AUTISM GENETIC TESTING: PSYCHOLOGICAL FACTORS ASSOCIATED WITH THE TEST DECISIONS AMONG PARENTS OF CHILDREN WITH AUTISM SPECTRUM DISORDERS (ASDs) IN TAIWAN

A Dissertation

by

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ABSTRACT

Autism spectrum disorders (ASDs) are a group of highly inheritable disorders. Genetic testing for ASD is anticipated to be offered in Taiwan in the near future. Therefore, it is critical to explore the psychological factors regarding the test decisions among the ASD-affected population before the provision of the test. This study examined emotions, attitudes, and intention regarding ASD genetic testing among parents of children with ASD in Taiwan.

The purpose of this study was threefold: (i) systematically review the literature regarding the emotional responses, attitudes, and intention related to ASD genetic testing; (ii) examine the psychological factors, attitudes, and intention regarding ASD genetic testing among a sample of parents with autistic children in Taiwan; and (iii) utilize structural equation modeling (SEM) analyses to (a) examine the associations between the emotional and attitudinal factors that determine parents' intentions to undergo ASD genetic testing and (b) test the overall "fit" of the model.

The first study systematically synthesized a decade (2003-2013) of empirical studies regarding the emotional factors, attitudes, and intention associated with undergoing ASD genetic testing and summarized the methodological quality of the included articles. This study indicated a lack of literature on this research area as well as the gap in the overall quality of the existing studies.

The second study was an empirical study among 444 parents of children with ASD from Taiwan in the preliminary data analysis. A SEM model was employed to

analyze the relationship between the variables and test the fit of the theoretical framework. This study demonstrated that anxiety, fear, and guilt were all determinants of test intention among parents of children with ASD.

In summary, the findings from this dissertation have direct implications for clinicians, psychiatrists, and other health professionals. Specifically, it will (i) help explain the potential psychological factors associated with undergoing ASD genetic testing, (ii) assist genetic professionals in becoming aware of the existing psychological concern, and (iii) help design appropriate pre-test educational programs. Educational materials addressing parents' emotional management should be developed. More significantly, policymakers should include and address parents' opinions properly in the official documents.

DEDICATION

Special thanks to my wonderful mother, my loving husband, and my two precious children.

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I would like to express my heartfelt thanks to the four most important mentors during my doctoral training. First of all, I owe my deepest gratitude to my advisor, Dr. Lei-Shih Chen, who has led me in this great transition of my life and inspired me in so many different ways. The legacy she left was not only her dedication and resolution in research, but also her great attitudes in transforming people's lives, especially those underserved populations through her dedicated work. Without her consistent guidance and mentoring, I could not be who I am today standing here presenting the fruits of my research. Second, I want to thank Dr. Goodson, one of the most brilliant and caring professors, a guiding star sparkling in my sky. I could never say enough words to describe what I learned from her in teaching and research, as well as in becoming a better person. I also want to give special thanks to Dr. Ward, who has been giving me long-lasting support whenever I need her, especially when I felt ups and downs, she has been with me throughout my doctoral study period. I had been so fortunate to have Dr. Ward with an amiable character and exceptional leadership. Also, Dr. Liew has given me wonderful support and guidance in my dissertation on so many occasions. I could never say enough about my wonderful dissertation committee for their generous support.

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This study is a secondary data analysis of a large research project directed by Dr. Lei-Shih Chen (PI) in the Department of Health and Kinesiology at Texas A&M University, USA and co-directed by Dr. Tse-yang Huang (Co-I) in the Department of Special Education, National Hsinchu University of Education, Taiwan. The research project is funded by the Chiang Ching-kuo Foundation for International Scholarly Exchange. The findings of this study are preliminary data analysis results.

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CHAPTER I

INTRODUCTION

Autism Spectrum Disorder (ASD) genetic testing is a component of clinical genetic care and an integral diagnostic tool to evaluate ASD in the United States. It is anticipated that similar ASD genetic testing will be provided to patients and their families in Taiwan in the foreseeable future, especially in the context of having a growing prevalence (12.3‰) among the entire population. Therefore, it is important to explore the attitudes and decisions as well as the factors associated with parents' decision-making process with regard to ASD genetic testing. However, to this date, little is known in the existing literature about this topic.

This dissertation examined emotional and attitudinal factors associated with the intent to undergo genetic testing for ASD. In a journal format, I presented two self-contained manuscripts to be submitted for publication in peer-reviewed journals. In the first manuscript, I systematically reviewed empirical studies during 2003-2013 that assessed emotions, attitudes, and intention with regard to genetic testing for ASD. In the second manuscript, I examined the emotional and attitudinal predictors about the intention to undergo genetic testing for ASD in a sample of parents of children with ASD in Taiwan.

The dissertation is composed of four chapters and two appendices. Chapter I presents an overview of the dissertation, introducing the content that follows. Chapter II provides the systematic literature review reporting emotions, attitudes, and intention

regarding undergoing autism genetic testing. To date, no systematic literature reviews (i.e., reviews that simultaneously summarize studies' findings and evaluate their quality) have been conducted on the topic. To summarize and evaluate the current state of the literature on the attitude and intention regarding undergoing autism genetic testing, I summarized the existing literature and reported the emotions, attitudes, and intention with regard to ASD genetic testing (including the three first-tier tests recommended for patients or families with ASD, i.e., Fragile X, G-banded Karyotype, and CMA). Second, this review used the methodological assessment to evaluate the quality of the reviewed articles by employing a 7-point (quantitative study) and a 6-point (qualitative study) criteria, respectively. Four electronic databases were searched using terms such as autism genetic testing, Fragile X, Karyotype, and CMA cognition (attitudes or perceptions) and decision-making (intention). The final number of studies included in this review was 17.

Chapter III particularly investigates the psychological factors that determine the test decisions among a sample of Taiwanese parents of children with ASD. Understanding the decisions regarding genetic testing for ASD is expected to have a broader impact in Taiwan, primarily due to (i) potential for misuse of genetic testing, (ii) the societal pressure or stigmatization associated with having children with mental disorders, and (iii) lack of policies or official guidelines to regulate ASD genetic testing. To ensure the appropriate use of genetic technology and reduce the concerns regarding ASD genetic testing, it is imperative to understand the psychological factors that determine the test uptake among parents of children with ASD.

For the above-mentioned study, a sample of 444 parents of children was used (preliminary data of a paper-and-pencil survey). Based on the current literature on factors determining the attitudes, beliefs, and decision-making regarding genetic testing, I chose a theoretical model for this study. This model encompassed three kinds of constructs, i.e., affect-type variables, attitudes, and intention. The theories used in this study included the Theory of Planned Behavior (TPB), Self-Regulation Theory (SRT), and the Transactional Model of Stress and Coping (TMSC). The model I chose was specifically designed to explain the emotional factors that facilitate or inhibit parents' decisions to undergo genetic testing for ASD. I used structural equation model (SEM) analysis to determine whether the observed data supported the hypothesized model.

Chapter IV presents the conclusion to this dissertation, based on discussions in Chapters II and III. Appendix A presents the characteristics of the 17 included studies investigating emotional factors, attitudes, and intention regarding autism genetic testing. Appendix B contains the matrix of the distributions of emotions, attitudes, and intention of undergoing genetic testing among the included 17 articles.

CHAPTER II

A SYSTEMATIC REVIEW OF THE EMOTIONAL RESPONSES, ATTITUDES, AND DECISIONS REGARDING THE GENETIC TESTS ASSOCIATED WITH AUTISM SPECTRUM DISORDERS

Introduction

As the number of genetic tests for multifactorial diseases continues to grow in clinical settings, individuals and family members at risk for these conditions face more and increasingly complex decisions.[1] In many instances, decisions to undergo genetic tests requires elaborate psychological and behavioral adjustments.[2,3] The current literature on psychological factors and decisions to undergo genetic testing has been heavily centered on (i) cancers as the disease focus, such as hereditary breast, ovarian, and colon cancers,[4-7] (ii) single-gene disorders with identified etiology, such as Down syndrome and Fragile X syndrome,[8,9] and (iii) the psychological and behavioral impact after genetic testing.[10,11] Less attention has been paid to the psychological determinants associated with decisions to undergo genetic testing for the complex neurodevelopmental disorders, specifically for autism spectrum disorders (ASDs).

Autism is a range of conditions characterized by social, communicational, and behavioral impairments.[12] Strong evidence suggests that ASD is among the most heritable of all neurodevelopmental conditions with high prevalence (one in sixty-eight children) in the United States.[13,14] Parents of children with ASD are at an increased risk of having another affected pregnancy. The recurrence risk of ASD is between 2-9% if

one child was diagnosed with ASD and is 25-35% if two or more affected children were identified in one family.[15]

Current genetic tests recommended for ASD

Until recently, there was no single laboratory test, such as the BRCA gene test for breast cancer and FMR1 screening for Fragile X,[16,17] which can be exclusively used for diagnosing ASD. The clinical genetic tests recommended for identifying the etiology of ASD vary by medical authorities. American Academy of Neurology and American Academy of Pediatrics recommend traditional cytogenetic tests[18,19] including G-banded karyotyping and Fragile X screening in patients with ASD. Recently, Chromosomal microarray technology (CMA) is a relatively novel technology providing higher resolution and better diagnostic yield than traditional tests.[20] Both the American College of Medical Genetics and Genomics (ACMG) and the International Standard Cytogenetic Array Consortium recommend CMA as the first-tier test for people affected with ASD.[21]

Overall, autism genetic testing can potentially help identify the causes of ASD, promote early diagnosis, and develop timely treatment plans.[22] As noted by ACMG clinical guidelines (2013 revisions), "using current knowledge and technology, a thorough clinical genetics evaluation of patients with ASD is estimated to result in an identified etiology in 30-40% of individuals."[23(p404)] However, similar to other genetic tests, autism genetic testing might also involve a number of ethical, legal, and social implications, such as genetic discrimination and insurance concerns.[24]

Decisions regarding undergoing autism genetic testing

The decisions to undergo genetic testing of specific conditions might vary widely among at-risk populations.[4] Previous literature has shown that the uptake of genetic tests were likely to be predicted by a number of psychological factors, such as higher perceived disease risk, greater level of anxiety over the disease or desire for emotional relief.[4,24,25] Unfortunately, psychological factors associated with decisions regarding testing for ASD are largely unknown in the existing literature. Decisions to undergo autism genetic testing can be more complicated than other conditions due to the following reasons: (i) The multifactorial nature of ASD (with more than one single gene involved), (ii) the relatively low detection rate with the current technology (compared with single-gene disorders, such as Down syndrome and cystic fibrosis), (iii) the inability to test for disease severity,[26] and (iv) lack of evidence for clinical utility.[26,27] Due to all these test constraints, ASD-affected people, their families, and at-risk populations might experience a host of unique psychological factors associated with the decision to undergo genetic testing for ASD.[24,28]

The purpose of this review was to (i) systematically evaluate a decade of empirical literature (2003-2013) regarding the emotional factors, attitudes, and intention toward autism genetic testing, including the first-tier genetic tests recommended for ASD-affected population (Fragile X, Karyotype, and CMA) and (ii) assess the methodological quality of reviewed studies, including the study design, utilization of theory, sample size/sample diversity, data validity, data reliability and trustworthiness. It

is critical to assess methodological quality to identify the strength of the existing literature and provide useful information for future studies in the topic area.

Method

Search strategy and process

The Garrard's Matrix method[29] guided the procedural framework for this review. Key search terms included "autism genetic testing," "genetic testing for ASD," the three first-tier tests, "Fragile X," "Karyotype," and "CMA" for ASD, "cognition" ("attitudes" or "perceptions"), and "decision-making" ("intention"). I used various combinations of the key terms as well as their variations and Boolean connections. The search process comprised three main steps. First, I screened the four primary OVID databases including MEDLINE (OVID), EMBASE (OVID), PsycINFO (PROQUEST), and CINAHL (Ebsco). All the identified articles from these four databases were exported to RefWorks (Refworks Co, Bethesada, MD), a citation management software, for further coding and eliminating of duplicates. Second, I assessed the studies that met the inclusion and exclusion criteria. Third, I searched Scopus, a database that can search reference lists electronically and conducted backward and forward searches.

Inclusion criteria

The studies included in this review met the following criteria: (i) they reported empirical data related to emotional factors, attitudes, and decisions for undergoing genetic testing; (ii) they were published after 2003 (the year in which researchers completed the human genome project; (iii) they reported human studies only; and (iv) they were published in English. Studies were excluded if (i) they focused on emotional

factors, attitudes, or decisions unrelated to undergoing autism genetic testing, such as people's attitudes/decisions after obtaining the genetic test results, as well as treatment decisions, clinical decisions, or reproductive decisions; (ii) they focused on health care providers' emotions, attitudes, and intention regarding autism genetic testing; and (iii) they were reviews, abstracts, brief reports, commentaries, or letters to the editors. I also did not include articles that investigated the psychological well-being and coping strategies of having a child or children with genetic disorders such as autism and Fragile X syndrome. In addition, studies were excluded if they only examined post-test psychological states, such as worries about the test results and anxiety over carrying faulty genes.

Data extraction and synthesis

Data from the selected articles were extracted and organized into standardized matrices by the first author (LX) independently. Appendix A presents the matrix with data for each study according to the following categories: first authors, targeted genetic tests, recruitment criteria and sample source, sample size, study design, pre-test counseling, as well as test uptake/acceptance rate. Appendix B displays each study according to the factors we examined in this review, namely, emotional factors, attitudes, and intention of undergoing genetic testing. During the data extraction period, the first two authors (LX and PG) met to discuss questions or concerns. To assure the reliability of the coding process, two of the authors, extracted data from four of the 17 reviewed studies (approximately 23%) independently and compared their findings. Cohen's kappa (a measure of inter-rater reliability/consistency) was 0.80, indicating

adequate inter-rater reliability.[30] Differences in ratings were discussed and consensus was achieved prior to the final report.

Methodological quality assessment

Five criteria were used to assess each reviewed study's methodological quality. Criteria evaluated sample size, response rate, data validity, data reliability, and theory use for quantitative studies. Similarly, I assessed sample diversity, data saturation, data trustworthiness, research disclosure, and theory use among qualitative studies. All studies were assigned a methodological quality score (MQS) with the maximum score of 7 points (quantitative study) and 6 points (qualitative study), respectively (Table 1).

Results

Figure 1 describes the study selection process. Altogether, 2291 articles were identified through database searching, of which 503 were duplicates. After eliminating duplication, the title and abstracts of 1788 articles were reviewed, resulting in 31 eligible studies. After applying the inclusion/exclusion criteria, 17 articles remained. Then I used Scopus to screen the references of these selected articles and the articles that referenced them. The final sample consisted of 17 articles. Findings are synthesized below in three sections and demonstrated in three separate tables: (i) the study characteristics (Appendix A), (ii) emotions, attitudes, and intention related to the tests (Appendix B), and (iii) methodological quality assessment (Table 1).

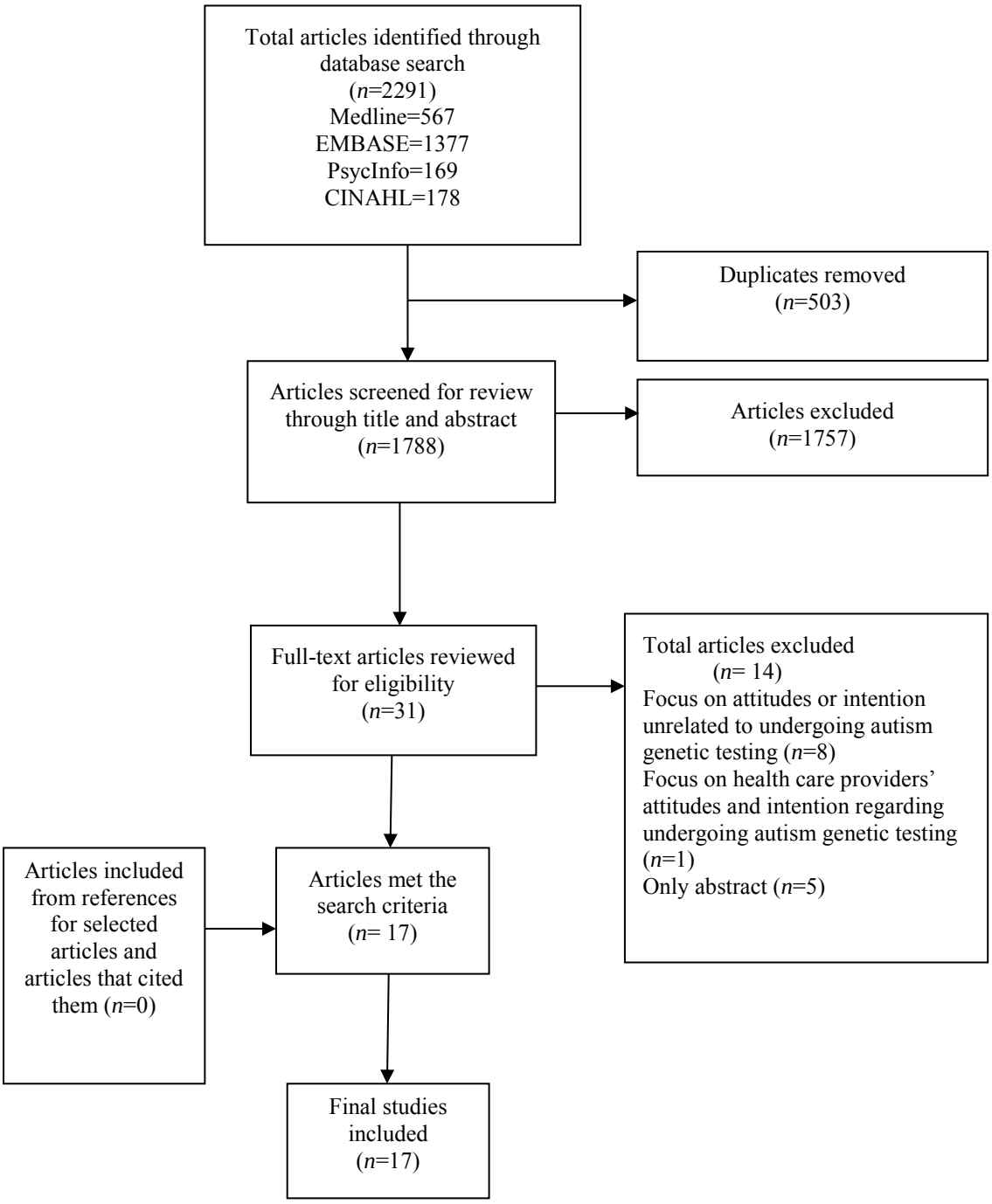

Figure 1 Flowchart of selection process.

