	Significance level for t-test set at 0.001	Carriers felt more afraid, worse, weaker, less relieved, less happy, more marked, and angrier then test-negative individuals. However there was no difference on the guilty, ashamed, ability, activity and health scales. No difference was found between carriers and non-carriers relating to feeling guilty, ashamed, ability, activity and health scales. Carriers did not have a poorer perception of their current health than non-carriers. Carriers described more positive feelings about themselves when they considered their own result compared to feelings they attributed to most carriers—'unrealistic optimism'. Non-carriers tended to be slightly more negative about 'most carriers' than carriers.
Henneman et al. 2002	Impact, understanding of test-results and satisfaction among participating couples in a preconception CF carrier screening project.	Longitudinal survey. Self completed postal questionnaire at three time points.	Recruitment of individuals aged 20–35 years, through GP or Municipal Health Service between 1997–2000. Five hundred and fifty-nine couples gave written consent to CF testing after education. Testing was step-wise. Eighteen carriers identified. Partners tested negative. Response rate for completion of all three questionnaires was 17 carriers, 15 partners with negative test results and 794 other participants.	Three self-administered questionnaires at three Time points. Time One = before pretest education and counseling; Time Two = before receiving test results, Time Three = six months after receiving test results.	X^2 or Fisher exact tests. P Values of $p<0.05$ considered significant. Multiple logistical regression.	Carriers and partners reported no impact of the test results on their reproductive plans. One hundred and fifty-four (19%) felt worried when waiting for results; women worried more than men. Six months after results only eight felt wor ried, four of whom were carriers. Seven out of 17 carriers reported feeling less health due to test results. Ninety-eight percent (98%) perceived no impact on

Table 1 (continued)

Reference	Purpose of study	Study design	Sample and size	Data collection	Method of analysis	Results
						relationship with partner. The other 2% perceived a positive influence (improvement in communication, increased certainty in having children) All carriers and 95% of the other participants would have the test again. Ten carriersshared info with their brothers and sisters, all but one had told parents. Only two shared info with more distant relatives.
Honnor et al. 2000	Acceptance of carrier testing for CF in the community when offered in a primary care setting.	Longitudinal, self completed postal questionnaire survey at two time points (pre and post test)	Five thousand one hundred and two individuals age 18–50 years, recruited through 20 general practices and a family planning clinic in Western Australia completed questionnaire at Time One. Two thousand, two hundred and twenty (43.5%) took test, 69 carriers identified. Response rate at three to six month follow up was 58.4%.	Two questionnaires administered at two time points. Time One = before testing and both before and after receiving information about CF; Time Two = three to six months after receiving test results. STAI used to measure anxiety at both time points.	X^2 test used to compare proportions and odds rations (OR) and 95% confidence intervals (CI) were calculated using SPSS.	There were no significant differences between counseled and un-counseled carriers; carriers and test-negative individuals; or test-negative and untested individuals for State Anxiety Inventory scores.
James et al. 2006	A survey of family members with chronic granulomatous disease and Duchenne/Becker muscular dystrophy and spinal muscular atrophy types II/III	Cross sectional study. Self completed postal questionnaire survey.	Recruitment of 'adults' (no age range given) was through US registries, participants in other studies and patient organizations. Consisted of 112 members of 51 families (59% response) with granulomatous disease and 96 members of 51 families with Duchenne/Becker muscular dystrophy and spinal muscular atrophy types II/III.	Cross-sectional mail survey of adults with the conditions mentioned. Included Multiscore Depression Inventory and the HOS.	X^2 tests Two-tailed *t* test Mann-Whitney Logistic and linear regressions	Mothers carrying X linked conditions were more worried about risks to future generations than mothers carrying recessive conditions. X linked mothers were more likely to feel guilty (both currently and in the past) and blame themselves. X linked fathers blamed their child's mother and X linked mothers felt more blamed by fathers. There were no differences in level of guilt or self-blame between autosomal recessive mothers and fathers. X linked family-members were more likely to consider being a carrier stigmatizing.
Lakeman et al. 2008	To study outcomes, knowledge, recall and understanding of test results, satisfaction, and reproductive intentions among 97 Western and 46 non-Western partici pants undergoing pre-conceptual ancestry-based carrier couple screening for CF and hemoglobinopathies in the Netherlands.	Longitudinal, self completed postal questionnaire survey at four time points (before and after pre-test consultation, one week after and three months after receiving test results).	Screening offered to 9453 individuals (20–35 years) in Amsterdam from January-December 2005. Invitees who had a partner with whom they were planning a pregnancy were eligible for participation. It was estimated that 33% (3120) belonged to the 'target population' based on reply forms and telephone survey. Eighty-seven participated in testing, providing a total of 72 couples. Forty seven couples were eligible for CF screening only, six for HbP's only, and 19 for both disorders. CF carrier testing was carried out step-wise. For HbP's carrier testing, both partners were tested. Three CF carriers and seven HbP carriers were identified, but no carrier couples. One hundred and ten participants completed all four questionnaires.	Questionnaire at four time points (before and after pre-test consulta tion, one week after and three months after receiving test results). Questionnaire included six item STAI. reproductive intentions, and satisfaction.	Independent sample T-tests or ANOVA analysis were performed to compare the mean scores for the variables between groups at the same measurement moment. T-test(s) and General Linear Model-analysis for repeated measurements for longitudinal comparison. X^2 test for statistical comparison of proportions.	Participants reported low levels of anxiety at the start, which decreased further during the study. Carriers felt anxious one week after receiving test results and only one was still anxious at the three month follow-up. Seven out of ten carriers felt relieved one week after receiving test results. None of the partic ipants, including carriers, perceived themselves as being less healthy after receiving the test-results. Sixty-eight per cent felt relieved at Time Three, and 62% at Time Four. Four participants, including two carriers, were disappointed one week after receiving results at Time Three, but none were disappointed at Time Four (three month follow up). Four other respondents reported feelings of disappointment at Time Four, including two non carrier partners of CF carriers. Twenty-seven percent of participants stated they would have considered not having more children if found to be in a carrier couple, although majority reported

