

PERCEPTIONS OF GENETIC COUNSELING FROM ADULTS WITH BIPOLAR DISORDER

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Bipolar disorder is a mood disorder that affects about 1% of the population, representing a significant public health issue. Bipolar disorder can be associated with substance abuse, unemployment, increased marital dysfunction, and increased use of health services. Twin studies provide evidence that genetics plays a role in the etiology of bipolar disorder with heritability estimates as high as 93% in some studies. Molecular genetic studies were initially promising, but no genes with large effect sizes have been discovered. There is also evidence that suggests a multifactorial inheritance pattern. Consequently, genetic testing is not yet available. However, as advances are made in the understanding the connections between genetics and psychiatric disorders, it is expected that the demand for genetic counseling for bipolar disorder will increase. Genetic counselors are well-equipped to educate patients and family members about the condition, to discuss their concerns about the risk of bipolar disorder, and to offer genetic testing should it become available. For this qualitative study, interviews were conducted to explore the opinions and perceptions of individuals with bipolar disorder and/or their siblings. The open-ended questions were designed to elicit the thoughts and attitudes about bipolar disorder and genetic counseling. Thematic analysis was performed on the transcripts from 10 interviews and the following themes were identified: excessive disease burden, variable causal attributions, desire for diagnostic test for BPD, and reproductive considerations.

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PREFACE

I would like to thank Holly Peay, MS, CGC for allowing me to duplicate her study and for providing me with great information. I would also like to thank my thesis committee for their wonderful advice and cooperation.

1.0 INTRODUCTION

Bipolar disorder (BPD) is a mood disorder that was first described in 1899 by Emil Kraepelin (Austin & Honer, 2005). Affecting 1% of the population, bipolar disorder is a major public health concern (Baron, 2002) and its prevalence warrants further study to identify strategies to improve the quality of life for individuals who struggle with this disorder. Both affected individuals and their family members can encounter significant challenges with the problems associated with it. BPD can be associated with psychosis during both phases of the disorder (Baron, 2002). Also, approximately 50% of individuals with BPD can have substance abuse problems (Carlson-Sabelli & Lessick, 2001). Other public health concerns include a higher rate of unemployment, increased marital dysfunction, and increased use of health services (McQueen, et al., 2005). Medical co-morbidities are also a significant public health concern for this population (Alda, Hajek, Calkin, & O'Donovan, 2009). These include conditions such as obesity, insulin-dependent diabetes mellitus, hypertension, and dyslipidemia (Alda, et al., 2009). The psychiatric disturbances and associated medical conditions contribute to the daily strain of living with this condition.

The current treatment for BPD will be discussed in more detail, but is fraught with potential negative side effects and can be inadequate for some individuals (Alda, et al., 2009). Therefore, this disorder deserves more research and attention to determine how to help affected individuals lead healthier, more productive lives. This study was designed to explore the

perceptions of affected individuals as well as their siblings with regards to BPD and genetics. A previous study was completed by Holly Peay et al. and published in 2009 in the *American Journal of Medical Genetics Part A* (Peay, Hooker, Kassem, & Biesecker, 2009). Peay et al. (2009) had conclusions that are relevant to the genetic counseling practice and there is value in conducting a similar study. Therefore, the current study used the same interview guide as Peay et al. (2009), along with a different population and different data analysis to accomplish research goals.

The research goals of this study were to explore the thoughts and opinions of individuals with BPD and their siblings about genetics and genetic testing, determine what information individuals with BPD and their siblings would want to learn from a genetic counselor, learn more about the daily burden of BPD to heighten awareness for better management options, and learn the cause to which individuals with BPD and their siblings attribute the disease. The open-ended questionnaire was designed to ascertain this information through a series of related questions.

1.1 SPECIFIC AIM

The aim of this qualitative research study is to identify perceptions and opinions of adults diagnosed with BPD and/or their siblings with regard to genetics and genetic counseling for BPD.

2.0 BACKGROUND AND SIGNIFICANCE

2.1 BIPOLAR DISORDER

2.1.1 Natural History

Bipolar disorder (BPD) is a psychiatric illness that results in a recurrent pathological disturbance in mood (Austin & Honer, 2005). This disorder can have detrimental effects on the life of the individual who is diagnosed, his/her family members, and society as a whole (Lish, Dime-Meenan, Whybrow, Price, & Hirschfeld, 1994). BPD was first described by Emil Kraepelin in 1899 (Austin & Honer, 2005). The two ends of the mood spectrum of this condition are depression and mania, or extreme elation (Craddock & Sklar, 2009).

The hallmark features of depression are social withdrawal, lack of energy and motivation, disturbances in sleep and appetite, decreased concentration, and impaired memory (Alda, et al., 2009). These features are distinct from the features of the type of depression that would be associated with grief or sadness (Alda, et al., 2009). The features of mania include elevated, irritable, or expansive mood, increased goal-directed activity, pleasure-seeking behavior, and impaired judgment (Alda, et al., 2009). Individuals who are experiencing a manic episode tend to have a diminished need for sleep and are frequently hyperactive and easily distracted (Alda, et al., 2009). They are also usually talkative and are apt to have an unrestrained, accelerated flow

of ideas (Alda, et al., 2009). Both moods are associated with a risk of suicide (Alda, et al., 2009).

BPD is categorized as, BPD I and BPD II. BPD I is associated with both depression and mania whereas BPD II is associated with depression and hypomania (Craddock & Sklar, 2009). Hypomania is a manic condition that is less severe than the typical mania (Craddock & Jones, 1999). The two forms of BPD are diagnosed based on the appearance of the specific episodes (Bebbington & Ramana, 1995).

2.1.2 Diagnosis

The diagnosis of BPD is based solely on clinical observation as there is no diagnostic test available (Craddock & Sklar, 2009). This is not ideal because it is not based on any anatomical or physiological evidence (Reus & Freimer, 1997). This difficulty with the diagnosis of psychiatric illnesses sets them apart from most disorders that are diagnosed based on physiological signs or symptoms (Reus & Freimer, 1997). The Diagnostic and Statistical Manual (DSM) IV - TR has listed the diagnostic criteria for BPD. A diagnosis of BPD I is made when a patient has experienced or exhibited one or more manic or mixed episodes (Association, 2000). BPD II is diagnosed when a patient has disabling depression and at least one hypomanic episode (Association, 2000). (See Appendix D for diagnostic criteria.)

Initial symptoms can vary from mania to depression or could also be a mixed episode (Rush, 2003). The clinical course can also vary among individuals with BPD (Alda, et al., 2009). Some individuals with BPD have regular mood cycles while others experience random mood shifts (Alda, et al., 2009). Other individuals undergo rapid cycling, (Carlson-Sabelli & Lessick, 2001) which is defined as having at least four manic or depressive episodes in one year

(Alda, et al., 2009). In addition to the timing, variability also exists in the type of mood. Some experience mixed episodes which occur when the criteria are met for both mania and depression (Barnett & Smoller, 2009). There are also some individuals who experience more episodes of depression than mania or the reverse situation. These factors combined can make it challenging for some people to accept the validity of a diagnosis and in fact, some patients are misdiagnosed with major depressive disorder for quite some time before they have their first manic episode (Lish, et al., 1994; Rush, 2003).

2.1.3 Prevalence

BPD affects approximately 1% of the population (Austin & Honer, 2005). The prevalence of BPD is about equal across ethnicities (Rush, 2003) and discrepancies in prevalence estimates are often attributed to diagnostic procedures (Tsuchiya, Byrne, & Mortensen, 2003). Of those with BPD, the percentage of individuals with BPD I is 35-40% and about 40-45% have BPD II (Carlson-Sabelli & Lessick, 2001). Most individuals are diagnosed in their early 20s (Carlson-Sabelli & Lessick, 2001) and the average age at diagnosis is 21 years (Craddock & Jones, 1999). About 13-20% of individuals with BPD undergo rapid cycling (Carlson-Sabelli & Lessick, 2001). This is more common in women than men and there is also evidence indicating that women have more depressive episodes than men (Carlson-Sabelli & Lessick, 2001).

2.1.4 Etiology

The etiology of BPD is currently unknown (Baron, 2002) but BPD is thought to be caused by some interaction between genetic and environmental factors (Rush, 2003). General observations

and scientific studies have shown that BPD has a genetic component (Austin & Honer, 2005). It is believed that some individuals are predisposed based on their genetic makeup and are at risk of developing BPD following an environmental trigger (Baum, Akula, et al., 2008). The genetics are not well defined and will be discussed in more detail in the following sections.

2.1.5 Treatment

The current treatment for BPD consists of medications, psychotherapy, education, and life-style modification (Alda, et al., 2009). The focus of current treatments is to control an acute phase of illness and to prevent long-term recurrences (Alda, et al., 2009) to provide the best quality of life. The existing methods are sufficient for most individuals with BPD, but others struggle to get the most effective medication regimen (Alda, et al., 2009). Some individuals are diagnosed with major depression and prescribed antidepressants before they have a manic episode that then prompts the diagnosis of BPD. Antidepressants can be detrimental for individuals with BPD; they can induce a manic episode, lead to rapid cycling, or worsen the depression (Alda, et al., 2009). This means that having a physical test instead of waiting for a manic episode to confirm a diagnosis would most likely be beneficial for this population (Lish, et al., 1994). It seems that learning more about the genetics and etiology of BPD would enhance understanding of the pathogenesis of the disorder and possibly lead to additional, more effective treatments.

2.2 GENETICS OF BIPOLAR DISORDER

2.2.1 Genetic Studies of Bipolar Disorder

The genetics of BPD are still unclear and as a result there is no genetic test for BPD. Clinicians have known for a long time that bipolar and other affective disorders tend to run in families (Craddock & Jones, 2001). However, genetic studies had disappointing results for many years until the advent of molecular genetic testing (Craddock & Jones, 2001). Molecular genetic studies have provided the tools to discover susceptibility genes and initially had promising results (Craddock & Jones, 2001). Unfortunately, there have been few susceptibility genes or chromosomal regions discovered that could be replicated in other studies.