Study characteristics

Study origins. According to the screening criteria, only studies published since 2003 were included. All 17 articles in this review were published after 2005. Sixty-five percent (*n*=11) of the studies were published in the past five years; 76.5 % (*n*=13) of the studies were conducted in the United States and the remainder (*n*=4) in Australia. Barley contributed four articles and Skinner[17, 31-33] as well as Metcalf[34-36] published three articles.

Targeted tests. Two studies (11.8%) specifically targeted autism genetic testing. For instance, Chen and colleagues[37] recruited 42 parents of children with at least one child diagnosed with ASD to explore their awareness and attitudes toward autism genetic testing.

Most studies (88.2%) examined their participants' perspectives related to genetic testing for Fragile X (FX) syndrome. Among 15 studies on FX screening, altogether 60% (*n*=9) examined participants' attitudes or test intention regarding carrier testing (*n*=7) or prenatal screening (*n*=2). For example, Anido et al[38] conducted a survey among the general public exploring its attitudes toward FX carrier testing. Three studies (20%) specifically focused on newborn screening. Christie and colleagues[39] invited mothers to participate in their study about maternal attitudes toward FX newborn screening in the postnatal wards. Three studies (20%) investigated the screening in general, including three different stages, i.e., carrier, prenatal, and newborn screening. For instance, Skinner et al[31] investigated caregivers of children with FX syndrome or FX carriers about

whether population screening should be offered in preconception, prenatal, and newborn stages.

Recruitment and sample source. Participants in the majority (70.1%, *n*=12) of the studies from the chosen studies were females and the remaining studies (*n*=5) were for both mothers and fathers of children either with FX syndrome or with ASD. More than half of the studies (53%, *n*=9) did not specify the carrier or non-carrier status of their samples. For example, Skinner and colleagues[17]surveyed mothers within 24 hours of their newborns' births, without specifying the mothers' carrier status. Six studies (35.3%) were among an affected population (either the participants were FX carriers or had children affected with genetic disorders). Two studies (11.7%) had mixed populations, including participants who were both FX carriers and non-carriers.

Altogether, 41.2% of the studies (*n*=7) recruited samples from clinical settings, such as hospitals or medical centers. For example, Christie and colleagues[39] conducted research among mothers in a postnatal ward at a children's hospital in Australia. Five studies (29.4%) examined samples from the general population. For instance, Barley and colleagues[32] recruited families of children with FX and the participants responded to a large national survey. Three studies (17.7%) reported their participants were from university or national research centers. For example, Anido et al[40] enrolled female participants from a large research project based at Emory University's School of Medicine. Altogether, two studies (11.8%) used community-based samples. For instance, Johnson et al[41] used a community-based participatory approach to reach church

attendees in various cities and towns in Oklahoma. Narcisa and her colleagues[42] recruited ethnic minorities directly from local or regional autism advocacy groups.

Sample. The sample size extended from 12 to 29103. Participants' age ranged from 21-89 years. Twelve studies (70.6%) gave detailed information about ethnicity of their participants and eight studies (47.1%) were predominantly conducted with a White sample. For instance, Barley et al[32] reported 92% of the parents in the FX screening study were White. As indicated in Chen et al's study,[37] half of their participants were ethnic minorities, including African Americans, Hispanics, and Asians. Among the eight (47.1%) studies that reported participants' educational level, most mentioned that more than half of their participants received education higher than a college diploma. Six (35.3%) studies discussed the annual household income and most of the participants from these studies had high annual incomes. For example, Narcisa et al[42] reported that 97.6% of the parents of children with autism had an annual household income higher than $50K in their study.

Study design. Seven (41.2%) studies employed qualitative design, utilizing focus groups and semi-structured interviews. Ten (58.8%) studies used quantitative design such as questionnaires or surveys. One study by Metcalf and colleagues[36] utilized both qualitative and quantitative designs. Altogether, three (17.6%) studies relied on existing theories to guide their investigations. These theories included Adult Learning Theory, Modified Health Belief Model and Grounded Theory.

Pre-test counseling. Eight studies (47.1%, *n*=8) provided genetic education and counseling to the participants prior to the study in a variety of forms. For instance, as

indicated by Anido et al,[38] basic disease characteristic and risks were disseminated among the mothers who agreed to participate in the FX carrier screening study. The contents of the pre-test counseling contained basic disease characteristics and potential risks as well as knowledge or information about the tests.

Test uptake/acceptance rate. Altogether, ten studies (58.8%) reported the acceptance rate ranged from 7.9% to 94%. The highest level of consent (94%) was reported by Christie et al[39] in a study on mothers' attitudes toward newborn screening for FX syndrome. The lowest rate (7.9%) was the acceptance of carrier screening in the prenatal genetic counseling setting with a national sample throughout the United States.[43] Pastore and colleagues[44] found more women with diminished ovarian reserve (75%) desired to have the FX carrier test than the comparison group with the premature ovarian failure or early menopause (43%). Bailey et al[33] evaluated a brochure that can help with parents' decisions regarding FX newborn screening; 61.9% parents agreed to test their children with the assistance of the information provided by the brochure.

Emotions, attitudes, and intention

Emotions. As detailed in Appendix B among the 17 studies, 12 emotions were identified. Most of the emotions were adverse psychological conditions, for example, anxiety, worry, and fear. The majority of the studies (72.8%, *n*=14) were conducted prospectively, but three (27.2%) were retrospective studies that collected participants' emotional responses after offering the tests to them.

Anxiety. The most frequently reported emotion was anxiety (29.4%, *n*=5). For example, Archibald and colleagues[36] reported carrier testing might cause anxiety during

pregnancy and impact future family plans. Christie et al's [39] study claimed that some mothers felt anxious about possible test outcomes about newborn screening for FX syndrome, although no variability was found based on different social economic status or educational levels. Metcalf et al[37] identified a reduced anxiety score for women who tested for FX syndrome.

Uncertainty. Five studies (29.4%) mentioned uncertainty. For instance, Christie et al[39] found that a small number of parents (10/173) encountered uncertainty and concern about the consequences of their newborns' test outcomes with FX syndrome. Parents used the words "horrible" or "grief and initial confusion" to describe how they might feel about knowing the positive test result about their newborns. Furthermore, participants (non-pregnant women) in Archibald et al's study[34] also mentioned the uncertainty about the features of FX syndrome might have impacted their test decisions.

Worry. The emotional factor of worry was mentioned in three studies (17.6%). As Barley et al[32] discussed, a substantial portion (44.4%) of the parents in their study did not want to participate in newborn screening for FX, because they "did not want to worry." Similarly, Skinner and his colleagues[17] also found that parents worried about a number of negative consequences related to genetic screening for FX; for instance, how others might treat them and how they might treat their children.

Feelings about the parent-child bonding. Three studies (17.6%) described feelings about the parent-child bonding, aiming at knowing parents' attitudes toward prenatal screening and newborn screening for FX. All three studies concluded that most parents mentioned the bonding with the newborns would not be disrupted. For instance,

Christie et al[39] found that most respondents (84%) considered the disclosure of a positive screening result would not affect parent-newborn bonding.

Fear. The emotion of fear was discussed in two (11.8%) studies. The specific kind of fear mentioned included fear of lacking feedback with regard to the test, fear of being discriminated, and fear about the insurance issue.[37,41] As Chen et al[37] pinpointed, a few parents of children with ASD mentioned that they feared that their life insurance would be suspended or they would have to pay more if the genetic test showed positive results.

The remaining emotions were only discussed by one study (5.8%). These emotions varied among studies and most of them had a negative impact on participants' attitudes and intention regarding undergoing genetic testing. For instance, Pastore and colleagues[45] reported three emotional responses, i.e., *feeling regretful* or *feeling angry* about not learning sooner that FX might be related to their infertility and *feeling upset* if FX runs in the family. Anido et al[40] reported a "*grieving period"* among FX-carriers prior to pursing the test. Johnson et al[41] identified a feeling of *distrust* was associated with participating in FX and other genomics-related research among both Native Americans and African Americans. *Frustration* was how the parents of children with ASD in Chen et al's study[37]depicted their feeling about the long waiting process for ASD genetic testing. The study by Barley et al[32] indicated that a high level of *depression* was not associated with caregivers' opinions about FX population screening.

Attitudes. Altogether eight studies investigated participants' attitudes toward undergoing genetic testing. Both positive (41.2%, *n*=7) and negative attitudes (35.3%, *n*=7) were reported.

Positive attitudes. All eight studies reporting positive attitudes listed participants' perceived benefits or outcomes pertaining to the test. These perceived benefits or outcomes can be categorized into five groups. First, the test might help obtain information about parents' carrier status (29.4%, *n*=5). Metcalf and his colleagues[36] identified that most test proponents wanted to know both their own health conditions and how likely they might have a child with FX syndrome. Second, the test might help with reproductive decisions (29.4%, *n*=5). In the study by Christie and colleagues,[39] about two thirds of the mothers responded that they would like to use information from the newborn screening for FX syndrome when planning for more children. Third, the test might help with research (23.5%, *n*=4). Anido and colleagues[38] found participating research was the biggest motivator for women who underwent screening toward FX carrier testing. Fourth, the test might help with early diagnosis, intervention, and timely treatment (23.5%, *n*=4). Parents in Chen et al's study[37] considered the benefits of having their children undergo ASD genetic testing to locate the genetic cause of ASD and to obtain timely medical treatment for their affected children, and lastly, parents mentioned that the test might help them with better preparation for birth of an affected child (17.6%, *n*=3); for instance, to get more family support or obtain health insurance coverage.

Negative attitudes. Six studies discussed perceived barriers or concerns related to the uptake of the test. These specific barriers were related to (i) concerns related to the potential harm brought by undergoing the test (29.4%, *n*=5); Archibald et al[36] mentioned the potential emotional impact as well as possible labeling and stigma related to undergoing genetic testing for FX syndrome; (ii) concerns related to the characteristics of the current tests (11.8%, *n*=2), such as parents' questions regarding the existence and reliability of the test;[36,37] (iii) concerns related to the values of the test (11.8%, *n*=2). As quoted by one mother of children with autism,[37(p278)] "I mean it [testing] would make no difference… it would make no difference in the way the school interacted with him, it would not make difference in any of the way he lived"; (iv) concerns about the societal implications regarding the genetic test (11.8%, *n*=2), such as eugenics issues and dilemma for people with disabilities and their families;[34,36] and lastly, (v) concerns related to the religion and culture beliefs (5.9%, *n*=1). Chen and colleagues[38] mentioned that religion and culture influence such as destiny played a role in Asian parents' negative attitudes toward genetic testing.

Intention to undergo genetic testing

Altogether, nine studies (52.9%) discussed the intention to test and provided the reasons for accepting and declining the tests. I categorized the underlying reasons under the constructs from Health Belief Model and Theory of Planned Behavior,[46,47] i.e., perceived benefits, perceived barriers, perceived risk, and subjective norms. Since emotions were not included in either of these two dominant health theories, emotional factors were added as a separate category.

Primary reasons for accepting to undergo testing. The categories of reasons for accepting were: (i) Perceived benefits were mentioned in nine studies (52.9%, *n*=9). These perceived benefits were primarily related to early diagnosis, better preparation, and informed reproductive decisions. Most women (91.7%) agreed to participate in newborn screening tests in Bailey et al's study,[33] and they mentioned that knowing the baby's carrier status with FX could help them prepare better for the possible challenges. Narcisa and her colleagues[42] found parents wanted to pursue genetic testing for earlier diagnosis and closer monitoring of their children with autism. (ii) Perceived risk was discussed in four studies. In the investigation by Johnson et al,[41] participants favored undergoing FX testing due to the perceived risk of passing the genes to the next generations. In Bailey et al and Skinner et al's studies,[31,32] participants considered FX screening would pose minimal risk. Therefore, they would support undergoing the tests. (iii) Subjective norms were identified by three studies. Chen and colleagues[37] found that recommendations from health care providers and influence by other family members could affect the participants' decisions regarding autism genetic testing. (iv) Perceived barriers were discussed by three studies. Metcalf et al[36] mentioned that since testing is free of charge, the mothers would like to be tested for carrier screening for FX syndrome. (v) Emotional factors were listed by one study. Narcisa et al[42] reported that the possibility of reducing anxiety levels was mentioned as one key reason for parents' interest in testing the younger siblings of their autistic children.

Primary reasons for declining to undergo testing. As described in Appendix B, among the seven studies reporting the primary reasons for declining genetic testing,

perceived barriers was the most frequently cited reason (47.1%, *n*=7).[17,33,35-37,41,44] These perceived barriers included lack of convenience (29.4%), issues with the current status of genetic testing (17.6%), lack of relevance (17.6%), confidentiality (11.8%), bad timing (11.8%), issues with the diseases (11.8%), and cost (5.8%).

The second most cited reason (23.5%, *n*=4) was the negative emotions associated with the test. These emotional factors were "do not want to worry," "fear," "lack of trust," and "feeling uncertain."[31,33,35,41] As demonstrated by Bailey et al[33] and Skinner et al,[17] participants considered testing might induce worry; therefore in order to avoid worrying, they would decline testing newborns for FX. This viewpoint was echoed in another study by Skinner et al[31] about parents' decisions toward population screening for FX. The parents of children with FX syndrome rated increased worry as the most likely negative outcome with regard to the genetic test for FX syndrome. They worried about their child's future health condition and development as well as the way their children might be treated after knowing the test results. Another kind of emotion mentioned by Johnson et al[41] was fear of lack of feedback and fear of absence of follow-up and ostracism. As quoted by one Native-American male participant, "excessive horror stories" given by people with previous testing experience terrified him from undergoing genetic testing. Lastly, subjective norms, which included lack of encouragement from health professionals and culture/family impact, were the concerns raised by three studies (17.6%).

Methodological quality

All 17 studies were divided into two broad groups for methodological quality assessment, i.e., quantitative studies and qualitative studies. The methodological characteristics for quantitative studies included sample size, response rate, data validity, data reliability, and utilization of the theoretical framework. In contrast, I measured the five aspects of the qualitative studies, i.e., sample diversity, data saturation, data trustworthiness, researcher disclosure, and theoretical framework (see Table 1). Metcalf et al[36]reported both qualitative and quantitative data; therefore, I coded the two kinds of data separately. The average MQS was 2.56 (*SD*=1.8; maximum potential score=7) for quantitative study and 3.25 (*SD*=1.4; maximum potential score=6) for qualitative study.

Quantitative studies. Altogether, 60% (6/10) of the quantitative studies utilized large samples (>300). Only one study (10%) reported the response rate. Among the 10 quantitative studies, two studies reported data validity (content validity) and none of them discussed data reliability. Also, none of the studies reported coefficients for the data analyzed. None of the quantitative studies reported the utilizing of theoretical framework.

Qualitative studies. A sample diversity measurement included four characteristics of the participants: gender, ethnicity, educational level and annual household income. If the study included less than two items, then the samples were considered homogenous. About 62.5% of the studies (*n*=5) were categorized into this group. Three studies reported more than two characteristics and were, thus, considered to be heterogeneous.

Table 1 Methodological criteria and frequency distribution of each criterion among the 17 selected articles

Quantitative studies				Qualitative studies			
Methodological characteristics	Scoring options	Distribution of characteristics Frequency (*n*)	%	Methodological characteristics	Scoring options	Distribution of characteristics Frequency (*n*)	%
Sample size	Small sample (<100)=1 point	3	30%	Sample diversity (i.e., gender, ethnicity, education level, annual household income)	Homogeneous=0 points	5	62.5%
	Medium sample (>100 and <300)= 2 points	1	10%		Heterogeneous Reported = 1 point	3	37.5%
	Large sample (>300)= 3 points	6	60%				
Response rate	Not reported =0 point	9	90%	Data Saturation	Not reported=0 points	3	*37.5%*
	Reported =1 point	1	10%		Reported= 1 point	5	62.5%
Data validity	Not reported =0 points	8	80%	Data trustworthiness(e.g., triangulation, respondent validation, credibility, and/or dependability)	Not reported=0 points	1	12.5%
	Reported=1 point	2	20%		Reported= 1 point	7	87.5%
Data reliability	Not reported =0 points	10	100%	Researcher disclosure	Not reported= 0 points	7	87.5%
	Reported=1 point	0	0%		Reported=1 point	1	12.5%
Theoretical framework	Not reported=0 points	10	100%	Theoretical framework	Not reported=0 points	4	50%
	Reported=1 point	0	0%		Implicit use of theories=1	2	25%
					Explicit use of theories: Reported= 2 points	2	25%

Metcalf et al (2008) included both qualitative and quantitative data. The qualitative and quantitative part of the data was coded separately.
MQS: 2.56 (*SD*=1.8; Maximum possible score=7 for quantitative study MQS: 3.25(*SD*=1.4; Maximum possible score=6) for qualitative study

Five studies (62.5%) mentioned their data reached saturation. Most studies (87.5%) provided evidence about the methods they used to maintain the credibility of their data collection and analysis, including triangulation, member checking, and the involvement of more than one person in the data analysis. Reporter disclosure is important in qualitative research due to the impact of the potential occurrence of researcher bias. Only one study (12.5%) reported this criterion. Two studies (25%) mentioned the use of theoretical framework as the guidance for their investigation. Researcher bias needs to be noted for giving credit to the studies that reported the use of theoretical framework, since qualitative studies usually do not need to have a prior theory to guide the investigation. However, I gave credit for studies showing efforts in using theoretical framework or validated constructs in the process of data synthesis.

Discussion

As the first review explored emotions, attitudes, and intention regarding autism genetic testing, this study performed two distinct tasks. First, it synthesized the existing literature within the past decade (2003-2013) on the emotions, attitudes, and intention with regard to autism genetic testing (including the three first-tier tests recommended for patients with ASD, i.e., Fragile X, G-banded Karyotype, and CMA). Second, this review used a methodological assessment to evaluate the quality of these studies using either qualitative or quantitative methodologies.

The overall quality assessment of this body of knowledge indicates mixed methodological quality. The majority of the quantitative study had a large sample size (N>300). However, among the nine quantitative studies, only two reported data's

validity, one mentioned response rate, and none reported data's reliability. In addition, none of these studies utilized a theoretical framework to guide their investigations. Therefore, consumers of these studies might have difficulty in assuring the validity and reliability of the studies.