						no change. At three month follow-up, 93% of all participants including all carriers, states that the test results had not changed their ideas about having children. Western compared with non-Western participants generally reported lower levels of anxiety.
Marteau et al. 1992	A study to determine how carriers of a recessive gene for Tay-Sachs perceived their health related to non-carriers.	Cross sectional study. Self completed postal questionnaire survey.	Three groups screened for Tay-Sachs. One group recruited from cultural exhibition for Jewish community, another through the local synagogue, the third group included relatives (Jewish and non-Jewish) of previously affected children, and previously identified carriers as well as persons identified by routine screening. Twenty-seven carriers and 55 non-carriers responded to the questionnaire. Mean age=29 years (non-carriers) and 39.5 years (carriers).	Questionnaire including three questions from SF-36 Health Status Questionnaire and two questions developed for the study. Multiple choice questions.	X^2 test for statistical comparison of proportions.	No differences between the three groups in how they perceived their current health. Contrasting current health with health status two years previously showed no difference between the groups. Groups altered in their expectations about future health. Carriers of Tay-Sachs held the least optimistic view of their future health compared to the other two groups. Carriers were less optimistic about their risk of developing something wrong in the future.
McConkie-Rosell et al. 2001 (same cohort as McConkie-Rosell 2000)	A study of women at-risk to inherit the FX mutation.	Mixed methods, longitudinal study at two time points. Interview included open and closed questions.	Women all had 50% a priori risk of being a carrier. Study sample=42 Caucasian women (20 carriers and 22 noncarriers) from 17 families. Women aged 18+ years, mean age 42.3 years, 81% married and 71% had at least one child. All women had a family member diagnosed with the condition.	Questionnaire including Fragile X VAS developed by principle investigator and her colleagues, and structured interview with open and closed ended questions including: How do you feel about your carrier status?'	Analysis of variance. Mann Whitney U procedure. Two-tailed *t* test Open ended interview data analyzed using thematic analysis.	Being at risk was upsetting, frightening and scary. At Time Two non-carriers reported feeling happy, relieved, grateful. Relief related to no longer having to worry about their children or grandchildren's risk. Carriers said they were upset and concerned, mainly for their children, grandchildren or own reproduction. Fifty-five percent used active coping statements in discussing feelings about being a carrier. Possible 'survivor guilt' reported by one non-carrier. Significant difference between carrier and non-carrier at Time Two was result of changed perceptions of the non-carrier women. Women who were carriers were equally as upset learning their at-risk status as learning they were in fact carriers. Carriers said initially learning carrier status was upsetting. Carriers reported an improvement in level of upset at Time Two. At Time Two non-carriers viewed condition as more serious than at Time One.
McConkie-Rosell et al. 2000 (same cohort as McConkie-Rosell 2001)	A study to explore self-concept of women at risk for inheriting the FX mutation.	Mixed methods, longitudinal study at two time points (before testing and six months after). Interview included open and closed questions.	Women all had 50% a priori risk of being a carrier. Study sample=42 Caucasian women (20 carriers and 22 non-carriers) from 17 families. Women 18 years +, mean age 42.3 yrs, 81% married and 71% had at least one child. All women had a family member diagnosed with the condition.	Questionnaire Including Tennessee Self-Concept Scale, Fragile X VAS. Structured interview consisting of 50 questions including: Has finding out your carrier status changed the way you view yourself?	Analysis of variance. Mann Whitney U procedure. Two-tailed *t* test Open ended interview data analyzed using thematic analysis.	No evidence of diminished social self related to at-risk status or to actual carrier status at Times One and Two on Tennessee Self-Concept Scale. Fifty nine percent of the non-carriers reported feeling better after five months using the Fragile X Visual Analog Scale. There was no evidence that being at risk or being a carrier altered perception of health. Some anecdotal evidence to suggest that carriers at Time Two believed they had mild clinical features of FX. Carriers did not report feeling worse about themselves than they had reported at Time One. The difference between carriers and non-carriers at Time Two occurred because non-carriers felt better about themselves and not because the carriers felt worse.

Table 1 (continued)