2.2.1.1 Twin Studies

Twin studies are useful for studying complex traits that have both a genetic component and environmental influences to help determine the heritability of the disease (Boomsma, Busjahn, & Peltonen, 2002). Classic twin studies involve identical twins (monozygotic) and fraternal twins (dizygotic) (Boomsma, et al., 2002). Monozygotic (MZ) twins develop from one fertilized egg and so have the same genetic makeup. Dizygotic (DZ) twins develop from two separate fertilized eggs; this means that they share approximately 50% of the same genes, much like two siblings. The measurement in twin studies is called the concordance rate (Boomsma, et al., 2002). Concordance is defined as “the occurrence of the same trait in both members of a pair of twins (Boomsma, et al., 2002).” The concordance rate allows us to gain an estimate of the heritability, or amount of genetic variability, of complex traits (Boomsma, et al., 2002). Since the concordance rate for BPD is greater in MZ twins when compared to DZ twins, it can be

assumed that there are genetic factors that play a role in the pathogenesis of BPD (Barnett & Smoller, 2009). These were the first studies to provide evidence of a genetic component (Craddock & Jones, 1999).

The results from the most recent and largest twin studies indicate that the heritability of BPD is estimated to be between 79% and 93% (Barnett & Smoller, 2009). This means that between 79% and 93% of the risk for BPD is attributed to genetic variation. Other estimates have ranged from 60-90% (Alaerts & Del-Favero, 2009; Austin & Honer, 2005; Barnett & Smoller, 2009; Craddock & Forty, 2006; McQueen, et al., 2005). Importantly, these are all greater than 50% and less than 100%. Since siblings share 50% of their genes in common, heritability estimates of less than 50% would imply that genetics do not play a large role in the etiology of BPD and would indicate that environment plays a larger role than genetics. The heritability estimated from twin studies is not 100%, so it can be assumed that this is not a purely genetic condition (Craddock & Jones, 2001). The environmental factors that contribute to the risk of BPD are called “triggers” and include accumulation of stressful life events, childbirth with postnatal depression, difficult marriage, birth trauma leading to brain damage, difficult childhood (including child abuse), sexual abuse, personality factors, and seasonal effects (Meiser, Mitchell, McGirr, Van Herten, & Schofield, 2005). More recent advances in molecular genetics have provided us with additional tools to study complex disorders.

2.2.1.2 Molecular Genetic Studies

Several molecular genetic studies have implicated potential genes and regions on chromosomes that could be involved in the pathogenesis of BPD, but few of them have been replicated. Molecular genetic studies examine the genetic makeup of individuals with BPD and their family members to identify genes that appear to contribute to the disorder in question. The goal in these

studies is to find a difference in a gene or differences in several genes that are shared among individuals with BPD and absent in individuals without BPD. Over the past 20 years, molecular genetic studies including linkage analysis and association analysis with positional and/or functional candidate genes have implicated regions on all chromosomes as being related to the etiology of BPD (Alaerts & Del-Favero, 2009).

Linkage analysis is a type of genetic study that uses genetic information from families with multiple individuals with BPD with the intention of identifying regions of the genome that are segregating or “linked” with the disorder in question (Alaerts & Del-Favero, 2009). These are also called positional gene studies because they identify regions of the genome that could be related to BPD but are not necessarily related to the pathophysiology (Craddock & Jones, 1999). In fact, this type of study does not require any knowledge of the disease pathophysiology (Craddock & Jones, 1999). Linkage studies are useful for complex disorders because they can identify potential areas of interest in the genome. Genes implicated in these studies can be examined in an attempt to learn more about the pathophysiology of the disorder.

Association analysis is a similar type of genetic study that uses a patient group and a control group to look for statistically significant differences in the frequencies of genetic variants (Alaerts & Del-Favero, 2009). The participants in each group are matched for variables thought to be relevant to the study, for example, gender, age, or ethnicity (Craddock & Jones, 2001). Matching for these variables helps to increase the chance that an association discovered is a true association and not related to other variables. These studies are usually performed for candidate genes that are thought to be involved with the pathophysiology of the disorder (Craddock & Jones, 1999). Association studies can help to provide insights into the genetic contribution of complex disorders.

Linkage analysis and association studies have provided evidence of some potential genes involved in the pathogenesis of BPD. Unfortunately, most of the results were not replicated in other studies or were not found to be statistically significant in meta-analyses of the data (Jones & Craddock, 2001). Implicated genes have potential biological significance, but studies identifying them have been difficult to replicate for several reasons: heterogeneity (differences in the genetics) of the disorder, differences in the populations studied, varying number of individuals with BPD in each family, different ascertainment criteria for studies, different sets of marker genotypes, and dissimilar analytic methods (McQueen, et al., 2005). All of these factors can create differences between the studies that may prevent duplication of significant findings.

More recently, genome-wide association studies (GWAS) have been performed to search for genes involved in BPD. GWA studies use the technology of “SNP chips” to scan the genome for areas of agreement between individuals who have BPD (or any other genetic disorder) and a particular SNP. A SNP is a “single nucleotide polymorphism” or one of the hundreds to thousands of basepairs that constitute a gene that is different across individuals. SNPs are genotyped, or examined, to determine if they occur more frequently in individuals of the population who have a certain disorder compared to a control population of individuals who do not have BPD (Hirschhorn & Daly, 2005). This helps the researchers determine the potential importance of a gene if a SNP in that gene increases the risk for a disease (Hirschhorn & Daly, 2005).

A few GWA studies report similar results for genes that could be involved in BPD (Baum, Hamshere, et al., 2008). There was no statistical agreement across GWA studies, but upon close inspection of the methods, there could be genes of interest even if they are not

statistically significant (Baum, Hamshere, et al., 2008). Table 1 lists the genes that contain the strongest signals, listed numerically by chromosome location.

Table 1: Genes suspected to be related to bipolar disorder

Gene	Chromosome Location
SORCS2 (Baum, Akula, et al., 2008)	4p16.1
EGFR (Sklar, et al., 2008)	7p12.3-p12.1
ANK3 (Ferreira, et al., 2008)	10q21
DFNB21 (Baum, Akula, et al., 2008)	11q22-q24
JAM3 (Baum, Hamshere, et al., 2008; Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls," 2007)	11q25
CACNA1C(Ferreira, et al., 2008; Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls," 2007; Sklar, et al., 2008)	12p13
TSPAN8 (Sklar, et al., 2008)	12q14.1-q21.1
DGKH (Baum, Akula, et al., 2008)	13q14
VGCNL1 (Baum, Akula, et al., 2008)	13q
PALB2 ("Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls," 2007)	16p12
DCTN5 ("Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls," 2007)	16p12.2
NDUFAB1 ("Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls," 2007)	16p12.3-p12.1
MYO5B (Sklar, et al., 2008)	18q21
SLC39A3 (Baum, Hamshere, et al., 2008; Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls," 2007)	19p13.3

However, these genes are still likely to have small or modest effect sizes. Linkage analysis and association analysis are most efficient for detecting variants with modest or large effect sizes (Alaerts & Del-Favero, 2009) and the results are inconclusive, supporting the speculation that there are many risk alleles with small effect sizes. These observations lead to the belief that BPD is a polygenic or multifactorial condition with the involvement of several genes and environmental factors (Baum, Akula, et al., 2008).

2.2.1.3 Summary of gene hunting for bipolar disorder

Even though the results of genetic studies seem to be disappointing, it is important to continue research to determine the underlying susceptibility genes related to BPD. As previously outlined, early diagnosis and treatment are critical for appropriate care of individuals with this condition (Alda, et al., 2009). Determining the genetics involved in BPD may help clarify some issues related to BPD (Jones, Scourfield, McCandless, & Craddock, 2002). Knowing the susceptibility genes could help to better inform our understanding of the pathophysiology (Jones, et al., 2002) and aid in understanding the gene products that play a role in causing BPD (Craddock & Jones, 1999). This could also lead to characterization of the way in which environmental factors interact with these gene products (Craddock & Jones, 1999). Understanding the pathophysiology may help researchers develop more effective treatments (Alda, et al., 2009; Jones, et al., 2002). Therapeutic agents may be developed that specifically target the causative gene products or other biochemical lesions (Craddock & Jones, 1999). Finally, knowing the susceptibility genes could lead to the development of a diagnostic test (Jones, et al., 2002). Having a diagnostic test may improve the validity of psychiatric diagnoses and classification of other disorders (Jones, et al., 2002). Perception and attitudes related to genetic testing for BPD has received significant attention in the literature.

2.2.2 Genetic Testing for Bipolar Disorder

2.2.2.1 Inheritance

The current theorized inheritance of BPD is the polygenic threshold or multifactorial model (Baum, Akula, et al., 2008). This model hypothesizes that BPD develops when the allele burden crosses an unknown threshold and the person experiences an environmental trigger

(Baum, Akula, et al., 2008). Multiple risk alleles probably contribute small effect sizes to the genetics of BPD. In 1989, Gottesman and Bertelsen estimated that at-risk individuals carry approximately six risk alleles (Alda, et al., 2009). There has not been a more recent estimation of the number of risk alleles, but there are probably many risk alleles that modify the chance of a person developing BPD (Rush, 2003). It has been suggested that a person's risk depends on the number of risk alleles and the environment in which she lives (Baum, Akula, et al., 2008). Some researchers contend that the age of diagnosis negatively correlates with the number of risk alleles (Rush, 2003). Individuals with later onset would hypothetically have fewer risk alleles than those who were diagnosed at a young age (Rush, 2003). These risk alleles are most likely polymorphisms with small effect size and so they would not help determine an individual's risk (Craddock & Sklar, 2009). Regardless of the potential difficulties, there is still interest in developing a genetic test.