Among the qualitative studies, the majority did not provide the richness and nuances of the data by examining at least two characteristics of the sample, such as gender, ethnicity, educational level, and annual household income.[46,48] Data trustworthiness and data saturation were two other crucial indicators of rigorous qualitative research.[48] The majority in this review provided evidence for these two indicators. However, only one study provided the "researcher disclosure"— another important indicator for qualitative studies.[48] Researcher disclosure is a description of the research's status, such as being part of the community or belonging to the same ethnic group as their participants.[46] Researcher disclosure can make readers prepare for the potential researcher bias. Although qualitative research does not need to be anchored in scientific theories, half of the researchers employed a grounded theory approach or other validated theories.

Notably, both in the qualitative and quantitative studies, lack of theoretical framework makes it difficult to interpret the relationship of the correlated variables with the studies' outcomes. Recently, official genetics/genomics authorities, such as National Human Genome Research Institute, have recommended to expand the existing theories for better understanding of the factors that might affect people's intention to undergo genetic testing.[49,50] However, only one study in this review mentioned the use of

modified constructs from the Health Belief Model (HBM) to explain factors that might influence the decision-making process regarding screening. Another study mentioned Adult Learning Theory as its framework, because researchers postulated that women in FX screening programs might be unprepared and would need a significant amount of information about this disease and the screening. The remainders either implicitly articulated their theoretical rationale or simply ignored using theories to guide their investigations. It is also worth mentioning that, in this review, I intended to categorize the major factors that affect test decisions into the key constructs from the well-established health theories, such as HBM and TPB. These theories, however, did not contain a category under which emotions can be classified. Given the neglect of theories and emotional construct in explaining intention to undergo genetic testing, future researchers should consider adding emotional factors as a construct to their theoretical framework for exploring how emotions might affect genetic testing decisions.

In synthesizing the literature, I identified a few significant literature gaps: (i) the limited studies that have explored the associations between emotional factors and the test decisions, (ii) the limited studies that have focused on the attitudes and intention regarding autism genetic testing among the ASD affected population, and (iii) the lack of pre-test counseling or educational efforts for alleviating participants' negative emotions related to testing.

The most salient finding was the limited studies on exploring the associations between emotional factors and the test intention. The inattention to this kind of research might be partially attributed to the neglect of emotional factors for explaining genetic

testing or screening behaviors.[51-53] The studies that investigated decisions to undergo genetic testing were either non-theory-based or primarily based on value-expectancy theories, such as the HBM and the TPB.[51] However, emotional factors, such as fear and anxiety, were not adequately taken into consideration, given these theories did not emphasize emotions as predictors.[46,52]

Another reason for the literature gap might be due to lack of benchmarks or criteria for assessing emotional factors related to the uptake of autism genetic testing, specifically. Compared to a significant body of research that takes into account evaluating emotional responses to genetic tests for Huntington's Disease or inherited cancers[7,16,53,54] there were no similar studies of emotional responses to autism genetic testing. Official recommendations have been consistently emphasizing testing psychological states related to the uptake of cancer-related tests, which may have led to the proliferation of such studies related to cancers of various kinds.[5] Nevertheless, similar recommendations for autism genetic testing are not available. Hill and colleagues conducted a systematic literature review exploring psychosocial aspects related to the uptake of FX screening and mutation frequency.[9]Although this review demonstrated psychosocial beings with regard to the screening for FX syndrome, it was not designed to explore the emotional factors and attitudes that determine participants' decisions associated with FX test decisions.

With the development of more accurate autism genetic tests for clinical use,[20] one needs to understand the emotional factors associated with the decisions to undergo these tests. As indicated by Gooding and colleagues,[51] understanding the factors that

determine genetic testing decision-making processes can help with informed choices about the test uptake among at-risk patients. This review suggested an immediate need for empirical studies to add "emotions" as a component in determining decisions related to genetic testing. Specifically, health education efforts or counseling services should also consider how to alleviate the influence of negative emotions related to autism genetic testing, thus helping maximizing genetic testing utilization.

Notably, among the studies that reported "emotions," some used retrospective designs, either collecting data immediately after the test, or after the test results had been disseminated. These studies asked participants to recall their testing experiences after receiving the test results and give the reasons for taking or not taking the tests. Because participants were asked about their post-testing attitudes and feelings, the answers provided by the participants might not have been the same as if they were asked before testing. For instance, anxiety might only last for a short duration at the time of occurrence.[5] If one wants to know the pre-test emotional factors that affect the decisions to take the test, a prospective research design might provide more accurate information. Retrospective studies might yield a substantial amount of measurement error.

Another important finding was the limited studies on the attitudes and intention to undergo autism genetic testing among the ASD affected population. Surprisingly, most studies focused on the attitudes and intention about undergoing FX screening among the general population or those affected with the FX syndrome. Only two studies particularly explored the attitudes and intention toward autism genetic testing among parents of children with ASD. Prior studies showed that FX screening is associated with

ASD and accounts for 2% of ASD cases; therefore, FX screening has been used as a standard genetic test among patients with ASD.[21] However, none of the FX screening studies were conducted among patients or families affected with ASD; specifically, this phenomenon could be due to a number of reasons: (i) the constraints of the current tests to identify ASD,[28] (ii) the lack of consensus regarding clinical utility of these tests, and (iii) the multifactorial nature of ASD.[21] For example, unlike most genetic screenings for single gene disorders, such as Down syndrome and cystic fibrosis, the range of diagnostic yield for autism genetic testing ASD is limited to 0.5 to 18%.[21,54,55]

The third salient finding is related to pre-test counseling or educational efforts. Half of the studies provided rigorously-designed consent and educational materials covering the basic characteristics and knowledge/information about the diseases and the genetic tests. However, the review showed that the participants might not fully digest the information or comprehend the personal, familial, and social impacts related to the test, especially the benefits or potential harms of undergoing the test[31,38] Moreover, *none* of the studies mentioned any educational interventions for alleviating participants' psychological stress, and/or negative emotions, prior to the test. It is crucial for participants to be prepared emotionally for undergoing testing, getting ready for having the test results, and making behavioral changes based on the test results.[11,55] As indicated by Broadstock et al,[56]pre-test emotional evaluation is necessary for more targeted counseling services by health professionals. Therefore, genetic testing research should consider including a pre-test evaluation of emotional factors so that the genetic counseling can be timely implemented.

Additionally, this review found that most studies were conducted among samples of White patients/people. Among the limited studies that recruited ethnic minorities, variations among attitudes were identified between Caucasian and other ethnic groups. As Skinner et al[17] identified, African American participants tended to be less likely to accept screenings for FX compared with their White counterparts. Johnson and colleagues[41] purposely recruited Native Americans and African Americans in their study and contended that these minority groups appeared to be more hesitant to undergo genetic testing. These findings were in line with recent research on the attitudes toward genetic testing conducted in the United States that showed variability in viewpoints among ethnic minorities. Future research in autism genetic testing should consider investigating a wide spectrum of ethnicities to specifically address this role of ethnicity and culture in genetic-related inequities.

Moreover, the majority of the studies identified that the participants had positive attitudes toward genetic testing for ASD and FX syndrome.[17,42] In addition, the studies also documented a high acceptance rate that indicated participants' willingness to undergo the tests or the actual uptake of the tests. For example, Skinner and colleagues[17,31] identified a generally favorable attitude toward population screening for FX. However, their study reported that carrier testing was more acceptable than prenatal and newborn tests. This finding was consistent with other studies showing that the general public holds positive attitudes toward genetic testing for various conditions.[57,58] However, as pinpointed by Bailey et al,[32] timing of the testing, in other words, in which stage of the participants' life genetic testing is offered, was an important factor that

might influence the attitudes and decisions with testing. Considering the impact of stages of life on testing decisions, screening might need to be offered multiple times to facilitate better informed decisions.

In light of these findings and their implications, I have the following recommendations for future studies. First, future studies should investigate various factors associated with decisions regarding autism genetic testing. More recently, researchers started to make attempts to understand different stakeholders' perspectives related to genetic tests for ASD.[28,59] For instance, Reiff and colleagues[59]researched the perspectives of receiving the genetic testing results for CMA among health care providers and the patients in clinical settings. Another study by Bernhardt et al[60] focused on investigating women's experiences receiving their abnormal test results for CMA. However, since these studies either only discussed the after-test scenarios or focused on health care providers' attitudes toward genetic testing associated with ASD, I did not report these studies in this review. Given the absence of studies investigating decisions to undergo autism genetic testing among ASD-affected populations prior to the offering of the test, future research needs to consider investigating this issue. Second, future studies should consider (i) utilizing a theoretical framework to guide investigations, (ii) reporting the validity and reliability of the data, (iii) considering measuring the relationship between emotional factors and decisions to test, and (iv) increasing the ratio of ethnic minorities in study samples.

This review has two limitations. First, although I conducted an exhaustive search for relevant articles, I might have overlooked articles in the field due to the constraints of

the search terms. Second, I limited my search to empirical studies published in English; therefore, selection bias might have occurred and I might have missed articles published in other languages. However, the strength of this study is that it is the first review reporting the emotions, attitudes, and intention regarding autism genetic testing among the at-risk groups and the general population. I provided useful information for more rigorous research addressing this topic in the future.

This review indicated that I did not have sufficient evidence on the associations between emotional factors and decisions with regard to undergoing autism genetic testing. Also, theoretical framework is largely missing in most of the included studies in this review, which makes it difficult to interpret the relationship of the psychological variables and other correlated variables. Future studies need to consider using validated or self-synthesized theories to explore how emotional factors, attitudes, and decisions interact with each other among at-risk populations with ASD. The findings of this review have significant implications for genetic education and genetic counseling among populations, both affected and non-affected groups. Pre-test health education/genetic counseling should address the emotional responses and possible test outcomes associated with genetic testing for ASD among patients and families. Health professionals will need to carefully consider educating, counseling, or supporting parents of children with ASD and thus assisting them with making decisions about genetic testing for ASD.

CHAPTER III

AUTISM GENETIC TESTING: PSYCHOLOGICAL FACTORS ASSOCIATED WITH THE TEST DECISIONS AMONG PARENTS OF CHILDREN WITH AUTISM SPECTRUM DISORDERS (ASDs) IN TAIWAN

Introduction

As genetic technologies continue to advance in the post-genomics era, more genetic tests for Autism Spectrum Disorders (ASDs) have been used to predict the risk of developing ASD, provide information for early diagnosis, and open venues for timely medical interventions.[61-64] In the United States, although the official guidelines for genetic testing for ASD vary by medical authorities, a growing trend is the offering of more advanced genetic tests for patients and their families with ASD in clinical settings.[20] For instance, the American College of Medical Genetics and Genomics (ACMG) is currently recommending Chromosomal Microarray Analysis (CMA), a more robust technology, among patients with ASD to identify ASD-associated genes.[23] In a recent study, Australian researchers announced that they have developed a more accurate genetic test (detection rate: 70%) to assess the risk for having ASD, particularly among people with a family history of ASD or related conditions.[65] Additionally, a French bio-company, IntegraGen, is trying to establish clinical evidence for a novel genetic test among hundreds of patients with ASD. Although still extensively debated, direct-to-consumer (DTC) genetic testing for genetic susceptibility to ASD is already under development.[26]

Albeit genetic tests are currently available for ASD-affected populations, deciding to undergo autism genetic testing can be a challenging task for parents of children with ASD. The reasons might include the nature of this multifactorial disease (with a wide spectrum and different severity levels), the unclear clinical significance, the ambiguous interpretation of the test results, as well as a number of ethical, social, and legal questions pertaining to the test.[24,28,66] Given these conditions, it is more urgent to understand how affected individuals and their families view autism genetic testing and how their affective and cognitive perceptions might impact their decisions.

Multiple lines of studies in various diseases have explored factors that might determine people's decisions associated with the uptake of genetic testing, such as perceived severity, perceived barriers, perceived benefits, attitudes, and intention.[51,67,68] These factors were primarily illustrated in two validated health theories: Theory of Planned Behavior (TPB) and Health Belief Model (HBM).[51] As Robert and colleagues[69] claimed, based on the key constructs of the HBM, those who believed the benefits of testing outweighed the harms tend to be more interested in learning the risks for having Alzheimer's disease. Stein et al[70] identified that intention to undergo genetic testing for cervical cancer were best predicted by beliefs about the susceptibility of the disease conditions. In addition, a prior study systematically reviewed how individuals' positive attitudes were correlated with their intention to be tested for colorectal and breast/ovarian cancer.[51] Although evidence has shown that psychological factors might be an important factor to predict genetic testing decisions, the affect-type variables have been largely neglected in the well-established health theories.[52]

Despite the fact less frequently adopted for genetic testing research, two theories, the Common Sense Model of Regulation (CSM) and the Transactional Model of Stress and Coping (TMSC), have been validated and used to explain how individuals might exhibit emotional responses, such as stress and fear as well as how they might cope with emotional distress.[51,71,72] Theories of stress and coping are well suited for decisions to undergo genetic testing because they emphasize how to cope with people's cognitive and emotional concerns.[73] Researchers have used both CSM and TMSC to investigate how emotional factors might influence the intention to undergo genetic testing for various genetic conditions, such as Huntington's disease, Alzheimer's, and hereditary colorectal cancer.[74-76]

However, these studies have not yet been applied to genetic testing for ASD. The framework (Figure 2) in this study is used to particularly test emotional and attitudinal factors that might determine the intention to undergo autism genetic testing among a sample of Taiwanese parents of children with ASD.

Although the reported prevalence of ASD in Taiwan (12.3‰) was lower than the estimates from developed countries, a potential under-diagnosis and under-detection of ASD has made it an immediate public health concern.[77,78] This phenomenon might be explained by the lack of recognition of ASD among clinicians, the lack acceptance of ASD in Taiwanese society, as well as the potential cultural influence in Taiwan.[77] For instance, parents might feel ashamed or embarrassed by having a child with ASD, which can lead to the difficulty in acceptance of the diagnosis of ASD. A few epidemiologic studies focusing on enhancing the detection rate of ASD among the Taiwanese

population are being conducted.[78,79] However, until today, no recommended tests are available for patients and families with ASD in Taiwan. Since culture might have significant influence on Taiwanese people's perspectives toward genomic disorders and disabilities (such as eugenics and social stigma of having a child with birth defects), it is critical to examine the decision-making process with regard to ASD genetic testing before the provision of this test.

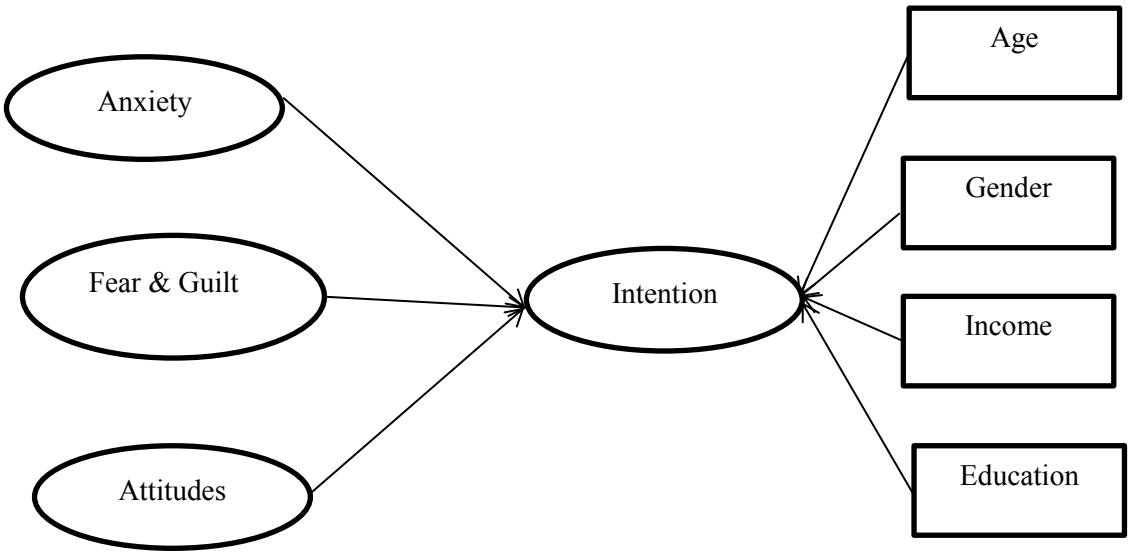

Figure 2. The integrative model of emotions, attitudes, and intention associated with undergoing autism genetic testing.

A better understanding of this decision-making process will provide information for (i) assisting genetic professionals to be aware of the existing psychological concerns among parents of children with ASD, (ii) establishing localized practice guidelines for health care providers to give appropriate referrals to ASD patients, and (iii) designing relevant educational interventions for parents of children with ASD prior to the offering

of the test. However, to date, little is known about factors regarding the intention to undergo autism genetic testing for parents of children with ASD in Taiwan.

The goals of this study were to address the gaps in the literature on the decisions to undergo autism genetic testing. In this study, I used a multivariate analytic technique, SEM, to examine the theoretical framework for explaining parents' emotional and attitudinal responses and their intention to undergo autism genetic testing. More specifically, this study explored the roles of (i) emotions, (ii) attitudes, and (iii) demographic variables in the decision-making process related to undergoing autism genetic testing among a sample of Taiwanese parents of children with ASD. The specific research questions and hypotheses were:

1. Does the model adequately explain parents' intention to undergo genetic testing for ASD? If this model is not adequate, what are the variables to be included in a refined model?

   H1a: The intent to undergo genetic testing for ASD can be positively predicted by parents' anxiety pertaining to the test.

   H1b: The intent to undergo genetic testing for ASD can be negatively predicted by fear and guilt.

   H1c: The intent to undergo genetic testing for ASD can be positively influenced by positive attitudes toward the test.

2. Will the model exhibit different patterns and values depending on participants' demographic information (i.e., age, gender, education, income)?

   H2a: SEM models differ for parents with age$\geq$ 35 years and < 35 years.

H2b: SEM models differ from mothers and fathers of children with ASD.

H2c: SEM models exhibit different values for parents with high and low educational level.

H2d: SEM models differ for parents with high annual household income and low annual household income.

3. Which variables in the model can best predict parents' intention to undergo autism genetic testing? Suppose both emotions and attitudes can predict intention, how much variability can be explained by parents' emotions (including anxiety, fear, and guilt)? How much variability can be explained by parents' attitudes toward testing?