Reference	Purpose of study	Study design	Sample and size	Data collection	Method of analysis	Results
McConkie-Rosell et al. 1997	A study of obligate carriers of the FX syndrome to ascertain opinions and attitudes regarding carrier testing.	Mixed methods study using 48 question structured interview.	Twenty-eight female carriers were recruited through the Fragile X Clinic at Duke University Medical Centre. All women had undergone genetic counseling and all knew they were carriers. Twenty-five premutation carriers, three full mutation carriers, mean age 41.8 years, mean number of children 2.28, mean number of years since diagnosis=5.9 years.	Structured interview with open and closed ended (multiple choice) questions at one time point. Questions were asked regarding family planning issues, how relatives should be told of genetic risk, and marital and family relationships. Also included an 11 item VAS.	Descriptive univariant analysis. Fisher's Exact test in the case of 2x2 frequency tables or Students t-test for differences between means.	Sixty-seven percent felt knowing about the condition had changed their plans about having more children. Eighty-nine percent felt that if they had known earlier they would have either reduced the size of their family or not have had any biological children. Eighty-two percent said they would have used prenatal diagnosis. Seventy-six percent said learning they were carriers had changed the way they viewed themselves; 53% in a positive way, 47% in a negative way. Subjects reported that over time there was a lessening in the intensity of the negative feelings associated with first learning carrier status. Eighty-seven percent indicated they did not feel guilty, however were sometimes angry or depressed and would change their carrier status if they could. Sixty-four percent noted a change in relationship with the partner; 72% a positive change, 27% a negative change. Sixty percent reported improvement in relationships with siblings.
Newman et al. 2002 (same cohort as Cheuvront 1998)	To assess how gender as well as carrier testing arrangements (home and clinic based) affected testing experience.	Randomized controlled trial comparing home education and testing with clinic education and testing.	Two hundred and ninety-nine accepted offer of free education and testing, aged 18+ (majority between 26–45 yrs). Participants were relatives of people with CF living in N. Carolina. Participants randomly assigned into two groups; those assigned to the clinic (91) and those assigned to education and testing at home (208).	Participants completed a baseline telephone interview, and completed a questionnaire at two time points: while waiting for their test results and immediately after learning their test results.	All reported regression analysis were conducted using SUDAAN software for clustered samples.	Women reported higher anxiety than men on the STAI administered at baseline but not at follow-up. Men tended to describe themselves with more positive adjectives than women while waiting for test results.
Pastore et al. 2008	A study assessing female FX premutation carriers.	Longitudinal, self completed postal questionnaire survey at two time points.	Female participants who had been diagnosed with diminished ovarian reserve aged 18–42 years and infertile. Women with a family history of FX were excluded. Twenty women completed questionnaire at baseline and 17 who were non-carriers and one carrier completed the questionnaire at three months.	Self administered questionnaires at baseline and three months after learning test results.	Exact Mann-Whitney U. Health Orientation Scale. McNemar tests.	Perception of the seriousness of FX premutations increased three months after learning they were not a carrier but this did not reach statistical significance. Non-carriers thought carriers would be more angry and regretful than they felt themselves three months after testing. Self esteem of non-carriers was essentially unchanged three months after learning they were not carriers.
Watson et al. 1992	A study assessing the effect of screening for CF carrier status on anxiety levels, attitudes, knowledge and actions of participants.	Longitudinal, self completed postal questionnaire at three time points.	Participants (men and women age 16–44) recruited through primary health care services. Three thousand one hundred and seventy-six individuals were screened identifying 100 carriers with no known history of CF. Eighty-eight carriers responded to questionnaire at Time Two. Sixty carriers responded to questionnaire at Time Three. Fifty one carriers (85%) have responded at Time Two and Three.	Self administered questionnaires. STAI used to measure anxiety. Time One = pre-test. Time Two = two weeks after results. Time Three = non-carriers after three months, carriers after six months.	Descriptive statistics were calculated.	Eighty-one percent of carriers said they were glad they had been tested. Carriers expressed being surprised (67%) at first, 25% said they were slightly anxious. Provision of written information and genetic counseling helpful (92% and 97% respectively). Twenty-two percent were worried (some still waiting for results of partner). At six months, 70% reported no anxiety or depression. Those not planning further children were either 'not worried' or 'indifferent' about their results. Eighty-nine percent of carriers told result to

						partner, 83% to parents, 82% to siblings, 48% to other relatives and 63% to friends. If found to be in an 'at risk' partnership 33% would consider not having children, 42% were unsure. Seventy-eight percent would request prenatal diagnosis. Thirty-six percent would consider termination.
Williams et al. 1997	A study examining experiences (emotional and social consequences) of adults requesting carrier testing for four autosomal recessive and X linked disorders.	Qualitative study. Interviews conducted at one time point.	Thirty-four adults recruited from a genetic counseling clinic. People requesting carrier testing for CF, TS, DMD, or FX from 1993 to 1996 were informed of study by genetic nurses and counselors. Ages of participants ranged from 18–71 years, the mean age was 32. Seventy-six percent were women.	Semi-structured interviews (17 face to face, 17 telephone) one month after learning test results. Questions included: Tell me about how your carrier testing turned out, positive and negative aspects of knowing their carrier status and to whom they disclosed test results.	Interviews transcribed, reviewed and coded. Each rater's codes were compared, and analysis continued until there was agreement on data codes. Codes then collapsed into more general categories.	Non-carriers experienced the freedom to look ahead regarding their own reproduction as well as relief from fear regarding the welfare of future generations. Carriers experienced loss of hope to have children or grandchildren who would be free of the condition. Most participants shared results with some members of their families, although members of both groups experienced some difficulties regarding disclosure of results to family members (e.g. non-carriers to relatives who had affected children) and expressed uncertainty regarding disclosure to insurance providers. Many participants who expressed feelings of grief and guilt were women who were carriers of FX or DMD.

CF cystic fibrosis, *DMD* Duchenne muscular dystrophy, *FX* fragile X, *HbP* hemoglobinopathies, *TS* Tay Sachs, *Fragile X VAS* Fragile X Visual Analog Scale, *HOS* Health Orientation Scale, *PANAS* Positive and Negative Affect Scale, *STAI* Spielberger Stait-Trait Anxiety Inventory

should be discarded on the grounds of poor quality). The studies included in the review had notable strengths. Validated questionnaires were used in many of the studies [e.g., Honnor et al. (2000)]. The use of a longitudinal study design enabled changes in psychosocial wellbeing to be measured over time [e.g., Lakeman et al. (2008)], and the use of in-depth qualitative interviews enabled rich and complex data to be acquired by the researchers [e.g., Anido et al. (2007)]. There were a number of study limitations that should be considered when interpreting the findings from these research studies. First, potential confounding variables, such as whether participants had completed their families at the time of testing (e.g., Bekker et al. 1994) or whether they knew anyone with the condition for which they were a carrier (e.g., Watson et al. 1992) were not addressed by some of the authors. In addition, authors of many studies did not justify their sample size (e.g., Pastore et al. 2008) while some studies lacked clear conceptual definitions and were not based on particular theoretical models (e.g., Henneman et al. 2002).

Data Synthesis

To enable comparison across the studies, a matrix (Miles and Huberman 1994) of studies was drawn up including aspects of each relevant study considered to be most important (study design, sample and size, methods, quality issues and findings related to the psychosocial impact of carrier testing). This matrix is summarized and displayed as Table 1. Due to the range of different quantitative measures and quantitative philosophical approaches used, a meta-analysis was not performed. Instead we used an approach based on Grounded Theory (Strauss and Corbin 1998), inductively deriving codes and themes from the data. We undertook a thematic analysis to elicit general overarching themes from the papers studied. The findings were discussed by the present authors and compared to identify areas of agreement and disagreement across studies; this resulted in a set of overarching themes. These themes were labeled using the terminology commonly contained in many of the studies, such as guilt, anxiety and stigmatization. Once this process was complete, a "spider diagram" or "mind map" (Burgess-Allen and Owen-Smith 2010) was drawn so that the key themes could be visualized and the relationships between them identified (Fig. 1). Finally, after reviewing the studies, we compared our results with well established psychological models relating to self concept (Shavelson et al. 1976) and coping (Lazarus and Folkman 1984). These two models have been used in other health-related studies looking at psychosocial adaptation (McConkie-Rosell et al. 2000; Street et al. 2010).