However, there are difficulties in developing a genetic test for BPD. When the effect size of a gene is small, the predictive ability of the test is limited and the test is not practical (Craddock & Sklar, 2009). The most likely result from a test for genes with small effect sizes would be a probability of developing BPD. In other words, the test would not provide a definitive result and may be unsatisfactory to patients and health professionals. Known risk alleles for BPD probably contribute small or modest effect sizes which makes it unlikely that genetic testing will become clinically available for BPD in the near future (Finn & Smoller, 2006; Meiser, et al., 2008). Nevertheless, there is still expectation that genetic testing will become available at some point and for that reason studies have explored the public's attitudes and opinions.

2.2.2.2 Opinions and Attitudes

Even though genetic testing for BPD may not be available for several years, studies have explored the opinions and perceptions of individuals with BPD, those with a family history of BPD, and the attitudes of psychiatrists towards testing. Three different settings for genetic testing and two types of genetic testing have been examined. The settings include clinical prenatal, pediatric, and adult settings and the two types of testing are diagnostic and presymptomatic (predictability). The prenatal testing would involve testing a fetus for the presence of BPD susceptibility genes. Pediatric testing would include testing anyone under the age of 18 years. Finally, adult testing would be testing individuals who are over 18 years of age.

The attitude toward presymptomatic testing of adults is mostly positive (Jones, et al., 2002). Based on the research, there appears to be a majority of participants who would pursue genetic testing for children. Eighty-nine percent of participants in study by Smith, et al. agreed that they would opt for presymptomatic testing for their children if there were effective drug treatments available (Smith, Sapers, Reus, & Freimer, 1996). Fifty-six percent would pursue testing for their children even if effective drug treatments were not available (Smith, et al., 1996). A more recent study explored the opinions of both patients and psychiatrists with regard to presymptomatic testing of children. The results of this study indicated that adult patients were more interested than psychiatrists in testing children (Jones, et al., 2002). This supports the notion that being a “sufferer” of the disorder makes one more focused on the potential benefits of genetic testing (Jones, et al., 2002). Meiser et al. (2008) reported a patient population with multiple individuals in one family with BPD; this contrasts with most studies regarding genetic testing perceptions because the participants were selected based on family history. In this study, 80% of the participants replied that they would probably or definitely test their children either at

birth or in early childhood (Meiser, et al., 2008). Some individuals would test children under certain conditions such as their child showing symptoms of BPD (Meiser, et al., 2005). Those who are opposed to testing children cited reasons that included potential harm if parents treated a child who carries a susceptibility gene differently from other children and wanting to wait until the child could decide for himself if he wants testing (Meiser, et al., 2005).

There is a high level of interest for most studies regarding genetic testing for adolescents, but conclusions about prenatal testing are different. As previously discussed, genetic testing for BPD is unlikely to be diagnostic, making decision-making challenging for prenatal testing. In general, when compared to pediatric testing, there is less interest in prenatal testing, 44% in one study (Trippitelli, Jamison, Folstein, Bartko, & DePaulo, 1998) and 29% in another (Jones, et al., 2002). A more recent study with participants selected for family history found that 54% of respondents would choose to pursue prenatal testing, if available (Meiser, et al., 2008). This suggests having a strong family history of BPD might correlate with a higher degree of interest in prenatal testing (Meiser, et al., 2008). Milner, et al. (1999) surveyed 227 individuals about prenatal genetic testing for psychiatric disorder, human traits, and neurological disorders. Approximately 75% to 85% of the respondents would agree to prenatal testing for BPD (Milner, Han, & Petty, 1999). Of those individuals who would agree to prenatal testing, some felt that it would be more useful if the test could predict the severity of the illness and the burden on the family, and if they believe that appropriate and timely intervention would lessen the severity (Milner, et al., 1999).

A positive test result could prompt some couples to choose to terminate the pregnancy (Smith, et al., 1996), but not all couples would choose this course of action (Meiser, et al., 2005). In fact, the results from Trippitelli et al. (1998) suggest that the majority would not terminate

(Trippitelli, et al., 1998). Reasons cited for opposition to pregnancy termination following a positive test result include personal objection to termination, not considering BPD serious enough to warrant termination, and not considering termination because of the increasing number of treatments available (Meiser, et al., 2005). Those who would choose to abort a fetus were more likely to do so when the risk is higher and when the degree of severity is higher (Smith, et al., 1996). In conclusion, the choice to pursue genetic testing would most likely depend on the setting and the type of testing available.

2.2.2.3 Potential Risks and Benefits of Genetic Testing

In addition to assessing public opinion about genetic testing (Meiser, et al., 2008; Meiser, et al., 2005; Milner, et al., 1999; Smith, et al., 1996; Trippitelli, et al., 1998; Wilde, Meiser, Mitchell, & Schofield, 2010), other researchers have explored the potential risks and benefits (Meiser, et al., 2005; Trippitelli, et al., 1998). Genetic testing is associated with potential risks and benefits. The benefits of genetic testing generally include reproductive planning (Meiser, et al., 2005), marriage decisions (Meiser, et al., 2005), planning for the future (Hill & Sahhar, 2006; Meiser, et al., 2008; Meiser, et al., 2005), helping research (Meiser, et al., 2005), and possible early intervention of treatment (Meiser, et al., 2005). There is also potential benefit for prevention of the disorder when the etiology is associated with a specific gene or genes (Hill & Sahhar, 2006; Meiser, et al., 2005). BPD might also be prevented by the avoidance of stressors or environmental triggers for an individual who tests positive (Meiser, et al., 2005). It is hypothesized that individuals who know that they carry a gene or genes that predispose them to BPD can try to avoid additional stressors that could trigger the onset of the disorder. Some have suggested that having a test that could confirm the diagnosis of BPD would be beneficial as it

would provide a sense of certainty (Meiser, et al., 2005) and could prove the validity of the diagnosis (Wilde, et al., 2010).

The risks of genetic testing for BPD include risks that are present for many genetic tests. These include increased worry in non-manifesting carriers (Meiser, et al., 2005), employment discrimination (Meiser, et al., 2005; Trippitelli, et al., 1998; Wilde, et al., 2010), impact on marriage or reproductive decisions (Meiser, et al., 2005), and insurance discrimination (Meiser, et al., 2005; Trippitelli, et al., 1998; Wilde, et al., 2010). Probabilistic genetic testing could confuse patients and cause anxiety related to living with uncertainty (Hill & Sahhar, 2006; Meiser, et al., 2005). Two other health risks that could be associated with a positive genetic test result for BPD include an increased risk for suicide in carriers and a lower threshold for stress with knowledge of increased vulnerability (Meiser, et al., 2005). When considering a genetic test for psychiatric conditions, some expressed a fear of developing a fatalistic view and not being able to achieve their goals (Trippitelli, et al., 1998; Wilde, et al., 2010). These risks should be elucidated before clinical testing is available so that health care professionals can discuss them with patients prior to testing and provide appropriate informed consent.

2.3 GENETIC COUNSELING FOR BIPOLAR DISORDER

2.3.1 Definition of Genetic Counseling

The National Society of Genetic Counselors (NSGC) is a professional organization for genetic counselors. The NSGC defines genetic counseling in this way:

Genetic counseling is the process of helping people understand and adapt to the medical, psychological, and familial implications of genetic contributions to disease. This process

integrates the following: interpretation of the family and medical histories to assess the chance of disease occurrence or recurrence; education about inheritance, testing, management, prevention, resources, and research; and counseling to promote informed choices and adaptation to the risk or condition.

Based on this definition of genetic counseling, this process could be beneficial for patients and families struggling with BPD. Therefore, researchers have explored the necessity for having genetic counseling available for individuals with BPD and their families.

2.3.2 Necessity

Clinicians are reporting that they are increasingly being asked questions by patients and their family members regarding recurrence risks for BPD for themselves and/or their children (Finn & Smoller, 2006). The American Psychiatric Association suggests that genetic counseling may be helpful for couples who have a history of BPD and are considering children (Finn & Smoller, 2006). To support this, various studies have conducted surveys regarding patient interest in genetic counseling and the results suggest that there is interest in genetic counseling (Finn & Smoller, 2006). Seventy-five percent of the participants in one study responded that they would opt for genetic counseling (Finn & Smoller, 2006).

Genetic counselors are health care professionals who specialize in communicating genetic information to patients (Fraser, 1974). Genetic counselors help their patients understand complex medical information about genetics, appreciate inheritance patterns, understand recurrence risks, understand the implications of genetic test results, and choose a course of action that is best suited for the patient (Fraser, 1974). Genetic counselors are able to explain complex traits and disorders and should be able to discuss psychiatric genetic concepts with their patients (Peay, et al., 2008). However, genetic counselors are not trained in psychiatry in most genetic

counseling programs and some people would argue that counseling for a psychiatric illness should be performed by someone who is trained specifically in that field (Finn & Smoller, 2006).

2.3.3 Who Should Counsel Patients about Psychiatric Genetics?

Genetic counseling for psychiatric conditions should be provided by genetics professionals or psychiatrists (Finn & Smoller, 2006). Genetics professionals include genetic counselors, clinical geneticists, and advanced practice nurses with specialized genetics training (Finn & Smoller, 2006). The genetic professionals are experts in understanding and relaying information regarding the genetic basis of disease, trained to facilitate decision making in a nondirective manner, and are able to provide supportive counseling as needed (Finn & Smoller, 2006). Finn et al. (2005) explored psychiatrists' knowledge regarding genetic information and has revealed that there are gaps in the psychiatrists' knowledge and so genetics professionals, may be the individuals who are more qualified to discuss psychiatric genetics with patients (Finn, et al., 2005).