Theoretical Perspective

Theoretical construction

Based on the current literature on factors determining the attitudes, beliefs, and decision-making regarding genetic testing,[31,50,73] I established an integrative model for this study (Figure 2). The key constructs included four latent variables (anxiety, fear & guilt, attitudes, intention) controlling for parents' age, gender, income, and education. I also tested the four demographic factors (parents' age, gender, education, and income) as moderators. The variables in this model are from the following validated theories: the Theory of Planned Behavior (TPB),[47] Self-Regulation Theory (SRT),[71] and the Transactional Model of Stress and Coping (TMSC).[72]

The model was specifically designed to explain the emotional factors that facilitate or inhibit parents' decisions to undergo autism genetic testing. The underlying

reason for constructing this combined model was as follows. Albeit preeminent health behavioral theories, such as the HBM and the TPB,[46] have been widely employed in examining the decision-making processes related to genetic testing, they lack an important component in predicting the intention or the behavioral change: emotions.[51,52]

Although less commonly used for genetic testing research, the two health psychology theories, SRT and the TMSC, have been employed to explain how people might exhibit emotional responses and cope with their emotional distress.[51] In this study, I added emotional factors as influences on the intention regarding autism genetic testing among parents of children with ASD.

The salient features of the model included the emphasis on emotional appraisal, coupled with attitudinal factors in assessing parents' decision-making processes.[51] This model highlighted the affect-type variables as important constructs to explain how people's decisions regarding genetic testing/screenings might be shaped.

Key constructs and demographic factors

The key outcome variable in the model was parents' behavioral intention to undergo genetic testing for ASD. Affect-type variables and attitudes were the predictor variables (Figure 2). It is hypothesized that in this model, parents' intention regarding ASD genetic testing was correlated with their emotional responses and attitudes toward the test. Each of the three kinds of variables (i.e., affect-type variables, attitudes, and intention) interacts and connects with one another. The affect-type variables were composed of three subdomains: anxiety, fear, and guilt. Anxiety has three subgroups: trait anxiety, anxiety caused by ASD, and anxiety caused by ASD genetic testing. Based

on past literature,[31,32,35] the parental attitudes are also further divided into three subdomains: (i) attitudes toward testing the immediate family of the affected child, (ii) attitudes toward carrier testing, prenatal diagnosis, and newborn screening, and (iii) attitudes toward testing individuals with a family history of ASD. Additionally, the overall moderating factors such as gender and age might influence these aforementioned factors. Below I will contextualize each of the variables employed in this model.

Affect-type factors. Based on the preliminary findings from my previous work[37] on parents' attitudes toward autism genetic testing and the reasons listed below, I specifically tested three emotional variables: fear, anxiety, and guilt.

Fear. Fear is defined as "an unpleasant emotional state characterized by anticipation of pain or great distress and accompanied by heightened autonomic activity especially involving the nervous system."[80] Both SRT and the TMSC delineate fear as an important predictor in making decisions when people experience a specific health situation.[51] Fear is among the most studied emotion in social science and can be a strong motivator for actions.[81] As Protection Motivation Theory (PMT) theorizes, "fear may be considered a relational construct, aroused in response to a situation that is judged as dangerous and toward which protective action is taken."[82(p157)] Evidence shows that stronger levels of fear can induce greater changes in attitudes, intention, and behaviors.[83] In this study, I tested the specific kind of fear related to negative consequences, privacy issues, genetic stigma, and discrimination caused by ASD genetic testing. Because the sample was from Taiwan, parents' perspectives could possibly be influenced by traditional Chinese culture and societal pressure related to birth defects. From the

perspectives of traditional Chinese culture, children with "birth defect," especially those with mental disorders, might be stigmatized and excluded from the mainstream society.[77]

Anxiety. Anxiety refers to "an emotion characterized by feelings of tension, worried thoughts, and physical changes like increased blood pressure. People with anxiety disorders usually have recurring intrusive thoughts or concerns. They may avoid certain situations out of worry."[84] Although anxiety is not specifically described as an affect-type variable in the constructs of SRT and the TMSC, previous literature has extensively described anxiety as one of the most common emotional responses related to genetic testing.[2,5]Anxiety has two related types: state anxiety and trait anxiety. The former one is a transitory emotional reaction that includes a subjective feeling of nervousness and worry.[85] However, trait anxiety refers to "an enduring characteristic of a person that can be used to explain a person's behavioral consistencies, and determines the likelihood a person will experience anxiety in stressful situations."[86] Previous studies have demonstrated that both state anxiety and trait anxiety were related to undergoing genetic testing for hereditary breast, ovarian, and colon cancers.[5] In this study, both trait anxiety and state anxiety were evaluated.

Guilt. Guilt is a "cognitive or an emotional experience that occurs when a person realizes or believes—accurately or not—that he or she has compromised his or her own standards of conduct or has violated a moral standard and bears significant responsibility for that violation."[87] Compared with anxiety and fear, the feeling of guilt is not well researched in genetic testing research. However, guilt is a prevalent emotional response to hereditary diseases across a wide range of genetic conditions.[88] In the context of

genetic screenings, guilt can be caused by feeling the passing of a faulty gene to children, causing them to have certain genetic diseases or the higher risk for developing the disease. A previous study indicates that the emotional responses to genetic conditions are often characterized by feelings of guilt.[88] Since genetic testing is meant to detect certain diseases running in the family, it is very likely to provoke the feeling of guilt among family members and affect their individual intention of undergoing genetic testing. I assessed guilt associated with having children with ASD and undergoing genetic testing for ASD in this study.

Attitudes. According to Eagly and Chaiken,[89] attitude is defined as the subjective evaluation of an object or action and it can be positive or negative. Attitude is a major determinant elucidated in TPB associated with people's engagement in a specific behavior.[47] Prior studies that explored the domains of TPB show individuals' positive attitudes are correlated with their intention to be tested for colorectal, breast/ovarian cancer, and Alzheimer's disease.[4,46,90] Two dimensions of attitudes can be measured: values and beliefs.[91] This study assessed both dimensions.

Intention. As depicted in the TPB, behavior is directly driven by people's intention. The TPB has been substantially used to predict and explain human behavior in diverse health-related contexts including genetic testing intention.[46] Similar to the TPB, the model of interpersonal behavior (MIP) also emphasizes the main construct of "intention" as the antecedent of individuals' behaviors.[81] The intention to be tested in this study was the intention of undergoing genetic testing for (i) children with ASD, (ii)

siblings of children with ASD, (iii) parents of children with ASD themselves, (iv) their spouses, (v) relatives from their biological family, and (vi) relatives of their spouses.

Demographic factors. As the HBM and TMSC theorize, a variety of socio-demographic factors (such as age, education, income, and ethnicity) might influence people's intention to undergo genetic screening. For instance, interest in and uptake of genetic testing for hereditary cancer has been related to education level, income, and better health insurance coverage.[51] In this study, age, gender, educational level, and annual household income were measured as moderating factors.

Methodology and Study Design

This study is a secondary data analysis of a larger research project initiated by Dr. Lei-Shih Chen in the Department of Health and Kinesiology at Texas A&M University and co-directed by Dr. Tse-yang Huang in the Department of Special Education, National Hsinchu University of Education, Taiwan. The research project, funded by the Chiang Ching-kuo Foundation for International Scholarly Exchange, was conducted with parents of autistic children in Taiwan.

Based on previous literature,[91-94] the research team developed a paper-and-pencil survey to investigate factors affecting the intention of undergoing genetic testing among the study population. This multi-part survey was designed to measure domains, including: (i) demographic information regarding the parents, the ASD-affected children, and the participants' knowledge of ASD genetic testing, (ii) parents and the families' previous experience with genetic services, (iii) affect-type factors that might influence parents' decisions to undergo genetic testing, (iv) parents' perceived benefits in

undertaking genetic testing, (v) parents' perceived barriers in undertaking genetic testing, (vi) perceived behavioral control, (vii) social support, (viii) parents' attitudes toward ASD genetic testing, and (ix) intention to undergo ASD genetic testing. The questionnaire was developed in traditional Chinese (the official language in Taiwan) for the convenience of the participants.

Once drafted, the preliminary survey was sent to two MDs (one family doctor and one genetic pediatrician), one special education expert, and one social behavioral specialist for assessing content validity of the items. After the revision based on the experts' suggestions, the survey was pilot tested in Taiwan. The research team invited seven parents of children with ASD to participate in the cognitive interview, four parents to participate in the retrospective interview, and one parent to participate in both cognitive and retrospective interviews. The questionnaire was then pilot tested with four parents.

Sample and Recruitment

The sampling and recruitment were carried out with the assistance of the Department of Special Education, National Hsinchu University of Education, Taiwan, which represented an extensive network of all the teachers and parents of special education classes in the Hsuichu area. Initially, the research team retrieved the list of all preschools and elementary schools with special education classes in the Hsinchu area and Taoyuan County from the official website of the Department of Education. Then, phone calls were made to the special education/resource teachers working in the

abovementioned schools to obtain the exact number of children with ASD in their schools.

Afterwards, parents of all the children with ASD enrolled in these schools were directly contacted by their special education/resource teachers and invited to participate in this study. Subsequently, a package containing the survey and information sheet was distributed to all the potential participants in the Hsuichu area and Taoyuan County by the teachers. In order to enlarge the sample size, the research team extended this study to Miaoli County and other areas in Taiwan. All participating parents were encouraged to complete the survey and return it to their children's teachers in two or three weeks to meet the deadline for entering the drawing. Each participant had the opportunity to enroll in the drawing and win gift vouchers for their participation. The first-place prize was for eight participants and each of them won a gift voucher of NT$ 3,000 ($100). The second-place prize was for 20 participants and the gift voucher was NT$ 2,000 ($67). Lastly, the third-place prize was for 200 participants and each winner received a gift voucher of NT$ 1,000 ($33).

Altogether 243 schools responded to the study, 862 surveys were sent to participants, and 454 were returned (response rate: 52.8%). Although the approval of an Institutional Review Board (IRB) is not mandatory in Taiwan, all research protocols for this study were approved by the IRB at Texas A&M University.

Measures

As illustrated in Figure 2, the conceptual model that was tested included two types of categories: (i) predicator variables and (ii) the outcome variable. The measures used in this model are summarized below.

Outcome variable: Parents' intention to undergo autism genetic testing

Six items were used in measuring parents' intention to take the test. Parents were asked to respond to the question asking the intention of testing the following people: (i) their children with ASD, (ii) the siblings of their children with ASD, (iii) themselves, (iv) their spouses, (v) relatives from their biological family, and (vi) relatives of their spouses. Possible responses were "very unlikely," "unlikely," "likely," "very likely," "children had been tested before [for participating research]," and "children had been tested before [not for participating research]." Responses were reported on a four-point scale ranging from "very unlikely," "unlikely," "likely," and "very likely."

Predicator variables: Affect-type variables and attitudes toward undergoing ASD genetic testing

First, affect-type variables included three subdomains of measurements: anxiety, fear, and guilt. Anxiety was composed of two elements that consisted of both trait anxiety and state anxiety. Trait anxiety was evaluated by six items. These six items assessed participants' enduring characteristics related to anxiety. State anxiety is the anxiety that lasts for a short period of time and it was evaluated by (i) six items related to the anxiety caused by the disease of ASD, (Anxiety-ASD) and (ii) five items associated with the anxiety caused by ASD genetic testing (Anxiety-GT). Parents were asked to

respond a four-point response format, from strongly agree to strongly disagree (e.g., "Thinking about ASD makes you feel worried" and "Thinking about the possible problems caused by ASD genetic testing, for instance, family disputes from knowing who has the ASD-associated genes and future marriage problems for children with ASD, makes you feel anxious.")

The five-items for fear assessed parents' perceptions about the possible consequences or social, legal concerns related to undergoing autism genetic testing. These items were as follows: "You are fearful of the negative consequences caused by ASD genetic testing (e.g., family disputes from knowing who has the ASD-associated genes and future marriage problems for children with ASD)," "You are fearful of the violation of your privacy caused by the ASD genetic testing (e.g., others might know my test results)," "You are fearful of genetic discrimination caused by ASD genetic testing," "You are fearful of stigmatization caused by ASD genetic testing," and "You are fearful that the general public will not accept individuals with ASD." All the responses in this section were divided into four categories: "Strongly disagree," "Disagree," "Agree," and "Strongly agree."

Guilt was assessed by nine items, for instance, "You feel guilty toward your child, because you brought this child to the world." "You feel guilty toward your child, because he or she has ASD, but you are healthy" "You feel guilty toward your child with ASD, because the biological father/mother or yourself might carry ASD-associated genes, which causes your child's ASD" and "Taking your child with ASD to undergo ASD genetic testing makes you feel guilty." Similar to the assessment with other affect-

type variables, all the responses in this section were also divided into four categories: "Strongly disagree," "Disagree," "Agree," and "Strongly agree."

Second, parents' attitudes toward genetic testing in children were composed of three subdomains: (i) Attitudes toward testing the immediate family, (ii) Attitudes toward carrier, prenatal, pre-implantation genetic diagnosis (PGT), and newborn screening for ASD, and (iii) Attitudes toward testing individuals with family history of ASD. Respondents were asked to indicate their personal beliefs and values in this construct. Items loading on each respective domain were summed to constitute both the belief and the value measures of attitudes. All the responses in this section were also divided into four categories: "Strongly disagree," "Disagree," "Agree," and "Strongly agree."

Data Analysis

Descriptive analyses and exploratory analyses

Before testing the hypothesized model presented in Figure 2, I conducted descriptive and exploratory analyses with the assistance of IBM SPSS version 22. For the variables (both predictor and outcome variables), the psychometric properties were calculated for examining the tendency in the data. Statistical significance of hypothesis testing is reported at the level of 0.05. Whenever possible, the actual *p*-values were provided.[95]

The two-step SEM modeling

After performing the descriptive as well as exploratory analyses, I used a two-step Structural Equation Modeling (SEM) analysis to evaluate whether the data

substantiated the hypothesized model (Figure 2). The reasons for choosing SEM data analysis are as follows: (i) SEM is a multivariate analytical technique designed to test theoretical models,[96] and (ii) SEM can capture the complexity of the social science phenomena more accurately. Testing the theoretical constructs can make contributions to advancement in the field of health behavioral research as theory-based programs are needed. In the model, SEM allows for testing and clarifying the dynamic relationship and interactions among multiple constructs, i.e., affect-type variables (anxiety, fear & guilt), attitudes, and intention. (iii) SEM is advantageous in controlling for the inflation of experimental (Type I) error, which potentially reduces the chance of falsely rejecting the null hypothesis.[96] (iv) Unlike path models that only involve observed variables, SEM is compatible for both observed and latent variables; thus, it can simultaneously test the measurement hypotheses (i.e., whether observed variables are good indicators of underlying factors) and structure relations (i.e., whether there are direct or indirect causal effects among latent factors) in a single model.[97,98]

Sample size needs to be considered adequately in estimating and interpreting the results of SEM. As indicated by Hair and colleagues,[99] the estimated number for a critical sample size that would meet with the requirement for maximum likelihood estimation is 200, with above 500 being "too sensitive" because it might detect too many differences.[100,101] The bare minimum for each estimated construct is 10 observations. In the hypothesized model, I needed to present a minimum of 190 observations. This study incorporated the responses from 444 parents of children, which is "sufficient to detect model fit without becoming 'too sensitive.'"[101(p52)]

The model was assessed with a powerful software package Mplus 7.11 due to its flexibility for handling different data structures and offering FIML (full information maximum likelihood) to deal with missing data. Mplus provides several indexes to diagnose the goodness-of-fit in the structural model, including chi-square, Comparative Fit Index (CFI), the Root Mean Square Root Error of Approximation (RMSEA), and Standardized Root Mean Square Residual (SRMR).[102] Chi-square statistic was not considered a primary index for evaluating the model fit due to a few widely acknowledged limitations, such as a high sensitivity to the sample size.[96] Both CFI and RMSEA have been proven to increase the likelihood of maintaining true-population models and to reduce the chance of rejecting fit models.[101] The cutoff values for these fit indexes were not consistently recommended.[97] However, based on previous literature, I used the following cutoff criteria-values of RMSEA less than .06, SRMR less than .05, and CFI more than .90.[102,103]

The initial SEM step comprised of a confirmatory factor analysis (CFA) which established a measurement model as well as determined latent model constructs.[49] Nine latent model constructs were evaluated through conducting CFA, i.e., trait anxiety by six items, state anxiety caused by ASD by six items, state anxiety caused by ASD genetic testing by five items, fear by five items, guilt caused by carrying ASD genes by three items, guilt caused by undergoing ASD genetic testing by six items, attitude toward testing the immediate family members by five items, attitudes toward carrier, prenatal, PGD, and newborn screening by six items, and intention by six items. The use of a latent variable "allows for the assessment of the measurement error associated with each

construct and the measurement model analysis provides a number of diagnostics to evaluate the validity of the constructs."[49(p435)] I utilized M*plus* MLR estimator as the statistical measurement tool. This estimator served several functions: (i) computed standard errors, (ii) allowed for FIML handling as well as producing maximum likelihood estimations, and (iii) provided diagnosis for model modifications.[49,98]

After establishing an adequate fit for the measurement model, I started to use the structural model to assess the underlying relationship between and among the variables [anxiety→ intention, fear & guilt → intention, attitude → intention]. To determine if the hypothesized model fit the observed data, I examined the following goodness-of-fit indexes: the chi-square, RMSEA, SRMR, based on the cutoff criteria-values of RMSEA less than .06, SRMR less than .05, and CFI more than .90.

Model modification method

Modifications of the model were then made by removing insignificant paths to make the model fit more sufficiently, after defining the final model, I tested the hypotheses by evaluating the reduced models. The researcher tested the hypotheses either by "evaluating the significance and magnitude of path coefficients or by model comparisons using fit statistics."[104(p1252)]

Both theoretical and statistical criteria were used to evaluate the simplification of the full model in Figure 2 into a reduced, more parsimoniously alternative model.[101] To eliminate a variable or a latent construct, one needs to consider theoretical merits as well as statistical properties simultaneously.[101,104]

Results

Participants

The final sample consisted of 444 parents of children with ASD in Taiwan and represented a total response rate of 52.3%. Participants were predominately females (77.5%) with an average age of 39.9 years (SD=5.4, range= 28-63). The average age of their spouses was 41.3 years (SD=5.6, range=26-63). This study involved 468 children diagnosed with ASD (88% were boys). The average age of these children with ASD was 9.5 ± 2.24. Most of the respondents (95.2%) claimed they were born in Taiwan, the remaining (4.8%) were from other countries, for instance, Mainland China, Burma, Indonesia, and Thailand. Participants' educational levels were diverse: most had not completed college (67.3%), and 32.7% had a college degree or postgraduate degrees. The majority of respondents were married (88.7%) and the others were either divorced or single.