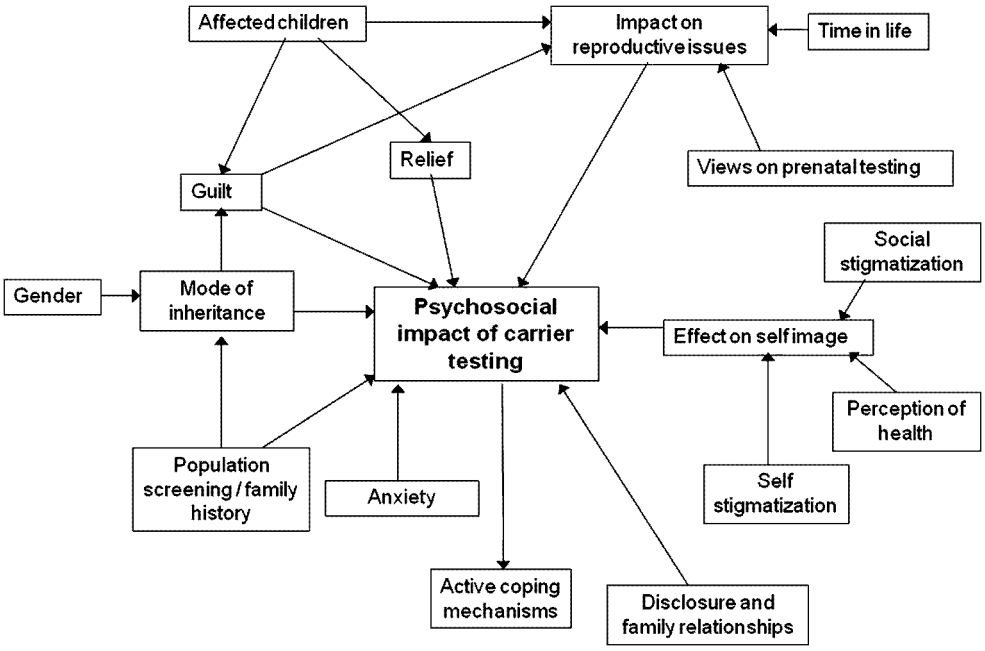

Fig. 1 Mindmap showing relationship between key themes

Results

The impact of carrier testing for cystic fibrosis was the condition most commonly investigated, with ten studies focusing on this condition, followed by carrier testing for fragile X (five studies), Tay Sachs (one study) and hemophilia A and B (one study). The focus of the remaining three studies was the effects of carrier testing for a number of conditions. No studies which assessed the impact of carrier testing on carriers of chromosomal abnormalities were identified from the literature review. Carrier testing for people who had a family history of a genetic condition (and were therefore at an increased risk) was assessed in 11 studies, risk in the general population was assessed in seven studies, and in two studies people in both groups were assessed. Only three of the studies included in the systematic review were intervention studies (Callanan et al. 1999; Cheuvront et al. 1998; Newman et al. 2002). All three compared levels of anxiety related to home education and testing with clinic education and testing. A number of overarching themes were identified. The most prominent were anxiety, guilt, relief, effect on self image, active coping mechanisms, impact on reproductive issues and disclosure of test results (Table 2).

Anxiety

Two categories of anxiety emerged; one related to testing and the other related to child health. In relation to testing, all longitudinal studies investigating patient anxiety over time either found no significant difference in anxiety between carriers and non carriers (Honnor et al. 2000), or found that any anxiety experienced by carriers upon first receiving their test result had, for the vast majority, dissipated by six months as assessed by the state STAI (Bekker et al. 1994; Callanan et al. 1999; Cheuvront et al. 1998; Lakeman et al. 2008; Watson et al. 1992), the Fragile X Visual Analog Scale (VAS) (McConkie-Rosell et al. 2001), or qualitative interviews (Anido et al. 2007; Anido et al. 2005).

Carrier anxiety dissipated for a number of reasons. Watson et al. (1992) found that the provision of written information and genetic counseling was helpful for most participants (92% and 97%, respectively). Bekker et al. (1994) found that the passage of time appeared to dissipate anxiety. Gender was also an issue discussed in relation to anxiety, in a number of studies. Newman et al. (2002) and Henneman et al. (2002) found that women reported higher anxiety than men while waiting for their test results (mean= 16.5 and 14.6, respectively on the STAI in the Newman study, $p<0.001$; and 24% versus 13%, $p<0.001$ measured on a five-point Likert scale in the Henneman study); however there was no significant difference between the genders once the test results had been received. Lakeman et al. (2008) found that Western participants generally reported lower levels of anxiety compared with non-Western participants (General Linear Model analysis at 4 time points, $p<0.001$).

Anxiety did however appear to be an issue for both carrier and non-carrier siblings of people with cystic fibrosis, in the interview-based study conducted by Fanos and Johnson (1995b). Identified carriers and non-carriers were equally likely to have moderate or severe anxiety around their child's health. Forty-one percent had had their