Psychiatrists have the benefit of being trained in psychiatric diagnosis and understand the course of illness, treatment options, and the psychodynamic issues related to counseling (Finn & Smoller, 2006). Researchers also discovered that most psychiatrists believe that it is their responsibility to discuss familial and genetic aspects of psychiatric conditions; however, they reported that they felt unprepared to do so (Finn, et al., 2005). The psychiatric community appears to make limited use of referral to genetics professionals in circumstances where they feel unprepared to discuss psychiatric genetics (Finn, et al., 2005) and psychiatrists without expertise in genetics may be directive (Finn & Smoller, 2006). Most psychiatrists expressed interest in further education in genetics (Finn, et al., 2005). In other words, psychiatrists may be open to

further education in genetic information relevant to their patients. This could remedy the problem, raised by Finn, of gaps in knowledge of non-genetics professionals.

2.3.4 Indications for Genetic Counseling

There could be several reasons that individuals would seek genetic counseling for BPD. One of those reasons might be to learn about recurrence risks (Finn & Smoller, 2006). Recurrence risks indicate the chance of other family members developing BPD (Finn & Smoller, 2006). Parents with BPD or their family members may be seeking this information to clarify risks to current or future children (Duffy, Grof, Robertson, & Alda, 2000). Individuals may be interested in learning more about the genetic causes of BPD and seek to have genetic testing (Finn & Smoller, 2006). If a pregnant woman has BPD, she may be taking psychiatric medications. This could pose a risk to the pregnancy, so her physicians may refer her for genetic counseling to discuss the potential risks posed by the medication (Finn & Smoller, 2006).

2.3.5 The Psychiatric Genetic Counseling Session

The main functions of genetic counseling in psychiatry include ascertainment of family history, education, risk estimation, and nondirective counseling to facilitate decision-making about options for dealing with recurrence risk (Finn & Smoller, 2006). Psychiatric genetic counseling can be useful for clients for other purposes as well, such as discussing their experiences with a health care professional (Finn & Smoller, 2006).

2.3.5.1 Family History

Taking a three-generation family health history is standard practice in almost every genetic counseling session regardless of the indication. This is relevant to psychiatric genetic counseling for two main reasons. First, clients often reveal the presence of psychiatric conditions during the process of eliciting the family history (Peay, et al., 2008). This means that potentially any genetic counseling session could evolve into counseling about psychiatric conditions because clients often have questions regarding recurrence risks. Second, the family history is an appropriate time to inquire about the condition of relatives who have psychiatric disorders (Peay, et al., 2008).

2.3.5.2 Education

Genetic counseling is intended to provide useful information so that individuals can make decisions that yield the best outcome for them and their family. Should the genetic cause of BPD be elucidated, there can be a vast improvement in patient education. Some individuals who seek genetic counseling for education may be relieved to learn of the genetic causes and find a support system (Finn & Smoller, 2006) where they get the most recent and accurate information (Peay, et al., 2008). Given the stigma associated with psychiatric illness, understanding that BPD has a genetic component and knowing what the cause is may help individuals and their family members deal with guilt or shame (Austin & Honer, 2005). Other individuals who seek genetic counseling for BPD may use the information for family planning purposes (Finn & Smoller, 2006).

Education is an important aspect of genetic counseling. Finn and Smoller (2006) have indicated that there is information that is important for clients to understand after a genetic counseling appointment for BPD. First, clients should learn about the complexities of genetic

and environmental interactions and how it relates to psychiatric illness (Finn & Smoller, 2006). This is not significantly different from a typical genetic counseling session with any complex disease and therefore, counselors are trained to communicate such an explanation (Peay, et al., 2008). Second, clients should understand the importance of accurate diagnosis for recurrence risk information (Finn & Smoller, 2006). Third, clients can learn about the limitations of using empiric risk information to calculate risks for individual families (Finn & Smoller, 2006). Next, genetic counselors are accustomed to researching and assimilating the necessary disease specifics before the appointment so that the client can be given accurate and complete information about their diagnosis (Finn & Smoller, 2006; Peay, et al., 2008). There are also opportunities for clients to learn about decision making based on risk information (Finn & Smoller, 2006). Genetic counselors are able to help clients interpret risk information so that clients can use it during a decision making process (Peay, et al., 2008). Finally, genetic counselors also serve as a source for additional information and referrals (Finn & Smoller, 2006; Peay, et al., 2008).

2.3.5.3 Risk Counseling

Risk counseling uses empiric risk information and factors from the family history to provide a range of risks. Empiric risks are calculated from family studies that combine data from multiple families in a certain population (Finn & Smoller, 2006). The risk estimates from large studies may not apply directly to individual families whose risk could be different based on certain factors that may be specific to that particular family (Finn & Smoller, 2006). Moreover, clients may seek different types of risk information, and it is important to determine which type most interests each client during the counseling session. Some families may be seeking a quantitative risk assessment based on current data, while others may just be looking for validation of their

thoughts (Austin, et al., 2008). They may want to be reassured that it is possible for them to have children without a psychiatric illness while others may want a qualitative evaluation (Austin, et al., 2008). It is important to also assess what the client intends to do with the information once he learn the recurrence risks (Austin, et al., 2008). For example, they may want it for family planning purposes, to make lifestyle choices, or to allow them to feel more in control as a result of better understanding (Austin, et al., 2008).

Clients should be given risk information in the form of a range of numbers collected from multiple sources because the inheritance pattern is not predictable since BPD does not follow a Mendelian inheritance pattern (Finn & Smoller, 2006). For example, a syndrome with a Mendelian inheritance pattern would have a known recurrence risk for that particular syndrome because the pattern would be predictable (Austin, et al., 2008). The following table lists the recurrence risks based on how many people in the family have BPD (Carlson-Sabelli & Lessick, 2001):

Table 2: Recurrence Risks

Category	Risk Percentage
Risk to offspring when <i>both parents</i> have BPD	30% (Carlson-Sabelli & Lessick, 2001) - 70% (Duffy, et al., 2000)
Risk to offspring when <i>one parent</i> has BPD	5% (Carlson-Sabelli & Lessick, 2001) - 10% (Craddock & Jones, 2001)
Risk to <i>sibling</i> of an individual with BPD	8% (Carlson-Sabelli & Lessick, 2001) - 10% (Craddock & Jones, 2001)
Risk to offspring when <i>neither parent</i> has BPD	1%

These risks are based on empirical data; they may be modified for each client. Some families have a history suggestive of a particular inheritance pattern and so the empiric risk can be modified based on the pattern that appears in a family (Duffy, et al., 2000). An earlier age of onset in the individual diagnosed with BPD may indicate a higher risk to relatives (Duffy, et al.,

2000; Finn & Smoller, 2006). There may be an increased risk to individuals born in a certain cohort, and this information is important because it may modify the risk of developing BPD (Duffy, et al., 2000). Finally, the presence of several family members with a psychiatric condition such as BPD may indicate a higher risk in relatives (Finn & Smoller, 2006) as opposed to families where only one relative has BPD. All of these factors can be elicited during the family history portion of the session and used to give a client a more personal risk assessment.

2.3.5.4 Complexities

Genetic counseling could be beneficial for families, but there could also be disadvantages. For example, couples that are seeking genetic counseling for prenatal testing could be faced with the decision to terminate an affected fetus or to continue the pregnancy. If the couple is not properly counseled about the risks and benefits of genetic testing, they could be faced with situations for which they are not prepared. Secondly, genetic counseling could increase the stigma and discrimination associated with psychiatric illness (Finn & Smoller, 2006). In conclusion, genetic counseling for psychiatric illness could produce benefits for clients, but the impact of counseling needs to be further evaluated.

3.0 METHODOLOGY

3.1 PATIENT RECRUITMENT

This study was approved by the University of Pittsburgh Institutional Review Board, IRB# PRO09070167. The approval letter can be found in Appendix E. Participants were recruited from three different sources. Flyers with the study information and the researcher's contact information were posted in Bellefield Hall, an outpatient clinic that serves individuals with BPD and other psychiatric conditions. The researcher contacted the leader of the Pittsburgh chapter of the Bipolar and Depression Support Alliance (DBSA), which holds support group meetings the second and fourth Wednesday of every month. The researcher asked permission to attend a meeting and to bring information about this study. Flyers with the study information and the researcher's contact information were distributed at the meeting (see Appendix C). The researcher was also able to explain the purpose of the study and answer questions that the meeting attendees had. One participant was also recruited through a mental health therapist who treats patients with BPD in the Pittsburgh area.

3.2 TELEPHONE INTERVIEWS WITH PARTICIPANTS

Potential participants made the initial contact with the researcher via email or a phone call and a mutual time for the phone interview was arranged. Prior to the start of the interview informed consent was obtained and any questions that participants had about the study were addressed. The informed consent document can be found in Appendix A. The participants were asked a series of open-ended questions and the interview was tape-recorded. The interview guides for affected individuals and their siblings are found in Appendix B.

3.3 INTERVIEW TRANSCRIPTION

Interviews were recorded and then transcribed using Microsoft Word. The same questions were asked of every participant and responses transcribed verbatim. Efforts were made to maintain the accuracy of the participant's responses and few revisions were made to the transcripts. The few revisions made included minor corrections to grammar and omissions of a few encouraging remarks during the interviews. These revisions were made only when it was felt the integrity of the interview or the meaning of the phrases were not distorted.

3.4 DATA ANALYSIS

The data for this research study are qualitative in nature, meaning that the responses to the questions were analyzed using a method of qualitative analysis. Qualitative research is well

suited for genetic counseling studies designed to elicit the feelings and perceptions of participants. Genetic counselors are trained to interpret and appreciate the emotions of their clients. They are capable of performing this type of research because it is designed to capture the complexities and nuances of the participants' thought processes and feelings (Beeson, 1997). The transcripts from the interviews were analyzed using a qualitative research method called thematic analysis. There are benefits to using thematic analysis. First, thematic analysis maintains the direct representation of the participants' own point of view and their personal experiences and perceptions (Luborsky, 1994). Second, thematic analysis is a flexible method that can be adapted to different types of research (e.g. focus groups or interviews) and is independent of any theoretical framework (Braun & Clarke, 2006). Thematic analysis is also an efficient method for reducing a long conversation into a series of short phrases or labels to highlight the main points (Luborsky, 1994).