Slightly more than half (50.2%) of the participants claimed they did not have full-time jobs (for example, were unemployed, had part-time jobs, or were retired). The remaining (49.8%) reported they had full-time jobs. Altogether, 33.6% of the parents reported making the equivalent of less than $20,000 annual household family income; 40.8% fell between $20,000 and $40,000, 14.6% reported incomes between $40,000 and $60,000, 5.6% fell between $60,000 and $80,000, 2.3% reported incomes over $80,000, and 13 participants (3.1%) refused to report their income.

In terms of their religious beliefs, 25.9% espoused Buddhism, Folk Religion (27.5%), and Christianity (9%). About 21.2% participants claimed to be Atheists or

Non-Believers, and 14.8% reported other religious beliefs. Table 2 summarizes the details of the demographic information of the 444 participants.

Along with having at least one child diagnosed with ASD, 8.1% of parents reported their family members (including themselves) had also been diagnosed with ASD, and 16.3% of parents reported their family members (including themselves) had ASD symptoms or traits of ASD. Similarly, 10.6% of parents reported their spouses' family members (including their spouses) had the diagnosis of ASD and 21.3% parents reported their spouses' family members (including their spouses) had ASD symptoms or traits.

Preliminary analyses

I first examined the data for missing values and patterns. The amount of missing data ranged from 2% to 7.6%. I used the most widely used technique for estimating SEM, full information maximum likelihood (FIML), to deal with the missing data. Under the assumption of multivariate normality, FIML produces parameter estimates that "perform optimally over ad hoc methods such as deletion or meansubstitution."[98(p68)] Following the procedure,[105] I imputed -99 to replace the missing values in the dataset.

Table 2 Study sample characteristics (*N*=444)

Characteristics	*n* (%)
Gender	
Female	334 (77.5)
Male	97 (22.5)
Age of parents, mean ± *SD* (range)	39 ± 5.4 (28-63)
Age of spouses, mean ± *SD* (range)	41.3 ± 5.6 (26-63)
Birth place	
Taiwan	413 (95.2)
Non-Taiwan	21(4.8)
Education	
Below college	292 (67.3)
Above college	141 (32.7)
Marital status	
Married	384 (88.7)
Others (divorced, single)	50 (11.3)
Current Employment Status	
Non-full time	218 (50.2)
Full time	216 (49.8)
Annual household income	
<TW$ 600K (~US$20K)	143 (33.6)
TW$ 600K (~US$20K) to < TW$1200K (~US$40K)	174 (40.8)
TW$1200K (~US$40K) to < TW$1800K (~US$60K)	62 (14.6)
TW$1800K (~US$60K) to < TW$ 2400K (~US$80K)	24 (5.6)
≥TW$ 2400K (~US$80K)	10 (2.3)
Others	13 (3.1)
Religion	
Buddhism	112 (25.9)
Folk religions	119 (27.5)
Atheists or Non-believers	92 (21.2)
Others	64 (14.8)
Christian (catholic)	39 (9)
I-kuan Tao	7 (1.6)

Note. The sample size (*N*=444) was used for the preliminary stage of the data analysis.

Based on Mardia's measure of relative multivariate kurtosis (MK),[95] I tested the normality of the variables and moderators (emotional factors, attitudes, and intention, as well as age, gender, education and income). I calculated the psychometric properties for emotions, attitudes, and intention (see Table 3 for details). The skewness and kurtosis

coefficients ranged from +1 to -1. The results indicated that the data did not violate the normality assumption.[95]

Table 3 Psychometric properties of all psychological variables

Variable	No. items	Response Range	M	SD	Skewness	Kurtosis
Emotions						
Trait anxiety	6	1-4	2.474	.538	-.019	.610
ASD anxiety	6	1-4	2.562	.617	.125	.287
ASD-GT anxiety	5	1-4	2.344	.619	.337	.717
Fear	5	1-4	2.641	.603	-.032	.228
Guilt	9	1-4	2.284	.496	.063	.712
Attitude						
Attitude A	5	1-16	7.873	3.458	.719	.347
Attitude B	6	1-16	6.076	2.995	.900	.898
Attitude C	3	1-16	9.244	3.564	.308	-.498
Intention	6	1-6	2.499	.662	.128	.528

Anxiety was primarily assessed by three subscales: trait anxiety (6 items), state anxiety caused by ASD (6 items), and state anxiety caused by ASD-GT (5 items). Higher scores indicated a higher level of anxiety. The composite mean score for trait anxiety was 2.48 (*SD*=.54), ASD anxiety 2.56 (*SD*=.62), and ASD-GT anxiety 2.34 (*SD*=.62). The anxiety statements with which most parents agreed were: "Thinking of ASD makes you feel worried" (75.8%; ASD anxiety), "You easily get worried" (61.8%, trait anxiety), and "Thinking about the possible problems caused by ASD genetic testing makes you feel stressed and worried during the past year" (50.3%, ASD-GT anxiety).

Fear & guilt was reflected by one fear scale (5 items) and two guilt scales (guilt 1 with three items, guilt 2 with 6 items). The composite mean score for fear was 2.64 (*SD*=.60) and for guilt was 2.28 (*SD*=.50). The fear statements with which most

participants agreed were: “You are fearful that the general public in Taiwan will not accept individuals with ASD” (70.4%). The guilt statements with which most participants agreed were: “You feel guilty toward your child with ASD, because you brought this child to the world” (65.1%). All the statements assessing emotional factors and the percentages of the agreement with these statements are listed in Table 4.

Attitudinal factors were examined with three subscales containing 14 items assessing respondents’ beliefs and another 14 items capturing respondents’ values. Table 5 depicts the frequency of agreement with each of the items. I first asked the respondents about their beliefs regarding undergoing genetic testing for ASD; subsequently, I asked about their values (how important they considered the testing to be). The belief statements with which the majority of the parents agreed was: “ASD genetic testing should be mandatory for newborn screenings” (84.8%), whereas the statement with the least amount of agreement was “All the relatives of children with ASD should undergo ASD genetic testing” (22.2%). Similar to these percentages, was the pattern of responses to the items assessing values. I used combined scores on the belief and value items for analyzing respondents’ attitudes. The composite mean score for Attitude A was 7.83 (*SD*=3.45), Attitude B was 6.07 (*SD*=2.99), and Attitude C was 9.24 (*SD*=5.56). Each of these items and their percentage distributions are shown in Table 5.

Table 4 Emotional factors (trait anxiety, state anxiety caused by ASD, state anxiety caused by ASD genetic testing, fear, and guilt) and the percentages of the individual statement

	Strongly Disagree (%)	Somewhat disagree (%)	Somewhat Agree (%)	Strongly Agree (%)
Trait anxiety				
You easily get worried	5.1	33.1	54.3	9.7
You are easily inclined to feel anxious (e.g., do not sleep well, irregular diet, irritable, etc.)	6.7	40.4	42.3	10.6
You tend to be pessimistic	11.5	61.2	24.5	3.8
You easily get worried	5.1	33.1	54.2	7.6
You cannot handle emergencies calmly	9.1	61.9	25.2	3.7
You felt nervous or worried during the past year	8.9	42.1	40.0	8.9
State anxiety caused by ASD				
Thinking of ASD makes you feel nervous	5.3	40.6	43.5	10.6
ASD causes you to feel anxious (e.g. do not sleep well, irregular diet, irritable, etc.)	6.5	45.9	38.0	9.7
ASD makes you feel pessimistic about life	7.4	51.4	33.9	7.4
Thinking about ASD makes you feel worried	3.7	20.5	63.2	12.6
Thinking about ASD can make you feel uneasy	6.2	52.7	34.2	6.9
Thinking about ASD made you feel stressed and worried during the past year	5.8	39.4	46.1	8.8
State anxiety caused by ASD genetic testing				
Suppose ASD genetic testing is available in the hospitals of Taiwan. Thinking about the possible problems caused by ASD genetic testing				
makes you easily feel nervous	7.2	49.7	38.1	5.1
makes you feel anxious	7.2	57.4	30.1	5.3
makes you feel pessimistic about life	9.0	63.8	22.3	4.9
makes you feel stressed and worried during the past year	6.7	42.9	44.3	6.0
makes you feel uneasy in your daily life	7.9	63.4	25.2	3.5

Table 4 Continued

	Strongly Disagree (%)	Somewhat disagree (%)	Somewhat Agree (%)	Strongly Agree (%)
Fear				
You are fearful of the negative consequences caused by ASD genetic testing (e.g., family disputes from knowing who has the ASD-associated genes and future marriage problems for children with ASD)	6.9	44.0	41.5	7.6
You are fearful of the violation of your privacy caused by the ASD genetic testing (e.g., others might know my test results)	4.1	42.4	45.6	8.0
You are fearful of genetic discrimination caused by ASD genetic testing	3.7	40.9	45.3	10.2
You are fearful of stigmatization caused by ASD genetic testing	3.7	34.3	50.8	11.2
You are fearful that the general public in Taiwan will not accept individuals with ASD	2.8	26.8	54.8	15.6
Guilt				
You feel guilty toward your child with ASD, because you brought this child to the world	6.2	28.8	51.6	13.5
You feel guilty toward your child with ASD, because he or she has ASD, but you are healthy	8.7	37.0	44.7	9.6
You feel guilty toward your child with ASD, because the biological father/mother or yourself might carry ASD-associated genes, which causes your child's ASD	9.8	47.1	35.7	7.3
Taking your child with ASD to undergo ASD genetic testing makes you feel guilty	11.7	68.3	18.6	1.4
Taking the siblings of your child with ASD to undergo ASD genetic testing makes you feel guilty	11.1	66.8	20.0	2.1
Taking the biological father of your child with ASD to undergo ASD genetic testing can make you feel guilty	11.3	66.9	18.6	3.2
If you undergo ASD genetic testing, you feel guilty	13.8	69.3	15.6	1.4
Taking your biological family members to undergo ASD genetic testing makes you feel guilty	10.8	60.8	25.2	3.2
Taking the biological family members of the biological father of your child with ASD to undergo ASD genetic testing makes you feel guilty	10.7	58.3	26.6	4.4

Table 5 Percentage distribution of the attitudes toward ASD genetic testing among parents of children with ASD

	Attitudes toward ASD genetic testing			
	Beliefs (%)		Values (%)	
Statements regarding parents' attitudes toward ASD genetic testing	Disagree	Agree	Not very Important	Important
Attitude A: testing the immediate family				
All children diagnosed with ASD should undergo genetic testing.	33.1%	66.9%	29.9%	70.1%
All children with characteristics or traits with ASD should undergo genetic testing.	35.5%	64.5%	31.2%	68.8%
All the siblings of child with ASD should undergo ASD genetic testing.	48.4%	51.6%	41.5%	57.5%
All the biological mothers of child with ASD should undergo ASD genetic testing.	39.4%	60.6%	37.5%	62.5%
All the biological fathers of child with ASD should undergo ASD genetic testing.	39%	60.9%	37.5%	62.5%
Attitude B: carrier, prenatal, pre-implantation genetic diagnosis (PGT),and newborn screening				
All the mothers of children with ASD should undergo ASD genetic testing during next pregnancy.	23.7%	76.3%	21.7%	78.3%
All the newborns of the parents of children with ASD should undergo genetic testing.	29.8%	70.2%	27.8%	72.2%
ASD genetic testing should be included in pre-marital heath examination.	29.8%	70.2%	29.0%	71%
All pregnant women should undergo ASD genetic testing during prenatal testing.	28.8%	71.2%	28.5%	71.5%
ASD genetic testing should be part of pre-implantation genetic diagnosis.	27%	73%	26.1%	73.9%
ASD genetic testing should be mandatory for newborns screenings.	15.2%	84.8%	15.9%	84.1%
Attitude C: testing individuals with family history of ASD				
All the relatives of the child with ASD should undergo ASD genetic testing.	77.8%	22.2%	73%	27%
An individual with at least one immediate family member of ASD (parents, siblings, or children) should undergo ASD genetic testing.	65%	35%	40.4%	59.6%
An individual with at least one family member of ASD (grandparents, uncles, aunts, cousins) should undergo genetic testing.	62.8%	37.2%	61.3%	38.7%

Intention was measured by six items assessing parents' likelihood to test with a possible score of 6. For this scale, great intention to undergo the test was indicated by higher scores. As indicated in Table 6, the mean score for each of the intention items was 3.15 (*SD*=0.83), 2.73 (*SD*=0.94), 2.86 (*SD*=0.92), 2.58 (*SD*=0.99), 1.92 (*SD*=.072), and 1.79 (*SD*=0.68) respectively. Overall, parents indicated that they would be "likely" or " very likely" to "bring your child with ASD to undergo ASD genetic test" (86.8%), "undergo the testing yourself" (68.5%), and "take your children without ASD (siblings of child with ASD) to undergo ASD genetic testing" (62.4%). Fewer parents indicated that they would bring "the relatives of your spouse to undergo genetic testing" (13.3%). The actual statements used in this survey and the frequency counts are reflected in Table 6.

Table 6 Percentage distributions of the likelihood of undergoing ASD genetic testing

	Likelihood of Undergoing ASD genetic testing (%)	
Individuals involved…	Likely	Unlikely
Your child with ASD	86.8%	13.2%
Your child without ASD (siblings of your child with ASD)	62.4%	37.6%
Yourself	68.5%	31.5%
Your spouse	52.5%	47.5%
Relatives from your biological family	18.4%	81.6%
Relatives of your spouse	13.3%	86.7%

Note. The answer options 'likely' and 'very likely' were combined into one category as were the options 'unlikely' and 'very unlikely.'

Confirmatory factor analysis

Correlation and reliability. Table 7 demonstrates the correlation matrix for these items related to emotions, attitude, and intention as well as participants' demographic information. The individual items comprising emotional and attitudinal factors primarily correlated among themselves. For instance, the highest correlation was found between the items for Attitude A and Attitude B ($r = 0.679$, $p<0.01$). ASD anxiety and trait anxiety ($r = 0.623$, $p<0.01$) were highly correlated also. In addition, the correlations between fear & guilt were significant ($r=0.442$, $p<0.01$), albeit not as high. These results provided evidence for hypothesized latent constructs in this study.

Construct validity. Because the model involved four latent variables, it was important to first establish measurement adequacy before testing the structural relationships in Figure 2. I conducted a series of confirmatory factor analyses (CFAs) to evaluate the factorial validity of the measurement scales used in this study. All factor loadings were significant at the .01level. Detailed information is demonstrated in Table 8.

Table 7 Correlation matrix for individual items related to the composite scores for gender, age, income, education, trait anxiety, ASD anxiety, GT anxiety, fear, guilt, Attitude A, Attitude B, and Attitude C, and intention

Indicator	Gender	Age	Income	Education	Trait anxiety	ASD Anxiety	GT Anxiety	Fear	Guilt	Attitude A	Attitude B	Attitude C	Intention
Gender													
Age	.328**												
Income	.026	.200**											
Education	.039	.153**	.443**										
Trait anxiety [a]	-.188**	-.099*	-.067	-.068									
ASD Anxiety [b]	-.089	.030	.009	.004	.623**								
GT Anxiety [C]	-.106*	-.102*	-.145**	-.223**	.458**	.567**							
Fear	-.075	-.053	-.082	-.120*	.265**	.343**	.585**						
Guilt	.017	-.008	-.121*	-.181**	.296**	.363**	.441**	.442**					
Attitude A [d]	-.032	-.129*	-.119*	-.164**	.144**	.129*	.095	.031	-.039				
Attitude B [e]	-.072	-.146**	-.038	-.101	.080	.070	.086	-.007	-.076	.679**			
Attitude C[f]	-.059	-.121*	-.054	-.120*	.095	.137**	.103*	.066	.035	.667**	.649**		
Intentions	-.001	-.094	.074	.040	.132**	.080	.065	-.092	-.057	.458**	.429**	.349**	.456**

***Note*. ** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed) ;[a] Anxiety related to the anxiety level as a personal characteristic;**
[b] Anxiety caused by Autism Spectrum Disorders; [c] Anxiety caused by genetic testing for ASD;[d] Attitudes toward testing the affected child and family members;
[e] Attitudes toward carrier testing, parental diagnosis and newborn testing; [f] Attitudes toward testing individuals with family history of ASD;

Table 8 Range of the standardized factor loadings, indicator reliability, and *N* of items for the Confirmatory Factor Analysis (CFA) model

Indicator	Standardized Factor Loading	Indicator Reliability (R^2)	*N* of Items
Trait anxiety	.582-.754	.850	6
ASD anxiety	.762-.850	.922	6
GT anxiety	.853-.929	.946	5
Fear	.648-.905	.895	5
Guilt1	.596-.924	.884	3
Guilt 2	.776-.874	.862	6
Attitude A	.862-.900	.946	5
Attitude B	.773-.853	.906	6
Attitude C	.580-.899	.824	3
Intention	.736-.912	.894	4

The results showed that, as I hypothesized, the measurement items testing trait anxiety loaded on one factor (range of factor loading: 0.582-0.754; 6 items), ASD-related anxiety loaded on one factor (range of factor loading: 0.762-0.850; 6 items) and GT-anxiety caused by ASD genetic testing also loaded on one factor (range of factor loading: 0.853-0.929, 5 items). Similarly, all five items regarding fear were loaded on one factor (range of factor loading=0.648-0.905). In addition, among the nine items for "guilt," the first three items–Guilt 1 loaded as one factor (range of factor loading: 0.596-0.924, three items), and the six remaining items–Guilt 2 loaded as a second factor (range of factor loading=0.776-0.874). The three items for Guilt 1 refer to the feeling of guilt brought by passing the ASD-associated genes to the family members; the remainders represented Guilt 2, which mainly discussed the feeling of guilt about taking the immediate and extended families to undergo autism genetic testing.

Factor loading also supported the hypotheses in dividing the "attitude" items into three categories. These three categories included Attitude A: Attitudes toward testing the immediate family members (range of factor loading=0.862-0.900; 5 items); Attitude B: Attitudes toward carrier, prenatal, PGD, and newborn screening (range of factor loading: 0.773-0.853, 6 items); and Attitude C: Attitudes toward testing individuals with family history of ASD (range of factor loading: 0.580-0.899, 3 items).

Although all these scales were adopted from previous literature, the initial CFAs of the intention scale (item1-6) showed two items that form intention did not load on the latent construct at an acceptable level (i.e., with loading below 0.45). Based on this finding and a recently published psychometric analysis, I removed these two items from the scale. The range of the factor loading for the remaining four items was 0.736-0.912.