Table 2 Themes by mode of inheritance

	Autosomal recessive		X linked	
	Family history	Population	Family history	Population
Anxiety dissipated by 6 months	Callanan 1999 Cheuvront 1998 Newman 2002	Bekker 1994; Henneman 2002; Honnor 2000; Lakeman 2008; Watson 1992	Anido 2005[a]; McConkie-Rosell 2001	Anido 2007
Guilt	Williams 1997[a]		Anido 2005[a]; Dunn 2008[a]; James 2006[a]; McConkie-Rosell 1997[a]; Williams 1997[a]	
Altered perception of health	Fanos 1995; Marteau 1992[a]	Bekker 1994; Henneman 2002; Marteau 1992	McConkie-Rosell 2000	
Evidence of self-stigmatisation		Gordon 2003	James 2006[a]; McConkie-Rosell 2000; McConkie-Rosell 1997[a]	
Evidence of social-stigmatisation		Gordon 2003	McConkie-Rosell 2001	
Use of active coping mechanisms			Anido 2005[a]; McConkie-Rosell 2001	Anido 2007
Impact on reproductive plans			Anido 2005[a]; Dunn 2008[a]; McConkie-Rosell 1997[a]	Dunn 2008[a]
No impact on reproductive plans	Callanan 1999	Henneman 2002; Watson 1992; Lakeman2008		Anido 2007
Disclosure of test results to family	Williams 1997[a]	Henneman 2002; Watson 1992	McConkie-Rosell 1997[a]; Williams 1997[a]	Anido 2007

Family History—Participants with a family history of the condition

Population—Participants identified from the general population

[a] Cohort included participants with affected children

children sweat-tested to rule out the condition, nine percent had had their child tested for carrier status, and 55% planned to do so before their child reached 18 years of age. Siblings who had had their children sweat-tested or tested for carrier status were equally divided between those who knew their own carrier status and those who did not.

Guilt

Guilt was a prominent theme in the data. Feelings of guilt associated with carrier status were cited as findings in five studies. These results were identified through interviews (Anido et al. 2005; McConkie-Rosell et al. 1997; Williams and Schutte 1997), an open-ended questionnaire (Dunn et al. 2008), a VAS (James et al. 2006; McConkie-Rosell et al. 1997) and the guilt subscale of the Multiscore Depression Inventory (sMDI) (James et al. 2006). Guilt is also an issue found to be closely associated with gender, mode of inheritance, and whether the participants had affected children. In the study conducted by Dunn et al. (2008) in which 81% of respondents had a son with hemophilia, 18 of 48 (38%) female carriers reported the timing of testing as negative. Reasons cited for the timing being negative included feeling blamed by their partner and a prolonged sense of guilt. James et al. (2006) found that mothers who were carriers of X-linked conditions felt substantial guilt and self-blame related to their child's condition. When measured on the VAS, mothers of children with X linked conditions had significantly higher levels of guilt than mothers of children with recessive conditions ($p<0.01$) and were more likely to blame themselves ($p<0.001$). A similar finding was identified in the Williams and Schutte study, in which it was found that many of the participants who expressed feelings of grief and guilt were women who were carriers of fragile X or Duchenne muscular dystrophy. Anido et al. (2005) also found that in families affected by fragile X, even those women without affected children experienced guilt to some extent, by virtue of the condition being in the family.

In one study (Gordon et al. 2003) there was no significant difference evident between carriers and non-carriers on the "guilt" scale (as measured by the HOS). The participants were from the general population, were

screened for cystic fibrosis, and did not have a family history of the condition.

Relief

Anido et al. (2005), McConkie-Rosell et al. (1997) and Lakeman et al. (2008) all identified that relief was an emotion experienced by carriers. In the study conducted by Anido et al. reactions of relief were expressed equally as strongly as reactions of guilt, with nearly all carriers expressing this emotion during interviews. For these individuals, finding out their carrier status was an inevitable result of finding a diagnosis for their child. Similarly, in the study by McConkie-Rosell et al. (1997), participants' responses indicated that while they felt angry or depressed about their carrier status, there was an "emotional relief in finding out the cause of the mental retardation in the family" (p. 65). Lakeman et al. (2008) found that 68% of participants, including seven out of ten carriers, felt relief one week after receiving their test results, as measured on a structured questionnaire assessing emotional outcomes.

Effect on Self-image

Three main issues arose within this theme: perception of health, self-stigmatization and social-stigmatization.

Perception of Health

Of the seven studies in which perception of health was measured, findings from three studies indicate that some carriers believed their current or future health to be significantly poorer after learning their carrier status (Fanos and Johnson 1995b; Henneman et al. 2002; Marteau et al. 1992). Seven out of 17 carriers (41%) in the study conducted by Henneman et al. (2002) felt less healthy (measured on a multiple-choice questionnaire) due to their test results, despite being informed both verbally and by letter that their carrier status would have no effect on their own health. Marteau et al. (1992), also using a multiple-choice questionnaire which measured perceived health from three time perspectives, identified that carriers of Tay Sachs held the least optimistic view of future health compared with non-carriers and the control group ($p<0.01$) and Fanos and Johnson (1995b) reported that during interviews, sibling carriers retrospectively redefined health problems as related to cystic fibrosis, although the authors do not report report how many.

Authors of four studies found that perception of health did not alter after learning one's carrier status, using measures such as the Tennessee Self Concept Scale (McConkie-Rosell et al. 2000), a multiple choice questionnaire (Bekker et al. 1994), the HOS (Gordon et al. 2003) and a five point Likert-scale (Lakeman et al. 2008). However, both McConkie-Rosell et al. and Bekker et al. do provide some anecdotal evidence to suggest that carriers might attribute previous health problems to their carrier status. McConkie-Rosell et al. found that 12% of participants at Time 1 and 20% of carriers at Time 2 reported feeling they had mild clinical features of fragile X. They felt that perhaps if they were carriers it would explain why they had to *"study hard in school"* (p. 340). A participant in the Bekker et al. cohort wondered whether her allergies and chest colds were in some way linked to her carrier status. Therefore, even though perception of health did not alter when measured quantitatively, during qualitative interviews there were some indications that it did in fact occur in a small number of cases. In fact, in the case of fragile X, it is possible that carriers did experience a mild manifestation of the disease due to skewed X-inactivation (Skirton et al. 2005). Furthermore, this finding may also be attributable to the repeat length itself which appears to be associated with toxicity due to elevated mRNA levels (Koldewyn et al. 2008).