While the literature is replete with qualitative studies that use thematic analysis, few articles address methods for performing thematic analysis. However, there is some literature that discusses general principles of thematic analysis (Braun & Clarke, 2006). This literature suggests that thematic analysis begins with a thorough reading and re-reading of the data during which the researcher begins to identify themes (Fereday & Muir-Cochrane, 2006). Codes, or descriptive labels attached to parts of the interview transcript, are utilized to organize the data into themes (Fereday & Muir-Cochrane, 2006). Several definitions of a theme exist in the literature. For example, Braun and Clarke (2006) define a theme as something important about the data in relation to the research question that represents patterns that appear in the responses. Another definition of a theme is "the generalized statements by informants about beliefs, attitudes, values, or sentiments (Luborsky, 1994)."

The specific process used for this research study is called inductive thematic analysis. This means that the identified themes are strongly linked to the original data, (Braun & Clarke, 2006) rather than being inferred from the data. The data were grouped into units of text called codes and the codes were then categorized into themes (Frith & Gleeson, 2004). This method was chosen because it was felt that being “data-driven” and making inferences would help clarify the significance of BPD in the participants’ lives, thoughts, and actions. The themes are semantic themes because they were identified within the explicit or surface meaning of the responses (Braun & Clarke, 2006). The responses were taken for what they meant without being forced into a preconceived theory in order to remain true to the responses of the participants.

3.4.1 Getting acquainted with the information

For some researchers, the first step in getting acquainted with the information is to transcribe the data (the interview recordings) (Braun & Clarke, 2006). The researchers may listen to the tapes and transcribe the interviews themselves or may invest in computer software that is able to transcribe. Another option is to have someone else transcribe the information. This researcher transcribed the interviews herself as outlined above in order to become more familiar with the information. The second part of this step involves reading and re-reading of all the transcripts (Luborsky, 1994). The transcripts from the interviews for this research were read four times before the coding process began and certain patterns or repeated responses may become apparent with re-reading.

3.4.2 Coding the data

Data coding began once the transcripts were read. Descriptive labels were used to identify main points and topics throughout the transcripts (Luborsky, 1994). This is the first part of analyzing the data (Braun & Clarke, 2006). The transcripts were coded using the focused coding method which is a process that allows the researcher to transform large portions of the data into small pieces that are organized into themes (Charmaz, 2006). The codes were put into a list with identifying information so that the researcher could find where they were originally read in each transcript. Most of the codes were utilized in several transcripts while others might have only been in one transcript. The unique codes were included because they were ideas that held significance for the participant and appeared to be compelling.

3.4.3 Analyzing the codes to identify themes

A list of codes was created and the codes were organized into groups that represented certain patterns or themes (Braun & Clarke, 2006). The codes were analyzed for similar ideas or comments that could be grouped into themes (Frith & Gleeson, 2004). This process was relatively straightforward because the questions addressed certain topics; however, the questions were sufficiently open-ended to allow participants to discuss issues that were meaningful to them.

4.0 RESULTS

4.1 DEMOGRAPHICS

Ten people participated in this study. Nine of the participants are over the age of 40 (mean age 48.6 years), nine reside in Pennsylvania, all of them are Caucasian four are male, and five have children. With regard to disease status, eight have been diagnosed with BPD and two of the participants are siblings of someone who was diagnosed with BPD. Of note, only one of the participants who had BPD is married.

Table 3: Demographics

Participant	Age	Sex	Race/ Ethnicity	State of Residence	Status	Children
1	49	Female	Caucasian	Pennsylvania	Affected	One daughter
2	41	Male	Caucasian	Pennsylvania	Affected	None
3	52	Male	Caucasian	Pennsylvania	Affected	None
4	53	Male	Caucasian	Pennsylvania	Affected	None
5	22	Female	Caucasian	Pennsylvania	Affected	None
6	42	Female	Caucasian	Pennsylvania	Sibling	None
7	56	Female	Caucasian	Pennsylvania	Affected	One son
8	50	Female	Caucasian	Pennsylvania	Affected	Two daughters
9	54	Female	Caucasian	Pennsylvania	Sibling	Two sons
10	67	Male	Caucasian	Illinois	Affected	Three children

4.2 THEMES

There were four themes identified using inductive thematic analysis and include excessive disease burden, variable causal attributions, desire for diagnostic test for BPD, perceived need for genetic counseling, and reproductive considerations.

4.2.1 Theme: Excessive Disease Burden

Based on the responses to questions, individuals with BPD experience excessive disease burden. BPD affects them on a daily basis and can prevent participation in common activities such as work or school. For these individuals, BPD causes a great deal of stress and requires daily coping skills.

4.2.1.1 Depression

Subjects responded to the question “what is the worst thing about BPD for you [or for your sibling].”. The worst aspect of BPD for six of the participants is depression. Depression prevented affected individuals from performing daily activities. For example, activities such as going to work, cleaning one’s home, and taking care of pets were difficult to perform. The following comments were made by two participants:

I don’t really take care of my house that well because I don’t, I just don’t like to focus on housework... And the depression, the depressive episodes; when they’re bad, they’re really bad. (Participant #2, affected male)

I can’t function. I can’t have relationships with friends. I can’t work. I have pets at home that I love, I can’t take care of them properly. My apartment becomes a total mess, cluttered. I can’t do dishes. I can’t do anything. (Participant #7, affected female)

4.2.1.2 Impact on relationships

Individuals with BPD indicated that it was difficult to maintain relationships with family and friends due to their condition. Difficulties maintaining relationships, combined with the stigma associated with BPD, can result in social isolation. Only one of the participants in this study who had BPD is married and he was diagnosed later in life, at age 62. Two of the participants were divorced after their diagnosis of BPD. One participant felt that it was difficult to maintain existing relationships because of his BPD symptoms:

Interviewer: What is the best thing for your family?

Participant: ...When I'm depressed they're worried sick and when I'm high it's a little hard to carry on a conversation with me. I want them to hurry up and complete their thoughts so I can get mine in. (Participant #3, affected male)

Two participants described the struggle to meet people due to their symptoms of BPD:

Interviewer: What is the worst thing about bipolar disorder for you?

Participant: Mostly being depressed and not wanting to do much of anything, not getting out and meeting people. (Participant #4, affected male)

A few years ago, I would go out, I would be angry at everybody else for no reason cause I thought they would be bothering me. (Participant #4, affected male)

It affects mostly I think my relationships with other people, which I think have always been really bad. I have just not very close relationships with anyone. I would have to say that if one thing marks my life, it's an absence of real friends or real love. I sort of prefer it that way and I don't prefer it that way. Relationships are so hard for me I would almost rather be alone. (Participant #2, affected male)

4.2.1.3 Limited positive aspects

When asked what the best thing about bipolar disorder is either for the individual or for his/her family, three participants responded that there was nothing positive but that they were okay when their medications kept their moods stable. This does not reflect benefits from having the disorder, but they were able to recognize the importance of medication.

I don't know if there is a best thing about having bipolar disorder...I guess as long as someone's on medication to try to stabilize it, I guess that could be the best thing. I'd rather someone not have it. (Participant #6, unaffected female)

When asked, "What is the best thing about bipolar disorder for you?" five of the participants responded that there is no positive aspect. One participant felt that there is no good aspect, but he was glad that his disorder was never really bad:

... I don't know if there is a best thing, best that it hasn't gotten any worse than it has. It's been, I think my condition has been fairly stable for a while and was never too extreme. (Participant #2, affected male)

One participant was able to share that being diagnosed with BPD has been beneficial to her life in at least one aspect. She is an artist who feels that BPD has enhanced her artistic abilities and allowed her to discover her true self as an artist. She is clearly the exception because the other participants were not able to claim any true benefits of having this condition.

4.2.1.4 Family challenges

Four of the participants commented on the difficulty of family interactions when one of the family members has BPD. The affected individuals were upset because their family members did not understand how BPD affects them. The siblings of an affected individual were upset because they did not know how to approach their sibling.

Interviewer: What is the worst thing for your family?

Affected Individual: ...Well, I can be hard to get along with, I think. I like to be by myself a lot and they don't always understand that. (Participant #2, affected male)

Affected Individual: They have trouble knowing how to approach this and how to interact with me. They do the best that they can but sometimes it's hard for them to understand because they don't deal with the same issues themselves. (Participant #5, affected female)

Sibling: It started out with us having no contact at all then when we realized there was a problem and my sister and I started to get involved I guess the worst part was we literally had to intervene and do things to help him...the worst part was there was no contact... (Participant #9, unaffected female)

Sibling: Well when he's in a depressed state, it was really hard to support him. Not because I didn't want to support him, but I didn't know how to support him...It was very hard because we wanted to help but he didn't want the help. (Participant #6, unaffected female)

Participants' responses suggested that they not only have difficulty meeting people and maintaining existing relationships, but also struggle when interacting with their own family members.

4.2.2 Theme: Variable Causal Attributions

There were basically three groups of causative factors proposed by the participants. The first is comprised of the participants who believe in a genetic etiology. These individuals felt that if the gene for BPD is present in someone at birth, then that person is destined to develop BPD. In their opinion, nothing can be done to change the risk of developing BPD if one is born with the gene. The second group is composed of the participants who felt that their risk to develop BPD was higher than other people because of their family history. These participants felt that a family history of any mental illness, including but not limited to BPD, increased their risk to develop BPD (or any other mental illness). In a sense, they do believe that genetics is the cause, but they concede that environmental factors such as home or work life affect the chance of someone developing BPD. Third, some of the participants felt that BPD does not have a genetic component and the cause of their BPD is the events that have occurred throughout their lives. This included their family life while growing up, social life, and work life.