A subsequent CFA containing all four constructs showed that the latent construct "anxiety," "fear & guilt," "attitudes," and "intention" and their observed measures were well supported. The resulting CFA fit statistics included a chi-square =2803.9, df =1112, p<.001, CFI=0.92, RMSEA=0.04, 90% confidence interval (CI) for RMSEA [0.043 0.049]), SRMR: 0.06. All fit indexes fell within acceptable ranges and all the factor loadings are significant (> 0.7).

Table 7 also shows the internal consistency of these observed items using Cronbach's alpha coefficient. All the indexes reached above the acceptance level. These indexes supported the use of these items to measure anxiety, fear & guilt, attitudes, and intention in this dataset. The Cronbach's alpha was as follows: trait anxiety (.85), ASD

anxiety (.92), GT anxiety (.95), fear (.90), guilt 1 (.88), and guilt 2 (.86), Attitude A (.95), Attitude B (.91), Attitude C (.82), and intention item 1-4 (.89).

Structural model

After confirming that the measurement model exhibited appropriate fit, I performed SEM to verify the structural relationships in this study.[49] I replaced the latent correlations in the measurement model. The hypothesized relationships were indicated in Figure 3.

Research question 1. Does the model adequately explain parents' intention to undergo autism genetic testing? If this model is not adequate, what are the variables to be included in the refined model?

The integrative model in this study contained four latent variables, i.e., anxiety, fear & guilt, attitudes, and intention. Latent variable anxiety expressed parents' tendency to experience anxiety, state anxiety caused by ASD, and state anxiety caused by ASD genetic testing. Latent variable fear & guilt was predicted by items depicting parents' fear about the social or legal implications caused by ASD genetic testing, guilt caused by passing down the genes associated with ASD, and guilt associated with undergoing genetic testing for ASD. Latent variable attitudes were predicted by three kinds of attitudes that included attitudes toward testing the immediate family of the affected children, attitudes toward carrier, prenatal, PGD, and newborn screening. Latent variable intention reflected the likelihood that parents might bring their child with ASD, bring their children without ASD, themselves, and their spouses to undergo ASD genetic testing. The result indicated that the model fit the data well: chi sq=2224.263, *df*=1109,

p<.001, CFI: 0.917, SRMR: 0.06, RMSEA: 0.048, 90% confidence interval (CI) for RMSEA [0.043, 0.049]. This model indicated that the hypothesized model provided a parsimonious but sufficient explanation of the observed data.

As is shown in Figure 3, parents' intention to undergo autism genetic testing had two predictors: anxiety, fear and guilt, when controlling for parents' age, gender, income, and education. Anxiety (β=0.46, p<.0001) including trait anxiety, anxiety caused by ASD, and anxiety related to ASD genetic testing can positively influence parents' intention to undergo ASD genetic testing. For instance, the greater anxiety parents have with regard to ASD genetic testing, the more likely they might undergo the test. Fear and guilt (β= -0.42, p=<.0001) appeared to negatively predict parents' intention to undergo ASD genetic testing. The more fear or guilt parents have, the less likely they might make the decision to undergo the test. Attitudes, which were predicted by the three kinds of attitudes (see Figure 3) did not predict behavioral intention to undergo the test. Older parents appeared less likely to undergo autism genetic testing, whereas parents with higher incomes were more likely to undergo the test.

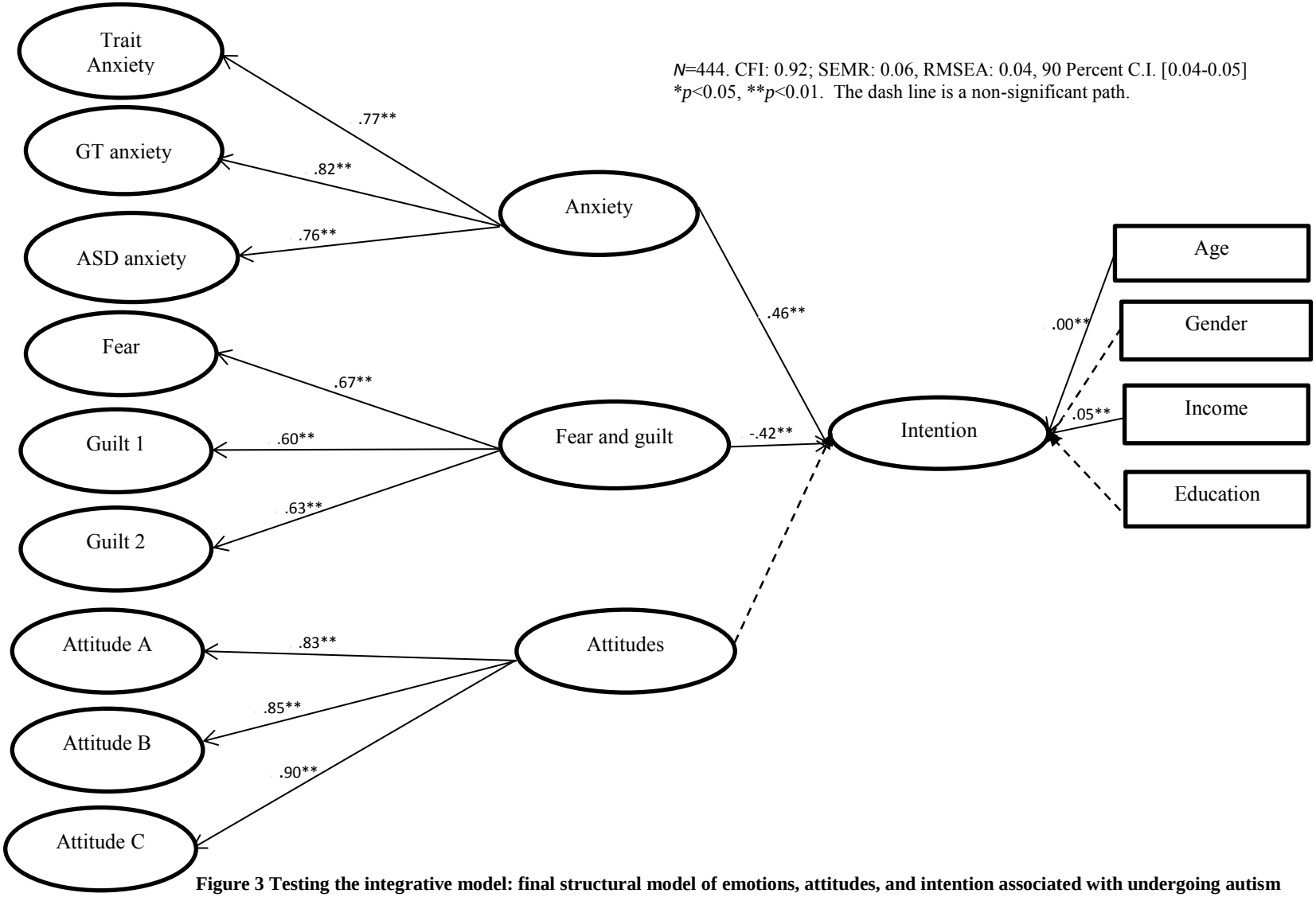

Figure 3 Testing the integrative model: final structural model of emotions, attitudes, and intention associated with undergoing autism genetic testing.

Research question 2. Will the model exhibit different patterns and values depending on participants' demographic information (i.e., age, gender, education, and income)?

I also examined the structural variation of anxiety, fear & guilt, attitudes, and intention using age, gender, education and income as moderators. In order to verify the structural invariant, I used MLR estimators to simultaneously assess both the constrained and unconstrained models. The structural paths were equally restricted across dichotomized groups, i.e., age≥ 35 years and < 35 years, male and female, high and low income (≥ 40K, <40K), as well as high education and low education (college graduates or below college). However, none of the moderating effects of age, gender, education, and income yielded Satorra-Bentler scaled chi-square value. The diagnosis from the output indicated no convergence due to exceeded interactions. These phenomena might be caused by the sparse of data for the dichotomized groups. Therefore, I was not able to infer age, gender, education, and income interacted significantly with the latent variables.

Research question 3. Which variables in the model can best predict parents' intention to undergo genetic testing for ASD? Suppose both emotions and attitudes can predict intention, how much variability can be explained by parents' emotions (including anxiety, fear, and guilt)? How much variability can be explained by parents' attitudes toward testing?

In the model, the largest predictor of intention was anxiety (β=0.46, p<.0001). In addition, fear & guilt were also predictors (β= -0.42, p<.0001). The use of the squared

multiple correlation (R^2), "the percentage of variance explained by one or more predicator variables on a dependent variable—in SEM is an ongoing area of research"[98(p71)] and a trend in explaining social phenomena. According to the model results, 10% of variance in parents' intention to undergo genetic testing for ASD can be explained by their emotional responses: anxiety, fear, and guilt.

Discussion

To the best of my knowledge, this is the first theory-driven study that examined emotional (anxiety, fear, and guilt) and attitudinal predictors of the intention to undergo ASD genetic testing among parents of children with ASD in Taiwan. The purpose of this study was not to promote the use of genetic testing for ASD, but to understand the factors that might influence parents' decisions with regard to undergoing ASD genetic testing before its full implementation in Taiwan. The findings extended existing literature on decision-making about undergoing genetic testing for ASD in two ways.

First, I used an integrative model and SEM analyses to understand how emotions and attitudes might influence parents' intention to undergo ASD genetic testing. The previous literature used validated health theories, for instance, the Theory of Planned Behavior and the Health Belief Model, for understanding the factors predicting intention toward genetic testing.[51] However, emotional factors have not been adequately addressed in these theoretical frameworks.[52] Notably, this study answered the call from the National Health Genomics Research Institute to expand beyond the existing conceptual models for exploring stronger predictors of genetic test decisions.[49] I added

affect-type variables, a largely overlooked factor in genetic testing decisions, as key constructs in the model.

It is noteworthy that the findings demonstrated the negative influence of fear and guilt on parents' intention to undergo ASD genetic testing. Past studies have shown that fear or guilt might potentially lead to a decline in genetic tests or refusal to participate in genetic research.[92,106] The particular kind of fear or social stigma in this study was associated with social, legal, and ethical concerns related to testing. For instance, I focused on assessing fear of genetic discrimination as well as fear of social stigma caused by genetic testing. In addition, I specifically measured guilt caused by passing the ASD-associated genes onto the affected child and guilt caused by undergoing genetic testing. The specific kinds of fear and guilt I assessed might be attributed to the culture and societal factors related to having a child with genetic disabilities.[106-108]

Related to the specific kind of fear and guilt I tested, the results might be explained by the unique Taiwanese culture and societal pressures related to having a child with genetic disabilities. These particular influences might play an important role in parents' decisions to undergo ASD genetic testing. Unlike the Western culture, the Taiwanese culture is traditionally embedded within Confucianism and influenced by the centrality of "face."[109] Parents of children with genetic disorders might consider having a child with disability a family stigma. Therefore, they might be inclined to forgo genetic testing because testing might verify they gave birth to "an abnormal child."[77] In addition, similar to other Asian societies, the Taiwanese society might also demonstrate discriminatory attitudes toward people with mental illness.[110] The findings were

consistent with previous studies showing that Asian cultures might significantly influence the decision whether to undergo genetic testing or utilize genetic services.[77] Also, autism genetic testing is still not available and officially recommended in Taiwan. Therefore, the feeling of fear and guilt might be caused by insufficient understanding about these yet-unknown tests.

The model tested in this study demonstrated that anxiety positively influenced parents' intention to undergo ASD genetic testing. The findings were in line with another study by Narcisa et al[42] that indicated the potential for reduced anxiety was one primary reason for parents' interest to be tested for ASD. The study showed that higher levels of anxiety were positively associated with increased likelihood of undergoing ASD genetic testing. This phenomenon can be potentially explained by stress and coping theories.[111]According to these frameworks, parents might consider undergoing ASD genetic testing as a coping mechanism.[111] For this particular sample, anxiety might be a positive influencing factor, predicting parents' test intention, once ASD genetic testing becomes available in Taiwan, researchers should examine whether testing does, in fact, function as a coping strategy.

A second way that the findings contributed to the existing literature for genetic testing was by having direct implications for public health genomics education and practice. The model suggested that educational interventions might be important based on the identified relationships among the factors. Although the sample did not allow me to generalize to the entire Taiwan population, the study provided support to the need of pre-test counseling and genetic education among the general public in Taiwan.

Despite limited generalizability, the findings also informed communications related to ASD genetic testing among health-care providers and parents of autistic children. For instance, in order to provide better genetic services for families affected with ASD, the multi-disciplinary team involved in the diagnostic process with ASD, such as pediatricians and psychologists, should proactively take into consideration the possible emotional distress among parents of children with ASD. To effectively address parents' fear, guilt, and anxiety, pre-test counseling or health education is needed; for example, using different modes of education such as website, DVD, lectures, and brochures to address negative emotions associated with the test is recommended.

Since healthcare providers or health educators can play a critical role in shaping people's decision to undergo genetic testing, it is also important to educate them and enhance their knowledge so that they can explain the tests to the parents of children with ASD. Health care providers' insufficient knowledge regarding genetic testing has been well documented in previous literature.[112-114] Less researched has been health care providers' ability to manage patients' emotions surrounding testing. Furthermore, to manage parents' concerns resulting from fear, policymakers and legislators also need to consider genetic discrimination laws in Taiwan, thus, alleviating the fear of genetic testing for ASD and ensuring the proper use of ASD genetic services. Laws and regulations that prevent the genetic discrimination have been in effect in the United States since 2008.[115] But similar regulations or laws need to be developed in Taiwan for protecting people from being genetically discriminated by employers or the society.

Moreover, race/ethnicity can be important factors that affect individuals' attitudes towards genetic testing. As the study indicated, the majority of the sample has favorable attitudes toward ASD genetic testing and these data supported a recent study on attitudes toward new genetic technology in Taiwan, which indicated that the general public in Taiwan held a positive attitude toward genetic testing.[77] Parents' positive attitudes toward testing were in line with the findings from our previous study that showed 67% of the participants (parents of children with ASD in the United States) exhibited favorable attitudes toward autism genetic testing and Asian parents tended to be more supportive of this test.[37] In this present study, I tested three kinds of attitudes: (i) attitudes toward testing the immediate family members of the child with ASD; (ii) attitudes toward carrier, prenatal, PGD and newborn screening; and (iii) lastly attitudes toward testing individuals with family health history. Parental positive attitudes might be explained by the fact that parents' perceived benefits of ASD genetic testing outweighed the perceived barriers. For instance, test proponents might expect that early detection provides information that can be used for medical interventions that can improve the conditions of their autistic children.

As discussed above, Chinese families are less likely to accept individuals with psychological/mental disorders. Therefore, parents might pursue genetic testing to make more informed reproductive decisions from ASD genetic testing. If the test results come positive, parents might have a high probability to terminate their pregnancies. Furthermore, the overall supportive attitudes toward ASD genetic testing could be explained by the perspectives of "eugenics" in the Asian society.[116,117] The findings were

also consistent with prior studies indicated Chinese Americans intended to have a stronger likelihood of supporting genetic research.[118,119] To ensure the appropriate utilization of ASD genetic testing, it is critical to examine the multiple factors that affect the decisions with ASD genetic testing prior to the provision of ASD genetic testing in Taiwan.

Interestingly, the findings showed that parents were highly supportive and very likely to take their affected children to undergo ASD genetic testing. However, a favorable attitude toward testing would not affect the decisions to take the test. This result differed from numerous previous studies testing the key variables (attitudes and intention) from the Theory of Planned Behavior, which identified the strong linkage between people's attitudes and their intention to undergo genetic testing.[76,120,121]

There were also trends toward participants with higher annual household incomes having greater interest in testing. Socio-economic status (SES) has been reported to be related with the decisions to undergo genetic testing, and previous research has shown that those with higher SES are more likely to use genetic services.[121,122] The findings indicated that heath inequities need to be addressed before implementing autism genetic services in Taiwan. We need to provide more resources for those with poor access to the genetic services and be aware of offering more affordable genetic services to patients with low SES.

Several limitations of this study deserve attention when interpreting the results from this study. First, this is a cross-sectional study conducted among a convenience sample. Since the participants were recruited through teachers at public schools listed on

the official website of the Department of Education in Taiwan, the sample might not adequately collect responses from autistic children's parents in private schools. However, we did make the attempt to reach every school child's parents in the designated area including private schools. Due to the location of this study, the generalization of the results was limited and the interpretation of these results needs to be considered more cautiously. Another limitation was that I only assessed pre-test emotional and attitudinal factors related to undergoing autism genetic testing; the future studies should also examine other predictors of intention, such as, perceived benefits, perceived barriers, and social norms. Also, although I identified that the majority of the parents hold positive attitudes toward genetic testing for ASD, the underlying reasons for parents' optimistic attitudes should be further studied.

Implications for Future Research

Several implications for future study in this area are noteworthy. First, this study assessed the impact of anxiety, fear, guilt, and attitudes on intention. However, social norms, perceived benefits, perceived barriers, and perceived behavioral control might also have influence on parents' intention to undergo genetic testing for ASD. Therefore, these factors might need to be examined further.

Second, this study evaluated parents' pre-test emotional responses to genetic testing for ASD; future studies should consider measuring both pre-test and post-test emotional responses when the test is available in Taiwan. In order to maximize the quality of counseling services and educational efforts in this research area, more studies are needed that focus on the specific needs of parents of children with ASD.

Third, the sample was a convenience sample recruited from Taiwan, thus the model might not be applied to other ethnic groups in other regions or countries. More empirical testing is needed to assess its application for parents of children in a wider range of geographical locations. It is of utmost importance that the theoretical model development should be in line with the actual understanding in diverse settings.

CHAPTER IV

CONCLUSIONS

The purpose of this dissertation was threefold: (i) to systematically synthesize the empirical literature regarding the emotional factors, attitudes, and intention associated with ASD genetic testing and summarize the methodological quality of the included studies, (ii) to examine the psychological factors, attitudes, and intention regarding ASD genetic testing among the sample of autistic children's parents in Taiwan, and (iii) to utilize structural equation modeling analyses to examine the associations between the emotions, attitudes, and intention, as well as test the overall "fit" of the model in this study.

This dissertation is composed of two studies that validate and support each other. Chapter II (the systematic literature review) informed Chapter III (the empirical study on emotional factors and attitudinal factors on intention to undergo genetic testing for ASD) in a few ways. These included the selection of targeted variables, examination of direct effects, and methodological quality issues, such as the use of theoretical frameworks and reporting of data's psychometric properties. Results from Chapter III, in turn, supported and validated those of Chapter II.