Self-stigmatization

There is evidence from four studies to indicate that self-stigmatization occurred in carriers to some extent (Gordon et al. 2003; James et al. 2006; McConkie-Rosell et al. 1997, 2000). Gordon et al. identified that carriers experienced less positive feelings; more afraid, worse, weaker, less relieved, less happy, more marked (although the authors do not explain what is meant by this) and angrier, compared to those who tested negative, on the HOS. Similarly, James et al. found that carrier status is associated with stigma and is significantly associated with mode of inheritance using the same scale. The only other study (Pastore et al. 2008) specifically looking at stigma using the HOS consisted of just one carrier, and therefore findings were not significant. Stigma was also evident in two of the qualitative studies. Just under half (9/19) of the fragile X carriers in one study (McConkie-Rosell et al. 1997) indicated that there had been a negative change in the way that they viewed themselves. One reason cited for this change was a "feeling of being abnormal or inferior" (p. 64), a statement indicative of self-stigmatization.

Social Stigmatization

Evidence of social stigmatization was evident in two studies, one quantitative (Gordon et al. 2003) and one mixed methods (McConkie-Rosell et al. 2001). Gordon et al. found that carriers and non-carriers attributed significantly more negative feelings to cystic fibrosis carrier status than non-carrier status. This finding was significant for all emotional scales on the HOS ($p<0.001$).

Active Coping Mechanisms

Use of active coping mechanisms was identified in five studies, out of a possible seven studies in which qualitative research techniques were employed. These studies included participants from the general population without affected children (Anido et al. 2007) and participants with a family history (Anido et al. 2005; McConkie-Rosell et al. 1997, 2000, 2001). McConkie-Rosell et al. (2001) found no change in the level of distress or perceived seriousness of fragile X when women were "at risk" of being a carrier as when they were found to be carriers. The increase in perception of seriousness only occurred in the non-carriers when the threat was no longer present. This possibly indicates that "threat minimization" was used by the participants as an active coping mechanism in both situations. McConkie-Rosell et al. (2001) also found, during in-depth interviews, that 11 out of 20 (55%) carrier women used spontaneous coping statements such as "life goes on" (p.41) and "If I am, I am. I'll deal with it" (p.41). Coping behavior statements were also evident during interviews in the study conducted by Anido et al. (2007).

For carriers identified in the study by Anido et al. (2007), most appeared to be considering their carrier status over the course of the interview, having not given the subject much thought previously. The authors postulated that this attitude is consistent with the coping mechanism known as "just-in-time" learning, as described in Adult Learning Theory (Wlodkowski 1999), wherein adult learners process information which is relevant and applicable to them at the time they need it.

Impact on Reproductive Issues

The impact of carrier status on participants' views on reproductive issues varied depending on their life stage, their views on prenatal testing and abortion, whether their partners were also carriers, and whether they were carriers of an X-linked or recessive condition. Authors of four studies (Callanan et al. 1999; Henneman et al. 2002; Lakeman et al. 2008; Watson et al. 1992) of cystic fibrosis carriers identified from both high risk groups and the general population who did not have affected children, all reported that the majority of carriers showed no change in reproductive plans after testing, as measured on questionnaires which included multiple-choice options (Callanan et al. 1999; Watson et al. 1992) or a five point Likert-scale (Henneman et al. 2002; Lakeman et al. 2008). Reasons given included the availability of prenatal diagnosis (Henneman et al. 2002; Lakeman et al. 2008; Watson et al. 1992) and having completed their families (Watson et al. 1992). Furthermore, in two of the studies (Cheuvront et al. 1998; Henneman et al. 2002), only carrier by non-carrier couples were included. If one partner tests positive and the other negative, the risk of having a child with CF is about 1 in 640 (Watson et al. 1992).

However, in two interview-based studies, females carrying X-linked mutations, many of whom were mothers of affected children, were more likely to indicate their carrier status had caused a change to their reproductive plans (Anido et al. 2005; McConkie-Rosell et al. 1997). In the study conducted by McConkie-Rosell et al. (1997) 19 out of 28 (67%) fragile X carriers stated that they would not have any more children because of their carrier status, and 25 out of 28 (89%) would have either reduced the size of their families or not had any biological children, if they had known earlier. Anido et al. (2005) also found through in-depth interviews that many women with fragile X children stopped planning to have more children after receiving their test results. Furthermore, those without affected children expressed a strong desire *"to figure out a way to end it with me"* (p. 301). Dunn et al. (2008) also reported findings from open-ended questions that revealed some respondents felt they might not have had as many children if they had known their carrier status earlier.

Findings differed however, in the study conducted on fragile X carriers identified from the general population (Anido et al. 2007). Many carriers expressed that although the information could be relevant in the future, it was not relevant at this stage of their lives in terms of family planning. Some had not really considered the implications for family planning and their thoughts about prenatal testing, but for those that had, carrier status did not have an apparent effect on their attitudes about termination. The issue of premature ovarian failure appeared to be more prominent than the risk of having children affected with fragile X.

Disclosure of Test Results and Family Relationships

In six studies in which disclosure of test results was assessed, the researchers found that participants did share their test results with others, although this disclosure was selective (Anido et al. 2007; Dunn et al. 2008; Henneman et al. 2002; McConkie-Rosell et al. 1997; Watson et al. 1992; Williams and Schutte 1997). Anido et al. (2007) found that providing information to partners primarily depended on the seriousness of the relationship. Watson et al. (1992) found that 89% (47/53) of CF carriers informed their partners of their test results, 83% told their parents, 82% their siblings and 48% told other relatives. Henneman et al. (2002) reported that most CF carriers shared the information with parents and siblings. All but one of the carriers whose parents were still alive had told them about their test results. Ten carriers had shared the information

with their brothers and sisters, but two had not. With respect to participants who did not disclose carrier information to other family members, their reasons included not wanting to disclose results to relatives who had affected siblings, and not wanting to cause feelings of guilt (Williams and Schutte 1997).