4.2.2.1 Genetic

Three participants felt strongly that BPD is a hereditary condition that one either does or does not have at birth. The three individuals who had this belief about the cause for BPD indicated that their physician provided them with this information. Two of the participants shared the following:

Interviewer: What would you say caused your bipolar disorder?

Participant: I really don't know, other than the fact that the doctor says it's hereditary. Well, you're born with it, I don't know if it's hereditary. I shouldn't say that, I understand that it's something you're born with... (Participant #9, unaffected female)

Participant: I never knew until my last doctor's visit. I asked 'Was I born with this?' He said yes, I was born with this, it's nothing that I did. So I guess it's hereditary... (Participant #3, affected male)

I think there's nothing you can do about it. I think you're either going to get it when you're born with it or you're not. Before you're born you can't do anything about it and then after you're born you still can't do anything about it. (Participant #3, affected male)

In addition to believing that BPD is something present at birth, Participant #3 felt that children are only at risk of developing BPD if one of their parents is affected with this condition.

Two individuals indicated that nothing can be done to affect the chance of someone developing BPD or any mental illness. For them, BPD is a condition that cannot be prevented through any means available. In the words of one participant,

No, I really don't think anything can be done about that. Because I think that if they're going to have it, they're going to have it. I really don't think there's anything that can be done. (Participant #5, affected female)

These participants suggested that environmental factors, such as the work or home situation, do not affect the chance of someone developing BPD.

4.2.2.2 Family history

Three participants believed there was a predisposition to BPD based on family history of mental illness (not a family history of BPD). These participants felt any type of mental illness in the family history can predispose one to BPD. One participant said:

I think I was predisposed to it just because of other family members and just the conditions were right, I guess, and different things in my life built up. It occurred slowly, it didn't happen right away, so I mean, it's just something that occurred slowly over time, it just developed. But I think I've always had it but it just doesn't show signs until, well, for some people it doesn't show signs until later in life, like their 20s or 30s. For me it started when I was about 14... (Participant #5, affected female)

4.2.2.3 Social environment

Several participants were of the opinion that the environment plays a causative role in BPD. For example, one participant felt that his BPD was a direct result of a stressful situation at work. Others felt that the accumulation of stressful life events caused their BPD and that reducing stress can lower the chance of developing BPD in those who are at risk. Some participants stated that reducing tension within the home environment could help decrease the chance of a child's developing BPD. Some participants described that one's home life can affect the chances of developing BPD:

Well it just depends on how you get treated by your family members. Like if they're always bickering or something like that. (Participant #4, affected male)

Having a healthy and normal a life as possible. My father was extremely abusive and that was very traumatic for me all my life and it still is. (Participant #7, affected female)

They felt that their home environment while growing up contributed to their BPD. Also, one participant said that her social life caused her BPD.

Interviewer: What would you say caused your bipolar disorder?

Participant: I'm not really sure, I used to occasionally drink on the weekends. Not having too many social friends. I don't know, I really don't. I've always worked though. It gets really bad being by yourself all the time. (Participant #8, affected female)

Finally, one participant felt strongly that genetics do not play a large causative role in BPD. He feels that BPD is caused by changes in mood that have nothing to do with genes.

4.2.3 Theme: Desire for diagnostic testing

The responses of the participants in this study indicate a strong desire to have some type of diagnostic testing for BPD. Affected individuals agreed that having a test would validate their diagnosis. In their opinion, a test could also improve treatment for those who develop BPD.

4.2.3.1 Importance of testing

Three of the participants recognized that early intervention is crucial for treatment of BPD. They indicated that treatment can help one feel better and therefore it is important to get help right away. It can take time for a diagnosis of BPD to be made because one has to encounter a manic episode. In their opinion, a diagnostic test could eliminate the wait for treatment. Having a test for BPD seemed to be critical for some participants because they expressed a need for their diagnosis to be validated.

4.2.3.2 Probabilistic test less desirable

Most individuals agreed that a test is needed for BPD; however, some were concerned that living with a percentage would cause too much stress. For example, one participant responded to a question about someone who has a 20% chance to develop BPD by saying:

I don't [think it is useful information] because it's such a low chance, a low risk that someone else would get it in her family. Maybe it is that she knows it's a low risk probably so she doesn't have to worry. (Participant #7, affected female)

Interviewer: Do you think if the risk was higher, say an 80% chance to develop bipolar disorder, that would change the way you felt about it?

I think that's too scary. There's still a 20% chance that someone wouldn't get it so I don't think she needs to know if there's a high risk. It's not a sure thing, there are other factors involved, it's not just genetics. (Participant #7, affected female)

Of the individuals who felt that BPD does have a genetic component, there was a consensus that there is a positive correlation between the amount of genes tested and the accuracy of the test. Others felt that it was not possible to have a percentage as the result because they felt that BPD is something that is or is not present at birth. For them, a percentage does not make sense because they view BPD in a deterministic fashion.

4.2.4 Theme: Reproductive considerations

Based on the responses during the interviews, BPD can affect family planning decisions. Only one participant indicated that she has changed her plans to have children after she was diagnosed with BPD.

4.2.4.1 Family planning decisions

Even the participants who believe that BPD is a genetic condition that can run in a family would not have changed their plans to have children. One individual, however, has changed her family planning decisions based on her diagnosis of BPD. Since she was diagnosed, she has decided that there are too many risks for her. She expressed being saddened by making the decision to change her reproductive plans:

I really love kids and I've always thought about having kids down the line but after this last episode of depression that I had, I realized it probably wouldn't be a good idea. Number one, they might have the same condition and number two, if I'm severely depressed I wouldn't be able to take care of them how they should be taken care of. I wouldn't want to put someone in that situation. (Participant #5, affected female)

Three of the participants already had children when they were diagnosed, but said that it would not have changed their decision if they had been diagnosed prior to having children. The affected male participants, who are in their 40s and 50s, did not explicitly say that they have plans to have children. However, they also said that having BPD would not affect their decisions to have children.

4.2.4.2 Concern that bipolar disorder “runs in the family”

Only one participant was concerned that BPD runs in the family because her mother was also diagnosed. When asked if she is concerned that BPD runs in the family, she said,

No because I don't know my child and I won't be having children anymore. But yes, it is a concern because I have worried from time to time that my son might have bipolar. (Participant #7, affected female)

She does not know her only child because he was given up for adoption over thirty years ago. Another participant who does not feel that BPD runs in the family understands that BPD has a genetic component and is concerned that she would pass it onto her children. Her response to the same question was,

My main concern would be passing this on. That's why I don't want to have children because I would be afraid they would have this and they would have similar experiences. And I wouldn't want that for my child. (Participant #5, affected female)

Seven of the participants responded that they do not feel that BPD runs in the family because no one else was diagnosed. A few participants had other family members whom they thought had BPD (whether or not they were officially diagnosed) or some other mental illness. Finally, there

is one participant who feels that BPD is a heritable condition, but this does not concern her even though she has a daughter. There also was disagreement among those who believe BPD is a genetic condition. Some who felt this way were still unconcerned that it could be passed down through the family. However, this could be due to the fact that most of the participants did not have children.

5.0 DISCUSSION

This study used the same interview guide that was designed for the study by Peay et al. (2009). Peay et al. (2009) interviewed 48 individuals: 25 individuals with BPD and 23 siblings of affected individuals. The objectives of the previous study were to “explore perceptions of family vulnerability, perceived control, and coping strategies related to familial risk and needs from genetic counseling (Peay, et al., 2009).” Thematic analysis was also used in Peay et al. (2009) to identify themes from the interviews and also from interview summaries. The themes that emerged included perception that BPD is significantly burdensome, fairly consistent causal attributions, increased risk of mood disorders to family members, reproductive considerations, at-risk family members, desire to end illness cycle in family, desire to modify risk for other family members, coping strategies for familial vulnerability, and the importance of education to monitor family members for early symptoms (Peay, et al., 2009). A difference between these two studies is that the sample size is smaller in the current study. Also, the previous study initially used codes developed from the literature before refining them to code the interviews and summaries.

The four themes that emerged from the thematic analysis are excessive disease burden, variable causal attributions, desire for diagnostic test for BPD, and reproductive considerations. Each theme is described and discussed in relation to findings from previous studies. The potential need for genetic counseling for individuals with BPD and their family members is

discussed. Also, a concept called biographical disruption that has been described in the literature on chronic diseases is discussed in regard to the findings in this study. Finally, the limitations of this study and directions for future research are addressed.

5.1 STUDY FINDINGS IN THE CONTEXT OF PREVIOUS WORK

5.1.1 Theme: Excessive disease burden

Participants' responses suggest that individuals with BPD can experience diminished quality of life. BPD has the potential to affect almost every aspect of the lives of those with it, and in this study only one participant could describe a positive impact of BPD. This supports the results of another study that also came to the conclusion that most individuals with BPD experience significant burdens that affect their daily lives (Peay, et al., 2009). The participants in a study by Peay et al. (2009) responded that BPD moderately to strongly affects daily function, life plans, and relationships.

The current study supports the finding in previous research that relationships are negatively impacted by the symptoms of BPD. Smith et al. (1996) surveyed BPD support group members, medical students, and residents about the impact of BPD on daily life. The study asked participants to rate the impact of BPD on their life experience on a Likert scale with options ranging from 1-5 for categories including marriage/relationships, raising children, education, goals, career, and finances. An answer of 1 indicated that BPD does not affect daily life in that category and an answer of 5 indicated that BPD severely impacts daily life in that category. One of the aspects cited in Smith et al. (1996) that is affected by BPD is marriage/relationships (mean

3.8 on the Likert scale) (Smith, et al., 1996). The combination of the results from these studies indicates that this population can experience excessive disease burden and BPD can diminish quality of life.