For instance, in Chapter II, a number of negative emotional factors, for example, fear, lack of trust, and feeling uncertain, were identified to be associated with people's intention with genetic testing. Chapter III showed significant associations between negative emotions (anxiety, fear, and guilt) and the test intention to undergo genetic

testing for ASD. These results align with each other and jointly contribute to theory development by adding emotional predicators (such as anxiety, fear, and guilt) in the dominant health behavioral theories. The expanded framework better reflects empirical evidence and opens doors to reintegration of theories to explain decision-making processes related to genetic testing.

Furthermore, as noted in Chapter II, there is a significant literature gap in the studies that have explored the associations between emotional factors and the genetic test decisions and focused on the attitude and intention for ASD genetic testing among the affected populations. Chapter III helped to close the gap by providing theory-based evidence specifically addressing the emotions, attitudes, and intention among a sample of 444 parents of children with ASD in Taiwan. Chapter III also confirmed anxiety, fear, and guilt were associated with parents' test intention, and attitudes did not appear to be a factor in the decision-making process.

This study is useful in providing insight about parents' perspectives regarding ASD genetic testing prior to the full implementation of this test in Taiwan. It will also contribute to the development of better genetic services and research in Taiwan. The information revealed that it is important to design more culturally appropriate educational programs for parents of children with ASD in Taiwan. Most participants postulated favorable attitudes toward ASD genetic testing and were likely to take their affected children for ASD genetic testing. However, compared to the situation in the United States, where ASD genetic testing is offered as a routine health care service, there is a lack of valid and reliable ASD genetic testing procedures in Taiwan. Given

that the parents of children with ASD were interested in ASD genetic testing, there is an immediate need to develop valid and reliable testing methods in Taiwan and provide culturally appropriate pre-test educational interventions for parents of children with ASD.

Future studies on decisions about undergoing genetic testing can benefit from addressing gaps in research pointed out by this dissertation. More studies are needed to (i) examine emotions related to the intention to undergo genetic testing for ASD among the affected populations; (ii) test theories that integrate emotions and other under-investigated factors such as perceived barriers, perceived benefits, and social environmental factors associated with the test intention; and (iii) evaluate moderation effects of demographic information. Future studies will also benefit from addressing methodological quality dimensions, such as the employment of more rigorous designs and the use of comparison groups. Addressing these dimensions is crucial for achieving a clearer understanding of parents' intention with regard to genetic testing for ASD for ASD-affected families and communities in a wider range of geographical locations.

REFERENCES

1. Miller DT, Adam MP, Aradhya S, et al. Consensus statement: chromosomal microarray is a first-tier clinical diagnostic test for individuals with developmental disabilities or congenital anomalies. *Am J Hum Genet.*2010;86:749-764.
2. Lerman C, Croyle RT, Tercyak KP, Hamann H. Genetic testing: psychological aspects and implications. *J Consult Clin Psychol*. 2002;70:784-797.
3. Metcalfe A, Werrett J, Burgess L, Clifford C. Psychosocial impact of the lack of information given at referral about familial risk for cancer. *Psycho-oncology.* 2007;16:458-465.
4. Jones DL, Clayton EW. The role of distress in uptake and response to predisposition genetic testing: the BMPR2 experience. *Genet Test and Mol Biomarkers.* 2012;16:203-209.
5. Vadaparampil ST, Ropka M, Stefanek ME. Measurement of psychological factors associated with genetic testing for hereditary breast, ovarian and colon cancers. *Fam Cancer.* 2005;4:195-206.
6. Borry P, Stultiens L, Nys H, Dierickx K. Attitudes towards predictive genetic testing in minors for familial breast cancer: a systematic review. *Cric Rev Oncol Hematol.* 2007;64:173-181.

7. Schlich-Bakker KJ, Ten Kroode HF, Ausems MG. A literature review of the psychological impact of genetic testing on breast cancer patients. *Patient Educ Couns.* 2006;62:13-20.

8. Green JM, Hewison J, Bekker HL, et al. Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review. *Health Technol Assess.* 2004;8:1-4.

9. Hill MK, Archibald AD, Cohen J, Metcalf SA. A systematic review of population screening for fragile X syndrome. *Genet Med.* 2010;12:396-410.

10. Heshka JT, Palleschi C, Howley H, et al. A systematic review of perceived risks, psychological and behavioral impacts of genetic testing. *Genet Med.* 2008;10:19-32.

11. Aatre RD, Day SM. Psychological issues in genetic testing for inherited cardiovascular diseases. *Circ Cardiovas Genet*. 2011;4:81-90.

12. Miles JH. Autism spectrum disorders--a genetics review. *Genet Med.* 2011;13:278-294.

13. Vande Wydeven K, Kwan A, Hardan AY, Bernstein JA. Underutilization of genetics services for autism: the importance of parental awareness and provider recommendation. *J Genet Couns.* 2012;21:803-813.

14. Developmental Disabilities Monitoring Network Surveillance Year 2010 Principal Investigators. Prevalence of autism spectrum disorder among children aged 8 years autism and developmental disabilities monitoring network, 11 sites, United States, 2010. *MMWR Surveill Summ* 2014; 63 Suppl 2: 1-21.

15. Ozonoff S, Young GS, Carter A, et al. Recurrence risk for autism spectrum disorders: a baby siblings research consortium study. *Pediatrics.* 2011;128:e488-495.

16. Pasacreta JV. Psychosocial issues associated with genetic testing for breast and ovarian cancer risk: an integrative review. *Cancer Invest.* 2003;21:588-623.

17. Skinner D, Choudhury S, Sideris J, et al. Parents' decisions to screen newborns for FMR1 gene expansions in a pilot research project. *Pediatrics.* 2011;127:e1455-1463.

18. Myers SM, Johnson CP, Management of children with autism spectrum disorders. *Pediatrics.* 2007;120:1162-1182.

19. McGrew SG, Peters, BR, Crittendon JA, Veenstra-Vanderweele J. Diagnostic yield of chromosomal micrarray analysis in an autism primary care practice: which guidelines to implement? *J Autism Dev Disord*. 2012;42:1582-1591.

20. Shen Y, Dies KA, Holm IA, et al. Clinical genetic testing for patients with autism spectrum disorders. *Pediatrics.* 2010;125:e727-735.

21. Fiorentino F, Napoletao S, Caiazzo F, et al, Chromosomal microarray anaylsis as a firt-line test in pregnanies with a prior low risk for the detection of submicroscopic chormosomal abnormalities. *Eur J of Human Genet.* 2013; 21.725-730.

22. Johnson HM, Gaitanis J, Morrow EM. Genetics in autism diagnosis: adding molecular subtypes to neurobehavioral diagnoses. *Med Heatlth RI.* 2011;94:124-126.

23. Schaefer GB, Mendelsohn NJ, Clinical genetics evaluation in identifying the etiology of autism spectrum disorders: 2013 guideline revisions. *Genet Med.* 2013;15:399-407.

24. Marchant GE, Robert, SJ. Genetic testing for autism predisposition: ethical, legal and social challenges. *Houst J Health Law Policy.* 2009;9:203-35.

25. Lerman C, Schwartz MD, Lin TH, et al. The influence of psychological distress on use of genetic testing for cancer risk. *J Cousult & Clin Psychol.* 1997;65:414-420.

26. Jordan BR, Tsai DF. Whole-genome association studies for multigenic diseases: ethical dilemmas arising from commercialization-the case of genetic testing for autism. *J Med Ethics.* 2010;36:440-444.

27. Maya I, Davidov B, Gershovitz L, et al. Diagnostic utility of array-based comparative genomic hybridization (aCGH) in a prenatal setting. *Prenat Diagn.* 2010;30:1131-1137.

28. Reiff M, Bernhardt BA, Mulchandani S, et al. "What does it mean?": uncertainties in understanding results of chromosomal microarray testing. *Genet Med.* 2012;14:250-258.

29. Judith G. *Health Sciences Literature Review Made Easy: The Matrix Method. .* Gaithersburg, MD: Aspen Publishers; 1999.

30. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics.*1977; 33(1), 159-174.

31. Skinner D, Sparkman K, Bailey D. Screening for Fragile X Syndrome: parent attitudes and perspectives. *Genet Med.* 2003;5:378-384.

32. Bailey DB Jr, Bishop E, Raspa M, Skinner D. Caregiver opinions about fragile X population screening. *Genet Med.* 2012;14:115-121.

33. Bailey DB Jr, Lewis MA, Harris SL, et al. Design and evaluation of a decision aid for inviting parents to participate in a fragile X newborn screening pilot study. *J Genet Couns.* 2013;22:108-117.

34. Archibald AD, Hickerton CL, Jaques AM, et al. "It's about having the choice": stakeholder perceptions of population-based genetic carrier screening for fragile X syndrome. *Am J Med Genet. Part A.* 2013;161A:48-58.

35. Archibald AD, Jaques AM, Wake S, et al. "It's something I need to consider": decisions about carrier screening for fragile X syndrome in a population of non-pregnant women. *Am J Med Genet. Part A.* 2009;149A:2731-2738.

36. Metcalfe S, Jacques A, Archibald A, et al. A model for offering carrier screening for fragile X syndrome to nonpregnant women: results from a pilot study. *Genet Med.* 2008;10:525-535.

37. Chen LS, Xu L, Huang TY, Dhar SU. Autism genetic testing: a qualitative study of awareness, attitudes, and experiences among parents of children with autism spectrum disorders. *Genet Med.* 2013;15:274-281.

38. Anido A, Carlson LM, Sherman SL. Attitudes toward fragile X mutation carrier testing from women identified in a general population survey. *J Genet Couns.* 2007;16:97-104.

39. Christie L, Wotton T, Bennetts B, et al. Maternal attitudes to newborn screening for fragile X syndrome. *Am J Med Genet.Part A.* 2013;161A:301-311.

40. Anido A, Carlson LM, Taft L, et al. Women's attitudes toward testing for fragile X carrier status: a qualitative analysis. *J Genet Couns.* 2005;14:295-306.

41. Johnson VA, Edwards KA, Sherman SL, et al. Decisions to participate in fragile X and other genomics-related research: native American and African American voices. *J Cult Divers.* 2009;16:127-135.

42. Narcisa V, Discenza M, Vaccari E, Rosen-Sheidley B, et al. Parental interest in a genetic risk assessment test for autism spectrum disorders. *Clin Pediatr.* 2013;52:139-146.

43. Croniser A, DiMaio M, Mahoney MJ, et al. Fragilxe X syndrome carrier screening in the prenatal screening couseling setting. *Genet Med.*2005;7:246-250.

44. Pastore LM, Karns LB, Pinkerton JV, et al. Acceptance of fragile X premutation genetic screening in women with ovarian dysfunction. *Am J Obstet Gynecol.* 2006;194:738-743.

45. Pastore LM, Morris WL, Karns LB. Emotional reaction to fragile X premutation carrier tests among infertile women. *J Genet Count.* 2008;17:84-91.

46. Wolff K, Nordin K, Brun W, et al. Affective and cognitive attitudes, uncertainty avoidance and intention to obtain genetic testing: an extension of the Theory of Planned Behaviour. *Psychol Health.* 2011;26:1143-1155.

47. Ajen, I. The theory of planned behavior. *Organ Behav Hum.* 1991;50:179-211.

48. Lincoln YS, Guba EG. *Naturalistic inquiry.* Thousand Oaks, CA: Sage Publications; 1985.

49. Wade CH, Shiloh S, Woolford SW, et al. Modelling decisions to undergo genetic testing for susceptibility to common health conditions: an ancillary study of the Multiplex Initiative. *Psychol Health.* 2012;27:430-444.

50. Sagi M, Shiloh S, Cohen T. Application of the Health Belief Model in a study on parents' intentions to utilize prenatal diagnosis of cleft lip and/or palate. *Am J Med Genet.* 1992;44:326-333.

51. Gooding HC, Organista K, Burack J, et al. Genetic susceptibility testing from a stress and coping perspective. *Soc Sci Med.* 2006;62:1880-1890.

52. Goodson P. *Theory in Health Promotion Research and Practice.* Sudbury, MA: Jones and Bartlett Publishers; 2010.

53. 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.

54. Sebat J, Lakshmi B, Malhotra D, et al. Strong association of de novo copy number mutations with autism. *Science.*2007;316:445-449.

55. Roesser J. Diagnostic yield of genetic testing in children diagnosed with autism spectrum disorders at a regional referral center. *Clin Pediatr.* 2011;50:834-843.

56. Broadstock M, Michie S, Marteau T. Psychological consequences of predictive genetic testing: a systematic review. *Eur J Human Genet.* 2000;8:731-738.

57**.** Heshka J, Palleschi C, Wilson B, et al. Cognitive and behavioural effects of genetic testing for thrombophilia. *J Genet Count.* 2008;17:288-296.

58. Hudson K, Scott J, Brauch S, et al. Reproductive genetic testing: what America thinks. http://www.dnapolicy.org/pub.reports.php?action=detail&report_id=6. Published 2004. Accessed April 30, 2013.

59. Reiff M, Ross K, Mulchandani S, et al. Physicians' perspectives on the uncertainties and implications of chromosomal microarray testing of children and families. *Clin Genet.* 2013;83:23-30.

60. Bernhardt BA, Soucier D, Hanson K, et al. Women's experiences receiving abnormal prenatal chromosomal microarray testing results. *Genet Med.*2013;15:139-145.

61. Fan YS, Jayakar P. Zhu H, et al. Detection of pathogenic gene copy number variabionts in patients with metnal retardation by genomewide oligonucleotide array comarative genomic hybridization. *Hum Mutat.* 2007; 28:1124-1132

62. Szatmari P, Paterson AD, Zwaigenbaum L, et al. Mapping autism risk loci using genetic linkage and chromosomal rearrangements. *Nat Genet.* 2007; 39:319-328

63. Shevell M, Ashwal S. Donley D, et al. Practice parameter: evalation of the child with global developmenal delay: report of the Quality Standards Subcommittee of the Americian Academy of Neorology and the Practice Committee of the Child Neurology Society. *Neurology.* 2003; 60:367-380.

64. Abrahams BS, Geschwind DH. Advances in autism genetics: on the threshold of a new neurobiology. *Nat Rev Genet.* 2008;9:341-355.

65. Skafidas E, Testa R, Zantomio D,et al. Predicting the diagnosis of autism spectrum disorder using gene pathway analysis. *Mol Psychiatry*. 2014;19:504-510.

66. Muhle R, Trentacoste SV, Rapin I. The genetics of autism. *Pediatrics.* 2004;113:E472-E486.

67. Bosompra K, Ashikaga T, Flynn BS, et al. Psychosocial factors associated with the public's willingness to pay for genetic testing for cancer risk: a structural equations model. *Health Educ Res.*2001;16:157-172.

68. Frost S, Myers LB, Newman SP. Genetic screening for Alzheimer's disease: what factors predict intentions to take a test? *Behav Med.* 2001;27:101-109.

69. Roberts JS. Anticipating response to predictive genetic testing for Alzheimer's disease: a survey of first-degree relatives. *Gerontologist.* 2000;40:43-52.

70. Stein MD, Cunningham WE, Nakazono T, et al. Screening for cervical cancer in HIV-infected women receiving care in the United States. *J Acquir Immune Defic Syndr.* 2001;27:463-466.

71. Leventhal H, Cameron L. *Handbook of Health Psychology*. Mahwah, NJ: Lawrence Erlbaum Associates; 2001.

72. Lazarus RS FS. *Stress, Appraisal, and Coping.*New York: Springer Publishing Company, Inc.; 1984.

73. Lerman C, Croyle RT. Emotional and behavioral responses to genetic testing for susceptibility to cancer. *Oncology.* 1996;10:191-195, 199; discussion 200-202.

74. Decruyenaere M, Evers-Kiebooms G, Cloostermans T, et al. Psychological distress in the 5-year period after predictive testing for Huntington's disease. *Eur J Hum Genet.* 2003;11:30-38.

75. Broadstock M, Michie S, Marteau T. Psychological consequences of predictive genetic testing: a systematic review. *Eur J Hum Genet.* 2000;8:731-738.

76. Tibben A, Timman R, Bannink EC, et al. Three-year follow-up after presymptomatic testing for Huntington's disease in tested individuals and partners. *Health Psychol.*1997;16:20-35.

77. Sun X, Allison C, Matthews FE, et al. Prevalence of autism in mainland China, Hong Kong and Taiwan: a systematic review and meta-analysis. *Mol autism.* 2013;4:7.

78. Lin CR, Tsai YF, Chang HL. Coping mechanisms of parents of children recently diagnosed with autism in Taiwan: a qualitative study. *J Clin Nurs*. 2008;17:2733-2740.

79. Wang J, Lee LC, Chen YS, et al. Assessing autistic traits in a Taiwan preschool population: cross-cultural validation of the Social Responsiveness Scale (SRS). *J Autism Dev Disord*. 2012;42:2450-2459.

80. Merriam-Webster. Third New International Dictionary Unabridged. http://search.eb.con/mwu. Published 2002. Assessed on May 5, 2014.

81. Williams K. Fear appeal theory. *Res in Bus and Econ J.* 2012;5:1-21.

82. Rogers RW. Cognitive and physiological processes in fear appeals and attitude change: a revise theory of protection motivation. In: Cacciopo J and Petty R, ed. *Social Psychophysiology*. New York. NY: Guiford Press; 1983:153-177.

83. Witte K, Allen M. A meta-analysis of fear appeals: implications for effective public health campaigns. *Health Educ Behav.*2000;27:591-615.

84. American Psychological Assocation. Anxiety. http://www.apa.org/topics/anxiety/. Assessed Jan 12, 2014.

85. Marteau MT, Bekker H. The development of a six-item short-from of the state scale of the Spielberger State-Trait Anxiety Inventory (STAI). *Brit J Clin Psychol*. 1992. 31. 301-306

86. Kelvens K. California State University, Northridge. Fear and anxiety. http://www.csun.edu/~vcpsy00h/students/fear.htm?Assessed on Jan 12, 2014.

87. Encyclopedia of Psychology. Guilt. http://www.enotes.com/homework-help/psychology-what-guilt-what-stages-guilt-466309. Accessed May 6, 2014.

88. McAllister M, Davies L, Payne K, et al. The emotional effects of genetic diseases: implications for clinical genetics. *Am J Med Genet. Part A*. 2007;143A(22):2651-2661.