The effects of sharing information about one's carrier status with a partner and/or family members varied across the studies. Positive experiences related to disclosure of test results were documented by Dunn et al. (2008) and McConkie-Rosell et al. (1997). Of the 18 carriers who indicated in a change in their relationship with their husband in the McConkie-Rosell et al. (1997) study, 13 carriers (72%) indicated this change had been positive. Seventeen (61%) felt that there had been an improvement in their relationship with their siblings. Difficult or distressing experiences were highlighted in three studies (Dunn et al. 2008; McConkie-Rosell et al. 1997; Williams and Schutte 1997). Dunn et al. and McConkie-Rosell et al. identified a negative effect on the relationship with the partner in 13/31 (42%) and 5/18 (27%) of cases, respectively. Reasons cited included anxiety and anger from the male partner (Dunn et al.) and feeling blamed by their spouse (McConkie-Rosell et al.). In cases where the experience had a positive effect on the relationship (in 4/31 and 13/18 of cases respectively), the carrier felt completely accepted by her partner (Dunn et al. 2008) and there was an increase in understanding and communication. Henneman et al. (2002) found the majority of participants (98%) perceived no impact of carrier testing results on the relationship with their partner. For the majority of participants in the Anido et al. (2007) study, providing information about fragile X carrier status to family members was not problematic. However, providing the information to partners depended on the seriousness of the current relationship.

Discussion and Conclusion

Discussion

This review is useful in that it identifies a number of factors that seem to influence the emotional consequences of carrier testing. These include population group, whether the carrier has an affected child, stage of life, psychological coping mechanisms, and mode of inheritance. In this respect the results of this systematic review provide some interesting insights into how genetic testing for different conditions may have a varying psychological impact that is dependent on the context in which testing occurs.

Anxiety, an emotion frequently measured in studies investigating the impact of carrier testing on individuals, dissipated in the long term for the majority of participants in all studies. In addition, the reasons suggested by authors, another reason may have been because none of the participants were pregnant at the time of receiving their carrier test results and were therefore not anxious about the possibility that the fetus was affected. For carriers, knowledge that reproductive options were available to them if there was a risk of having an affected child may also have overridden any initial anxiety. Furthermore, good quality genetic counseling services may have lessened the impact of the test results.

Variables including mode of inheritance, gender and whether the carrier already had a child affected by the condition appear to be strongly linked to the issue of guilt. The finding that guilt was more dominant in women than men, indicates that it may be strongly connected with what Peters and Jackson (2009) describe as a unique emotion concerning a mother's relationship with her affected child. Guilt also appeared to be more commonly reported by mothers of children with X-linked conditions. One possible explanation lies in the close association of guilt and blame. In the case of X-linked conditions, it only takes a carrier mother to pass along an X-linked condition rather than having both parents contribute the "faulty" gene. Therefore the burden of having passed on a faulty gene cannot be shared with a partner. In these cases men may "externalize their emotional response to devastating news and blame, while women are likely to internalize their responses and to accept this blame" (James et al. 2006). Mothers are also more likely to self blame (Peters and Jackson 2009).

Guilt may also be an emotion linked to family history. Anido et al. (2005) found that women who did not have affected children but had the condition in the family, expressed feelings of guilt, which may indicate a form of "survivor guilt." Survivor guilt has also been identified in CF families. In a study (which was excluded from this review as it contained women who were pregnant at the time of testing) in which barriers to carrier testing for adult cystic fibrosis siblings were identified, carrier status served an important function in binding guilt, with 15% of siblings either hoping they were carriers or feeling guilty they were not (Fanos and Johnson 1995a).

There are conflicting results in the literature regarding the issue of perceptions of health. Yet even those studies in which carriers did not indicate feeling less healthy on surveys or questionnaires, during in-depth interviews, some participants reported clinical features of the disorder for which they were being tested or for which they were found to be a carrier. In the case of fragile X, it is possible that carriers did experience a mild manifestation of the disease due to skewed X-inactivation (Skirton et al. 2005). Furthermore, this finding may also be attributable to the repeat length itself which appears to be associated with

toxicity due to elevated mRNA levels (Koldewyn et al. 2008). However this finding also suggests that participants may have been seeking support for beliefs they held about themselves.

In interpreting this finding, McConkie-Rosell et al. (2000) refer to the theory of self-concept as described by Shavelson et al. (1976). Shavelson et al. hypothesize that self-concept is hierarchical, with perception of personal behavior in specific situations at the base of the hierarchy, inferences about the self in broader domains (e.g., social, physical) at the middle, and a global, general self-concept at the apex. Global self-concept is stable, but as one descends the hierarchy self-concept becomes increasingly situation specific and less stable. Seeking clinical features related to actual or possible carrier status might be indicative of situation-specific changes in feelings about self. Additionally, it may be the case that scales such as the HOS (used by Gordon et al. 2003) and TSCS (used by McConkie-Rosell et al. 2000) are not sensitive enough to detect the subtleties concerning how carriers perceive their own health, which are more likely to be expressed during in-depth interviews.

Reproductive intent also appeared to be closely linked to mode of inheritance, stage of life and whether the participant already had an affected child, with the greatest impact being identified for carriers of X-linked conditions with affected children. This group was most likely to refrain from having more children. One possible reason involves the documented psychological difficulties of raising a child with fragile X (Abbeduto et al. 2004; Lewis et al. 2006). When Anido et al. (2007) interviewed fragile X carriers who did not have affected children and were from the general population, the information did not appear to have an impact on family planning with many not having considered the issue. This is likely to be because they did not have any experience, either themselves or through other family members, of raising a child with the condition. It may be that these carriers would experience increased distress as they consider reproduction more seriously. Similarly, carriers of cystic fibrosis in the general population did not change their reproductive plans as a result of their carrier status. Participants in these studies did not have affected children, and even as a carrier, there would only be a risk to future children if the partner was also a carrier.

Active coping mechanisms, such as "threat minimization," significant changes to reproductive intentions and the use of active coping statements, were identified in those participants at an increased risk of carrying the fragile X gene. Lazarus and Folkman (1984) describe coping as consisting of two different strategies, problem-focused coping and emotional-focused coping. The findings from this systematic review suggest that women at high risk of being a carrier of fragile X engaged in problem-focused coping by managing their health threat through genetic testing, and if found to be carriers, by changing their reproductive intentions. They engaged in emotional-focused coping through threat minimization and active coping statements.