5.1.2 Theme: Variable causal attributions

Almost all of the participants had a different explanation for the cause of their BPD. The spectrum of causation ranged from solely genetic factors to purely environmental factors. Meiser et al. (2007) asked participants in their study what they perceived as the cause of their BPD and their responses also indicated a wide range of perceived etiologies (Meiser, et al., 2007). One response to the question of causal attributions in the current study is “I don’t know.” This was not reported in previous research, but this study asked an open-ended question about causal attributions where other studies asked participants to choose from a list of possibilities.

Meiser et al. (2007) reported that 85% of the participants felt that genetics was the cause. The present study revealed different conclusions, with three participants indicating that genetics was the cause of their BPD. Other causes cited in previous research that were also found in the present study include family environment, parental behavior, difficult or abusive childhood, accumulation of daily life stresses, and imbalance of chemicals in the brain (Meiser, et al., 2007). There is little agreement among affected individuals in regard to the cause of BPD; however, there is agreement across studies that most people have a variety of explanations.

5.1.3 Theme: Desire for testing

This theme emerged as multiple participants emphasized the desire to have a test to *prove* or confirm that they have a medical condition. As previously mentioned in the Background and Significance section, this is a common occurrence for individuals with a psychiatric illness. Individuals with BPD can lead productive lives between episodes of depression and mania. Therefore, it might be difficult for employers to understand that BPD is a medical condition which has the potential to cause serious problems for their affected employee. One participant commented, “there’s really no physical test which proves that I have it.” This individual had to leave his job because he was unable to deal with the stress, and the employer was not willing to provide accommodations because mental illness can be perceived differently than a physical disability. Several other individuals with BPD stated that they could not work because of their condition. A test to prove that they have BPD, which may encourage employers to be more lenient or make it easier to get disability benefits, was mentioned by participants. These comments are in contrast to other research that concluded that a diagnostic test could lead to employment discrimination (Meiser, et al., 2005; Trippitelli, et al., 1998; Wilde, et al., 2010). While the potential for discrimination due to genetic testing has received attention in the literature and the popular media, our participants offered an interesting perspective that suggests the benefits of diagnostic testing may outweigh the risks of discrimination in certain circumstances.

Another benefit of testing cited by the participants was the necessity for an earlier diagnosis. Previous research supports that early diagnosis/treatment and long-term follow-up minimizes the episode frequency (Lish, et al., 1994). Episodes can cause significant disruption in the lives of those with BPD and reduction of episodes could improve the quality of life.

Individuals with BPD have reported that they have fewer negative life events when there is infrequent recurrence while undergoing treatment for BPD (Lish, et al., 1994). Improving the lives of affected individuals by early detection and treatment is one beneficial aspect of a genetic test and is one reason why the search for susceptibility genes continues.

Unfortunately, most individuals with BPD are interested in testing that will provide a definitive diagnosis but current understanding of the genetics of BPD suggests that it is unlikely that a genetic test will have a high enough accuracy to be diagnostic in the near future and other biochemical markers may need to be identified for diagnostic testing (Lakhan, Vieira, & Hamlat, 2010). It is most likely that a genetic test would provide a probability or risk of developing BPD as opposed to a definitive answer. Should this type of susceptibility testing become available, uptake rates may be lower than estimated because some participants contend that living with uncertainty causes stress, which could in turn induce episodes. Even testing that provides a definitive answer has lower uptake than predicted. For example, prior to the release of genetic testing for Huntington's disease (HD), it was estimated that between 40% and 79% of at-risk individuals would opt for testing (Meiser & Dunn, 2000). Similar to BPD, there were concerns about possible negative impacts of predictability testing for HD, but it was felt that the benefits of knowing would outweigh the risks of testing (Meiser & Dunn, 2000). When the test became available the uptake was much lower than predicted (Meiser & Dunn, 2000).

When asked a question about a test revealing that someone has a 60% chance to develop BPD, one participant replied, "...I don't know that it would do any good to know that you *might* [emphasis added] get it. I think that would just, that would cause me to just be fearful of something that hasn't even happened yet." Similar sentiments were shared by several participants and previous research has provided similar evidence (Meiser, et al., 2005; Wilde, et

al., 2010). Nevertheless, it is still important to continue efforts to create a diagnostic test for BPD, and should it involve genetic testing, the accuracy and predictive value will need to be scrutinized before releasing the test for clinical use.

5.1.4 Theme: Reproductive considerations

Except for one individual (Participant #5), the participants in this study would not change their decisions to have children. This is similar to a previous study in which the majority of the participants would not change plans to have children even though they were diagnosed with BPD (Trippitelli, et al., 1998). The decision made by Participant #5 supports another study which found that 35% of the participants were “not at all willing” or “less willing” to have children (Meiser, et al., 2007).

Previous research has shown that half of the participants would have changed their decision to have children had they known about the increased risk for their children to be affected with BPD (Meiser, et al., 2005). Those who feel that the diagnosis of BPD would not affect their decision to have children might not find the risks to be significant. Those who are not concerned about passing BPD to future generations might not believe that it is a genetic condition (Meiser, et al., 2007). In conclusion, a diagnosis of BPD may change family planning decisions. Decision-making is likely dependent on factors such as the perceived stigma of BPD, risk perception, endorsement of a genetic model, and being affected with BPD (Meiser, et al., 2007).

5.2 GENETIC COUNSELING FOR BIPOLAR DISORDER

Since almost all of the participants expressed an interest in learning more information, it seems that genetic counseling could provide an opportunity for education and help clarify issues related to BPD genetics. The participants in this study were not specifically asked if they would attend a genetic counseling session for BPD, but the impression was that the majority of participants would be interested. In fact, previous research estimated that 75% of the participants would opt for genetic counseling (Quaid, Aschen, Smiley, & John I. Nurnberger, 2001).

The individuals with BPD in this study felt that their family members do not know how to interact with them because they do not understand the issues that affected individuals deal with on a daily basis. This is one of the worst aspects of BPD for some individuals. Similarly, it is difficult for siblings when they are unable to understand their own brother or sister. Educating family members about BPD can help them appreciate the impact of this chronic condition on individuals. This may help to improve relations with family members, which can be problematic for those with BPD. In addition to learning about the disorder, genetic counseling clients could learn about the early signs and symptoms to be sure to get family members treatment as soon as possible (Hill & Sahhar, 2006).

Some of the participants had already done significant research about BPD and had some understanding of genetics. Austin and Honer (2005) review important aspects of a psychiatric genetic counseling session. This research supports their claims that some clients who seek genetic counseling have an existing knowledge base regarding BPD. They state that counselors should discuss previous education with clients during a genetic counseling session (Austin & Honer, 2005). Genetic counseling could build on prior knowledge of genetics in order to help clients piece together the information currently known about BPD (Austin & Honer, 2005).

In addition, genetic counseling can be an effective way to dispel misperceptions (Austin & Honer, 2005). For example, in the present study, some participants felt that BPD is a condition that is present at birth and cannot be affected by environmental factors. Clients can be provided with information about multifactorial inheritance and the way in which environmental factors can combine with genetics to cause a condition. In fact, this is consistent with conclusions by Finn and Smoller (2006) that one of the functions of genetic counseling for psychiatric conditions is explaining the role of genetics in the etiology. In conclusion, genetic counseling could be useful for individuals with BPD and their family members.

5.3 BIOGRAPHICAL DISRUPTION

Michael Bury (1982) introduced the concept of “biographical disruption” when studying the impact of rheumatoid arthritis on the everyday lives of women. When chronic illness changes one’s sense of self and disrupts their “structures of everyday life,” it is considered a biographical disruption (Bury, 1982). There are three aspects of biographical disruption: the disruption of daily activities and behaviors, a reconfiguration of one’s identity (biography), and the response of mobilizing resources to manage the new daily situation (Bury, 1982). A biographical disruption, in the form of a chronic illness diagnosis, forces the individual to re-think future plans and usually he has to change aspects of daily life to deal with the new circumstances (Bury, 1982). This concept can be and has been used to analyze the way in which being diagnosed with a chronic illness can affect someone’s life (Wilson, 2007).

Studies have examined biographical disruption for other conditions such as HIV/AIDS, motherhood and HIV/AIDS, cystic fibrosis, terminal cancer, and hypertension. However, it has

not been studied in relation to a diagnosis of BPD, and the themes identified in this project offer some interesting comparisons. The challenges of living with episodes of depression and mania resemble those of other chronic illness. Indeed, being diagnosed with BPD appears to be a disruptive event for some individuals in this study.

5.3.1 Biographical Disruption in Bipolar Disorder

One of the themes that resulted from this study is that BPD causes disease burden that affects almost every aspect of daily life. This combined with the challenges of episodes of depression and mania, imply that BPD may constitute a biographical disruption to the individuals who are diagnosed. However, some may not experience a significant disruption in their lives. For example, one man who was diagnosed in his 60s has been married for a long time and has completed his family. His diagnosis of BPD has not changed his life dramatically for several reasons. His course of illness was short, only a few years. His family was already complete and he did not feel that his children were at risk for the same disorder. The only difference for him is the new medication regimen. In his case, BPD may not be considered a chronic illness that constituted a biographical disruption. In contrast, BPD for others created and continues to create significant disruptions to their lives. In the literature and with regard to BPD, it appears that biographical disruption can be caused by either the diagnosis or the symptoms related to the condition.