89. Eagly A CS. *The Psychology of Attitudes*. Fort Worth, TX: Harcourt Brace Jovanovich; 1993.

90. Price AS. Primary and secondary prevention of colorectal cancer. *Gastroenterology Nurs.* 2003;26:73-81.

91. Lierman LM, Young HM, Kasprzyk D, et al. Predicting breast self-examination using the theory of reasoned action. *Nurs Res.* 1990;39:97-101.

92. Chen LS, Goodson P. Public health genomics knowledge and attitudes: a survey of public health educators in the United States. *Genet Med.* 2007;9:496-503.

93. Levine FR, Coxworth JE, Stevenson DA, et al. Parental attitudes, beliefs, and percetpions about genetic testing for FAP and colorectral cancer survellance in minors. *J Genet Coun.* 2010:19:269-279.

94. 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.

95. Mega C, Ronconi, L, Beni R. What makes a good student? how emotions, self-regulated learning, and movivaiton contribute to academic achievement. *Am J Educ Psychol.*2013.106.121-131

96. Buhi ER, Goodson P, Neilands TB. Structural equation modeling: a primer for health behavior researchers. *Am J Health Behav.* 2007;31:74-85.

97. Schreiber JB, Nora A, Stage FK, et al. Reporting structural equation modeling and confirmatory factor analysis results: a review. *J Educ Res.* 2006;99:323-337.

98. Buhi ER, Goodson P, Neilands TB, Blunt H. Adolescent sexual abstinence: a test of an integrative theoretical framework. *Health Edu Behav.* 2011;38:63-79.

99. Hair JF, Black WC, Babin BJ, et al. *Multivariate Data Analysis.* Upper Saddle River, NJ: Prentice Hal; 2006.

100. Schumacker RE, Marcoulides GA. *Interaction and Nonlinear Effects in Structural Equation Modeling.* Mahwah: Lawrence Erlbaum Associates; 1998.

101. Wayne Mk. Factors Influencing Intention to Obtain a Genetic Test for Prostate Cancer Risk: A Structural Equation Modeling Approach [dissertation]. Philadelphia, PA: Drexel University; 2004.

102. Schumacker RL, R. *A Beginner's Guide to Structural Equation Modeling*. Mahwah: Lawrence Erlbaum Associates.; 1996.

103. Buhi ER, Goodson P. Predictors of adolescent sexual behavior and intention: a theory-guided systematic review. *J Adolescent Health.* 2007;40:4-21.

104. Coltman T, Devinney TM, Midegley DF, Venaik S. Formative verus reflective measurement models: two applications of formative measurement. *J Bus Res.* 2008, 1250-1262.

105. Yuan KH, Bentler PM. Finite normal mixture SEM analysis by fitting multiple conventional SEM models. *Sociol Methodol.* 2010;40:191-245.

106. Villagran M, Hajek C, Zhao X, Wittenberg-Lyles E. Communication and culture: predictors of treatment adherence among Mexican immigrant patients. *J Health Psychol.* 2012;17:443-452.

107. McBride CM, Alford SH, Reid RJ, et al. Putting science over supposition in the arena of personalized genomics. *Nat Genet.* 2008;40:939-942.

108. Aatre RD, Day SM. Psychological issues in genetic testing for inherited cardiovascular diseases. *Circ Cardiovasc Genet.* 2011;4:81-90.

109. Eisenbruch M, Yeo SS, Meiser B, et al. Optimising clinical practice in cancer genetics with cultural competence: lessons to be learned from ethnographic research with Chinese-Australians. *Soc Sci Med.* 2004;59:235-248.

110. Yang LH, Purdie-Vaughns V, Kotabe H, et al. Culture, threat, and mental illness stigma: identifying culture-specific threat among Chinese-American groups. *Soc Sci Med.* 2013;88:56-67.

111. Baum A, Friedman AL, Zakowski SG. Stress and genetic testing for disease risk. *Health Psychol.* 1997;16:8-19.

112. Suther S, Goodson P. Barriers to the provision of genetic services by primary care physicians: a systematic review of the literature.*Genet Med.* 2003;5:70-76.

113. Chen LS, Goodson P. Barriers to adopting genomics into public health education: a mixed methods study. *Genet Med.*2009;11:104-110.

114. Baars MJ, Henneman L, Ten Kate LP. Deficiency of knowledge of genetics and genetic tests among general practitioners, gynecologists, and pediatricians: a global problem. *Genet Med.*2005;7:605-610.

115. Hudson KL, Holohan MK, Collins FS. Keeping pace with the times--the Genetic Information Nondiscrimination Act of 2008. *N Engl J Med.* 2008;358:2661-2663.

116. Mao X. Chinese geneticists' views of ethical issues in genetic testing and screening: evidence for eugenics in China. *Am J Hum Genet.* 1998;63:688-695.

117. WonPat-Borja AJ, Yang LH, Link BG, Phelan JC. Eugenics, genetics, and mental illness stigma in Chinese Americans. *Soc Psychiatry Psychiatr Epidemiol.* 2012;47:145-156.

118. Catz DS, Green NS, Tobin JN, et al. Attitudes about genetics in underserved, culturally diverse populations. *Community Genet.* 2005;8:161-172.

119. Samuel M. Y. Ho JWCH, Cecilia LW, et al, Decisional consideration of hereditary colon cancer genetic test results among Hong Kong Chinese adults. *Cancer Epidemiol Biomarker Prevent.* 2003;12:426-432.

120. Armitage CJ, Conner M. Efficacy of the theory of planned behaviour: a meta-analytic review. *Br J Soc Psychol.* 2001;40:471-499.

121. Sutton S. Predicting and explaining intentions and behavior: how well are we doing? *J Appl Psychol*. 2006;28:1317-1338.

122. Bunn JY, Bosompra K, Ashikaga T, et al. Factors influencing intention to obtain a genetic test for colon cancer risk: a population-based study. *Prev Med.* 2002;34:567-577.

APPENDIX A

Characteristics of 17 Included Studies Investigating Emotional Factors, Attitudes, and Intention Regarding Autism Genetic Testing

Authors	Targeted genetic tests	Recruitment criteria and sample source	Sample (N, age, ethnicity, education, income)	Study Design (Method, theoretical framework)	Pre-test counseling (contents)	Test Uptake/ Acceptance Rate
1.Anido et al. 2005 [USA]	Fragile X (FX) carrier screening	• Females (18-50 years), both FX carriers and non-carriers • University Research Center	• N=40 • Range: 21-50 years • Non-Hispanic White: 77% Non-Hispanic Black: 23% • Education: not reported • Income level: not reported	• Qualitative: focus group • Theory: not reported	• Yes • Basic disease characteristic and risks	Not reported
2.Anido et al. 2007 [USA]	FX carrier screening	• Females (18-45 years), FX carriers • University research center	• N=12 • Range: 21-44 years • All White • Education: not reported • Income level: not reported	• Qualitative: interviews • Adult Learning Theory	Not reported	Not reported
3.Archibald et al. 2009 [Australia]	FX carrier screening	• Females (≥18 years), non-pregnant can read, speak or write English • General population	• N=31 • Range: 18-45 years (96.8%) >45 years (3.2%) • Ethnicity: not reported • College and above: 67.8% • Income level: not reported	• Qualitative: semi-structured interviews • Reframed constructs from the Health Belief Model	• Yes • Basic disease characteristic and risks	Not reported

4.Archibald et al. 2012 [Australia]	FX carrier screening	• Females(≥ 16 years), fluent in English; affected relatives with first, second or third degree relative with FXS (the diagnosis is within one year), and pregnant women at <10 weeks gestation • General population	• N=188 • ≥16 years • Ethnicity: not reported • Education: not reported • Income level: not reported	• Qualitative: semi-structured interviews/focus group • Grounded theory	• Yes • Knowledge or information about the tests	Not reported
5.Barley et al.2012 [USA]	FX carrier, prenatal and newborn screening	• Both males and females (parents of children with FX) • General population	• N=1099 • Range:16-89 years Mean= 47 years • White: 92% Hispanic:4% African Americans: 2% Others: 2% • College and above: 58% • Income level: 56% > $75K	• Quantitative: survey • Theory: not reported	Not reported	79% preferred carrier testing
6.Bailey et al. 2013 [USA]	FX newborn screening	• Females (pregnant mothers: 59%; recent mothers: within past six months) • General population	• N=118 • Range:18-43 years Mean= 30.4 years • White: 52.5% African American: 39.8% Latino: 7.6% • Education: not reported • Income level: $50K (median)	• Quantitative: survey • Theory: not reported	Not reported	61.9%
7.Christie et al. 2013 [Australia]	FX newborn screening	• Females (mothers in the postnatal ward) • Clinical setting	• N=1698 (questionnaire) N=173 (written documents) • Range: 21-30 years: 52%; >31 years: 39%; <21 years: 9% • White: 88% Aboriginal/ Torres Strait Islander:7% Others:5% • Education: not reported • Income level: not reported	• Quantitative: survey • Theory: not reported	• Yes • Basic disease characteristic and information about the test	94%

8. Cronister et al, 2005 [USA]	FX(prenatal) carrier screening	• Females (with no known family history of FX syndrome) • Clinical setting	• N=29103 • Age: not reported • Ethnicity: not reported • Education: not reported • Income level: not reported	• Quantitative: survey • Theory: not reported	• Yes • Basic disease characteristic and knowledge as well as information about the test	7.9%
9. Fanos et al, 2005 [USA]	FX prenatal screening	• Females (both with and without family history of FX syndrome) • Clinical setting	• N=20 • Range: 26-41years Mean: 35 years • White: 65% Latina:10% Asian:15% African American: 11% • Education: college degree (median) • Income level:$15K (median)	• Qualitative: interviews • Theory: not reported	• Yes. • Knowledge or information about the test	80%
10. Narcisa et al, 2012 [USA]	Autism genetic testing	• Both males and females (parents of children with at least one child with ASD) • General population	• N=162 • Age: reported • White: 84.3% African American: 7.2% Hispanic: 5.7% Mixed: 2.9% • College above 93.3 % • Income level: 97.6% > $50K	• Quantitative: survey • Theory: not reported	Not reported	80%
11.Johnson et al. 2009 [USA]	FX screening (other testing such as sickle cell is not included in this study)	• Both males and females (church attendees) • Local communities	• N=24 • Range:18-81 years; Mean:55.26 years (Native Americans) Range:18-73 years; Mean:45.67 years (African American) • Native Americans: 48% African Americans: 25% • Education: not reported • Income level: not reported	• Qualitative: focus groups • Reported but not further explained	Not reported	Not reported
12. Chen et al. 2012 [USA]	Autism genetic testing	• Both males and females (parents of children diagnosed with ASD)	• N=42 • Age: 44.3 years (24-58) • White: 50%	• Qualitative: semi-structured interviews • Theory: not reported	Not reported	69%

		• Local communities	Asian: 26% Hispanic: 14% Black: 7% Mixed: 2% • Some college above: 88% • Income level: 66.7%>$50K			
13. Metcalf et al. 2008 [Australia]	FX carrier screening	• Females • Clinical Setting	• N=30 (Phase I) N=318 (Phase II) N=31 (Phase III) • <45 years: 100% (Phase I) <45 years: 92.7% (Phase II) <45 years: 83.9% (Phase III) • Ethnicity: not reported • College diploma and above: 66.7% (Phase 1) 68.8% (Phase II) 67.8% (Phase II) • Income level: not reported	• Qualitative: focus group and interview) (Phase I and III) Quantitative: survey(Phase II) • Theory: not reported	• Yes • Knowledge or information about the test	20%
14.Pastore et al. 2006 [USA]	FX carrier screening	• Females (previous or current patients diagnosed with ovarian dysfunction) • Clinical setting	• N=40 • >18 years • White: (above 92.9%) • Education: not reported • Income Level: not reported	• Quantitative: cross-sectional survey • Theory: not reported	Not reported	Acceptance rate: 75% (women with diminished ovarian reserve); 42% (women with premature ovarian failure/early menopause)
15.Pastore et al. 2008 [USA]	FX carrier screening	• Females (diagnosed with diminished ovarian reserve before) • Clinical setting	• N=20 • Range: 32-44 years Mean: 39.5 years • White: 85% • Education: not reported • Income level: not reported	• Quantitative: survey • Theory: not reported	Not reported	Not reported
16.Skinner et al. 2003 [USA]	FX carrier, prenatal and newborn	• Both males and females (parents of children with FX syndrome)	• N=442 • Not reported • White: 94%	• Quantitative: survey • Theory: not reported	Not reported	Not reported

	screening	• National research centers	African Americans: 1.8% Hispanic/Latino:1.3% Asian: 0.6% Unknown: 2% • College degree above: 63.9% • Income level: 81.7%>$51K			
17.Skinner et al. 2011 [USA]	FX newborn screening	• Females (mothers of newborn within 24 hours' giving birth) • Clinical setting	• N=2137 • Not reported • White: 43.7% Latino: 37% Black: 4.4% Other: 7.8% • College degree above: 36.8% • Income level: not reported	• Quantitative: survey • Theory: not reported	• Yes. • Knowledge or information about the test	• 63% (the test uptake rate) • Black participants were less likely to accept screening

APPENDIX B

Distributions of emotions, attitudes, and intention of undergoing genetic testing among the 17 included studies

Factors	Percentage	Studies
Emotions		
Anxiety	29.4%	Archibald et al. 2013; Christie et al. 2013; Fano et al. 2006; Metcalf et al. 2008; Narcisa et al. 2012
Uncertainty	29.4%	Archibald et al. 2009; Archibald et al. 2013; Bailey et al. 2012; Bailey et al. 2013; Christie et al. 2013
Worry	17.6%	Bailey et al. 2012; Bailey et al. 2013; Skinner et al. 2011
Feelings about the parent-child bonding	17.6%	Barley et al. 2012; Christie et al. 2013; Skinner et al. 2011
Fear	11.8%	Chen et al. 2013; Johnson et al. 2009
Regret	5.9%	Pastore et al. 2008
Angry	5.9%	Pastore et al. 2008
Upset	5.9%	Pastore et al. 2008
Grief	5.9%	Anido et al. 2005
Distrust	5.9%	Johnson et al. 2009
Frustration	5.9%	Chen at al. 2013
Depression	5.9%	Bailey et al. 2012

Attitudes

Positive Attitudes *(Perceived benefits or outcomes)*	41.2%	Anido et al. 2005; Archbald et al.2013; Barley et al. 2013; Chen et al. 2013; Christie et al. 2012; Metcalf et al. 2008; Skinner et al. 2003
Help with information about carrier status	29.4%	Archibald et al. 2013; Bailey et al. 2013;Christie et al. 2012; Metcalf et al. 2008; Skinner et al. 2003
Help with reproductive choices/options	29.4%	Archibald et al. 2013; Bailey et al. 2013; Chen et al. 2013; Christie et al. 2012; Skinner et al. 2003
Help with research	23.5%	Andio et al. 2007; Chen et al. 2013; Christie et al. 2012; Metcalf et al. 2011
Help with early diagnosis and timely medical treatment	23.5%	Bailey et al. 2013, Chen et al. 2013; Christie et al. 2012; Skinner et al. 2003
Help with better preparing for the birth of the affected child	17.6%	Chen et al. 2013; Christie et al. 2012; Skinner et al.2003
Negative Attitudes *(Perceived barriers or outcomes)*	35.3%	Arichibald et al. 2013; Bailey et al. 2013; Chen et al. 2013; Christie et al. 2012; Metcalf et al.2008; Skinner et al. 2003
Concerns related to the harm brought by undergoing the test	29.4%	Arichibald et al. 2013; Bailey et al. 2013; Chen et al. 2013; Christie et al. 2012; Skinner et al. 2003
Concerns related to the characteristics of the current test	11.8%	Archibald et al. 2013; Chen et al. 2013
Concerns related to the value of the test	11.8%	Chen et al. 2013; Metcalf et al. 2008
Societal implications regarding the genetic test	11.8%	Archibald et al 2013; Metcalf et al. 2008
Concerns related to religion and culture beliefs	5.9%	Chen et al. 2013

Intention or Decision-making

Primary reasons or outcomes for accepting to undergo testing	52.9%	Anido et al. 2007； Archibald et al. 2009; Bailey et al. 2013; Chen et al. 2013; Johnson et al. 2009; Metcalf et al. 2008; Narcisa et al. 2012; Pastore et al. 2006; Skinner et al. 2011
Perceived test benefits	52.9%	Anido et al. 2007; Archibald et al. 2009; Bailey et al. 2013; Chen et al. 2013; Johnson et al. 2009; Metcalf et al. 2008; Narcisa et al. 2012; Pastore et al. 2006; Skinner et al. 2011
Perceived risk	23.5%	Archibal et al. 2009; Bailey et al. 2013; Johnson et al. 2009;Skinner et al. 2011

Subjective norms	17.6%	Chen et al. 2013; Bailey et al. 2013; Johnson et al. 2009
Perceived barriers	17.6%	Archibald et al.2009; Bailey et al. 2013; Metcalf et al. 2008
Emotional factor (lessened anxiety)	5.9%	Narcisa et al. 2012
Primary reasons or outcomes for declining to undergo testing	47.1%	Archibald et al. 2009; Bailey et al. 2013; Chen et al. 2013; Johnson et al. 2009; Metcalf et al. 2008, Pastore et al. 2005; Skinner et al. 2011
Perceived barriers	47.1%	Archibald et al. 2009; Bailey et al. 2013; Chen et al. 2013; Johnson et al. 2009; Metcalf et al. 2008, Pastore et al. 2006; Skinner et al. 2011
Lack of convenience	29.4%	Archibald et al. 2009; Chen et al. 2013; Metcalf et al. 2008 Bailey et al. 2013; Pastore et al. 2005
Issues with the current status of genetic testing	17.6%	Bailey et al. 2013; Metcalf et al. 2008; Skinner et al. 2011
Lack of relevance	17.6%	Bailey et al. 2013; Johnson et al. 2009; Skinner et al. 2011
Confidentiality	11.8%	Johnson et al.2009; Pastore et al. 2005
Bad timing	11.8%	Bailey et al. 2013; Skinner et al. 2011
Issues with the diseases	11.8%	Bailey et al. 2013; Skinner et al. 2011
Cost (e.g. pay out-of-the pocket)	5.9%	Pastore et al. 2006
Emotional factors associated with the test	29.4%	Archibald et al. 2009; Bailey et al. 2013; Johnson et al. 2009; Skinner et al. 2011
Subjective norms	17.6%	Bailey et al. 2013; Johnson et al. 2009; Skinner et al. 2011