In addition to these coping strategies aimed at lessening distress, Lazarus and Folkman describe a smaller group of cognitive strategies directed at increasing distress. For some individuals, there is a need to feel worse before they can feel better. Self-blame, a coping mechanism found to be used by carriers of X-linked conditions, is one such form of self-punishment individuals may use. This deliberate emotional distress may mobilize individuals into action. Evidence that women use self-blame as a coping strategy has been identified in other studies; for example, self-blame was found to be significantly correlated with both problem-focused and emotional-focused coping strategies in a study of patients with diabetes (Tuncay et al. 2008). Self-blame was also used as a strategy to cope with depression in a study of how primary care patients manage their illness (Brown et al. 2007).

Other studies, in which participants became aware of their carrier status through family history or newborn screening, have identified similar psychosocial issues to those in this review. Fanos and Mackintosh (1999) recognized a number of coping mechanisms used by parents of children with ataxia-telangiectasia, including rationalizing their child's condition as a "statistical quirk" (p.417), and imbuing the occurrence with meaning and significance through connecting it with the wider sphere of human suffering or to the spiritual world. Guilt was not however a common finding in their study, and surprisingly when it was mentioned, it was in reference to fathers. Undue concerns about the health of carriers was also identified in a minority of parents in a study assessing the impact of carrier status information following newborn screening (Kai et al. 2009), as was a sense of responsibility to share carrier status information with extended families. Stigmatization was also evident in a study which included participants from high risk CF families who did not want to learn their carrier status (Fanos and Johnson 1995a). For example, one untested woman was worried that she would be "less desirable" (p. 88) to men if they knew she was a carrier.

While this review provides an overview of the psychosocial experience of living as a carrier, it is important to keep in mind the limitations of making comparisons across different conditions, in particular cystic fibrosis and fragile X (the major conditions included in this review). These two conditions vary greatly in terms of their effects on the affected individual, the implications for the health of the carrier, and risk of the carrier having an affected child. Furthermore, variations in study design, the different population subsets compared, and the obvious complexities

of comparing qualitative and quantitative data, mean that the findings should be interpreted with some degree of caution. For example, there were indications from some studies using validated scales of no changes in perception of health. However, when the authors used in-depth interviews, changes in health perception were evident (Bekker et al. 1994; McConkie-Rosell et al. 2000). Some authors used the STAI to measure anxiety, whereas others using qualitative methods relied on participants' own terminology. Studies using the HOS were much more likely to identify evidence of stigmatization that those that did not use this scale, as this scale specifically measures aspects of self image. Future systematic reviews may therefore benefit from the inclusion of samples involving population groups which are more similar in kind in terms of risk to offspring, severity of the condition or family history. Future research studies may be better summarized if the studies focus on using similar groups of patients and validated tools.

Yet this does not necessarily mean the findings of the present review fail to provide valuable insight into the psychosocial experience of living as a carrier. In particular, the review provides an overview of the commonality of experiences across conditions with different inheritance patterns. Furthermore the overview identifies a number of issues that collectively apply to carriers as a group, because of the familial nature of genetics.

Strengths and Limitations

As stated previously, findings from the review should be considered in light of the difficulties and limitations of combining studies undertaken with different study designs, subsets of the population, measures and outcomes. These factors may have diluted the strength of the comparisons. Furthermore, many of the studies lacked theoretical models or presentation of a conceptual model to help place the variables and their possible interactions in context (Henneman et al. 2002; Pastore et al. 2008; Watson et al. 1992). Such omissions possibly weaken the validity of the results. Nevertheless, in the present systematic thematic analysis, the findings were able to be explained within established theoretical models of coping and self-concept (Lazarus and Folkman 1984; Shavelson et al. 1976).

The systematic review does have notable strengths. Seven databases were used to retrieve studies to maximize the chance of finding all relevant research. In addition, several iterations of the search were conducted using different combinations of keywords, to ensure the search was rigorous. At the present time there does not appear to be another systematic review in the literature that compares the psychosocial experience of carrier testing for autosomal recessive and X linked conditions; thus, this review provides unique and useful information.

Conclusion

The findings from this systematic review provide insight into the variety of psychosocial emotions experienced by individuals undergoing carrier testing and a general overview of the psychosocial impact of living as a carrier. Prominent themes that occur in the literature include anxiety, guilt, relief, effect on self image, active coping mechanisms, impact on reproductive issues and disclosure of test results. Variables that influence the psychosocial effects of carrier testing include whether the carrier has an affected child, mode of inheritance, genetic counseling and life stage. A key finding concerns the different emotions experienced by carriers who already had an affected child compared with carriers who did not. Studies indicated that carriers with affected children were more likely to experience guilt and self-blame. Furthermore, fragile X carriers with affected children were more likely to indicate that carrier status had affected their reproductive plans. In contrast, carriers identified from the general population did not change their reproductive plans as a result of their carrier status. Due to the commonality of experiences identified through this systematic review, it would appear that we can make certain assumptions about the psychosocial impact of living as a carrier. Yet at the same time it is important to bear in mind the limitations of making generalizations across different population groups and condition types.

Practical implications

Genetic counselors and other health professionals offering genetic testing should pay attention to the variety and complexity of psychosocial experiences that may be encountered by individuals undergoing carrier testing. One key finding from this systematic review is that carriers who already have an affected child often react differently when receiving their test results than carriers who do not. For those carriers who already have an affected child, the impact of receiving the test results in these cases may reinforce feelings of guilt, self-blame and maternal blame in the case of X linked conditions. Counselors therefore need to be aware of these issues when testing parents of affected children as these psychological issues may need to be addressed both before and after testing. In addition, counselors should look to address misconceptions related to health and carrier status; some individuals may seek support for beliefs they have about their health by identifying clinical features of the disorder for which they are being tested or are found to be a carrier. Furthermore, while some clients will effectively manage anxiety and their carrier status through threat minimization and other active coping mechanisms, professionals should ensure that those who appear to be managing well do not

minimize their threat to the extent that they disengage from protective health actions, particularly when it comes to reproductive issues.

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