5.3.1.1 Biographical disruption caused by diagnosis

One of the participants exemplifies biographical disruption in terms of her diagnosis of BPD. She is a 22-year-old woman who was diagnosed at 17 years of age. The following quote

depicts the way in which this disorder has truly disrupted her life course and the stability she wanted to establish:

Just feeling different from other people and it's very frustrating at times because I'm not able to do some of the things that I'd like to do and I'm not able to start something that's going to be long term because I don't know how my mood's going to be. I feel alright now but then three months from now I might be in a deep depression so I might not be able to do the things that I was able to do at the time when I started. (Participant #5, affected female)

Another way that this diagnosis has changed her life is in relation to family planning. Being diagnosed with a chronic illness can cause a woman to consider the effect of that illness on her ability to be a mother (Wilson, 2007).

Wilson (2007) explored biographical disruption in mothers with HIV/AIDS. Motherhood is crucial to the identity of most women, and the diagnosis affected their identity as mothers (Wilson, 2007). It seemed that their identity as a "good" mother was threatened by their illness (Wilson, 2007). These women expressed concern that they might not be able to care for their children in times of acute illness, and that fear threatened their sense of motherhood and therefore their identity (Wilson, 2007). The participant in the current study shared that she chooses not to have children because of her diagnosis. She stated two reasons for making this decision:

I really love kids and I've always thought about having kids down the line but after this last episode of depression that I had I realized it probably wouldn't be a good idea. Number one, they might have the same condition and number two, if I'm severely depressed I wouldn't be able to take care of them how they should be taken care of. I wouldn't want to put someone in that situation. (Participant #5, affected female)

This accentuates how serious BPD is and how it can alter the course of someone's life. Motherhood was not specifically discussed in relation to the affects of BPD, but it might be

interesting to explore in a future study. Based on the responses of one participant it might be possible that BPD causes a biographical disruption in terms of a woman's identity as a mother.

5.3.1.2 Biographical disruption caused by ongoing events

The disruption might not always be the diagnosis itself for individuals with BPD; there were disruptive events that occurred after the diagnosis. Since the length and number of episodes in BPD vary among individuals, it may create disruptions throughout the course of the individual's life. One participant was severely depressed for over two years and now lives in constant fear of becoming depressed again. Also, hospitalizations are common for both manic and depression episodes. Several of the participants have been hospitalized several times and constantly fear that another episode will put them back into the hospital.

This type of disruption is similar to experiences of those diagnosed with hypertension. Once they were diagnosed with a condition that increases their risk of heart attack and stroke, they became hypersensitive to bodily signs (Sangren, Reventlow, & Hetlevik, 2009). The diagnosis constituted a major life event, but the disruption is arguably the change in behavior. Individuals with BPD who live in fear of another severe episode or hospitalizations, as well as their family members, may become sensitive to any changes in their mood or behavior. These could be considered a biographical disruption because it forever changes one's identity and daily life.

This is supported by research about biographical disruption in the context of fibromyalgia and chronic fatigue syndrome (Asbring, 2001). These conditions are similar to BPD in that there is much uncertainty about etiology, treatment, and prognosis; the severity of symptoms varies across affected individuals; the illness is episodic; the diagnosis is based on criteria and not always physical testing; and affected individuals face considerable disruption in social

functioning. In the case of fibromyalgia and chronic fatigue syndrome, the biographical disruption occurred over a period of time as patients had to change from an active to a passive lifestyle (Asbring, 2001). Several of the participants with BPD underwent a similar lifestyle transformation.

For these participants, it was not the diagnosis of BPD that disrupted their lives, it was the change in lifestyle. Some of the participants worked full time jobs and led busy lives. After their first severe episode, they had to quit their jobs and lead a more passive lifestyle. The diagnosis, however, provided individuals with an understanding of why they needed to leave their employment. They felt like working was too much responsibility when there was a chance of having a severe episode any day. Not being able to accomplish the same goals once they have had an episode is what really altered the course of their lives.

5.3.2 Conclusion of biographical disruption in bipolar disorder

Considering biographical disruption in the context of BPD may add provide insights into the manner in which BPD affects the daily lives of those who are affected. The results of such a study may present new ways to help them cope with their daily lives. For some individuals with BPD, the actual diagnosis may cause a disruption to their identity. However, the disruption could also be caused by the symptoms of BPD that appear both before and after the diagnosis. In the case of BPD, similar to fibromyalgia and chronic fatigue syndrome, the diagnosis has the potential to provide relief because these conditions sometimes go unrecognized and affected individuals do not understand the cause of their symptoms. In conclusion, BPD may create a biographical disruption in the lives of those who are affected and this is a possible area for future research.

5.4 FUTURE DIRECTIONS AND LIMITATIONS

5.4.1 Limitations

There are several limitations to this research study. This was a qualitative research study, and it is possible that a researcher with more experience could have made more interpretive conclusions. Another limitation is interviewing experience. Over time, as the interviews were performed, they became more of a conversation as opposed to a question-and-answer session. More information was obtained from the participants in the later conversation-style interviews. There is some ascertainment bias because all of the individuals in this study are presumably undergoing treatment. Finally, the sample size is small and so the results are not generalizable to the entire BPD population. However, the results have led to several ideas for future research studies.

5.4.2 Future Directions

This study has interesting results and provided avenues for future research. First, it shows that individuals with BPD and their siblings are interested in learning more about BPD. Genetic counseling would be a good method for accomplishing education about this condition. Those who seemed less interested in genetic counseling could benefit from reading material that presents the information in an understandable and concise manner. An idea for a future project is creating educational materials geared toward affected individuals and their family members. Participants' responses suggest a need for, and an interest in, such educational materials. The majority of the knowledge deficit relates to the genetics of BPD. It is possible that psychiatrists

might not always discuss the genetics of BPD with their patients. Since some psychiatrists may not be aware of the current understanding of the genetics of BPD, a guide could also be created for physicians.

Future research using this interview guide could yield more data through several alterations to the guide. First, adding socioeconomic questions such as employment, income, and marital status would provide more data and could lead to more conclusions. As discussed, more information was gained when the interviews became more conversation-style as opposed to a question-and-answer session. Therefore, changing the interview guide so that it is more open-ended may provide more rich data for future studies. Finally, since it seems that genetic counseling could benefit this population, questions could be added to the guide that specifically ask about interest level. There are already questions about information that would be presented during a genetic counseling session that would easily lead into questions about interest.

6.0 CONCLUSION

This qualitative research study consisted of phone interviews using an interview guide from Peay et al. (2009). The goal of this study was to learn the perceptions of genetics and genetic counseling from adults with BPD and their siblings. Once the interviews were complete, they were transcribed and the data was analyzed using inductive thematic analysis. Four themes regarding BPD and genetics were identified from the responses to the questions during the interviews.

Patients with BPD can experience an excessive disease burden that affects their daily life. This is in agreement with previous research that concluded that BPD is a condition that significantly impacts the daily lives of individuals with BPD (Peay, et al., 2009; Smith, et al., 1996). The data from this study indicate that BPD can create a socially isolated lifestyle and that depression is the worst aspect of BPD for most of the participants. Causality varied among individuals with BPD, and the explanations were specific for each participant. Previous research has also concluded that individuals with BPD can endorse several models of causation (Meiser, et al., 2007). The participants expressed a high level of interest in testing for BPD. A diagnostic test is preferred over a probabilistic test because living with uncertainty can cause stress. These conclusions are in agreement with previous literature (Meiser, et al., 2005; Wilde, et al., 2010). Some individuals with BPD who are diagnosed prior to having children may reconsider their reproductive decisions. However, others may not change their reproductive planning decisions

regardless of their diagnosis of BPD. This is also consistent with previous research about the effect of BPD on family planning decisions (Meiser, et al., 2007; Meiser, et al., 2005).

Genetic counseling could be beneficial for individuals with BPD and their family members. Since some individuals with BPD have a basic understanding of genetic concepts, genetic counseling could build on that information to help them understand the multifactorial etiology. Also, genetic counseling could provide an opportunity to educate family members about the condition to help them understand how the condition affects the individuals who are diagnosed. Early intervention is important for a better prognosis (Lish, et al., 1994) and genetic counseling could help family members understand the signs and symptoms to get treatment earlier.

Finally, biographical disruption is a concept that could be studied in relation to BPD. The diagnosis of BPD could constitute a biographical disruption for some individuals. However, other individuals who are diagnosed with BPD may experience biographical disruptions throughout the course of their illness. The sample size of this study is too small to make conclusions for this population; however, these observations indicate that biographical disruption may be a relevant concept to study with respect to BPD.

APPENDIX A: Consent Form

Telephone Informed Consent Document

Script to be read to all telephone interviewees

I will now read you the informed consent for the study. The informed consent process is meant to help you understand what your participation in the study involves, as well as the risks and benefits.

This research study involves interviewing adults with bipolar disorder or adult brothers or sisters of individuals with bipolar disorder and asking them about their opinions and experiences. I plan to ask you questions related to your thoughts about the causes of bipolar disorder, your experiences with this illness, your concerns about the disorder happening again in your family, and your feelings about the value of discussing these issues with health care professionals. As part of the interview I will ask questions about the mental health of your close family members and about your own mental health.

The interview will take about 60 minutes to complete, and we will tape record the interviews. Other than the people directly involved in this research, no other individuals will be told that you participated in the study. Identifying information about you will not appear on any documents following the interview and we will keep all records confidential.

In research, we always try to help people understand the risks and potential benefits of participating. There are no physical risks to you because of participating in the study. It is possible that, because the interview includes personal issues, you may feel upset by the questions. You do not have to answer any question and you may stop the interview at any time. The main risk is to your privacy because we are asking questions about your personal experiences and the experiences of your family members with psychiatric illness. To address this, we are taking care to protect your privacy by keeping all of your personal information in a password-protected database accessible only to the study team. The tape recording and transcript we make today will not be labeled with your name or any other contact information. We will keep the tapes for two years and transcripts for three years; after that, we will destroy them.

Participating in this study will not provide any direct benefit to you. Sharing your thoughts and experiences will help us better understand what it is like to live with bipolar disorder in the family.

The alternative to being in this study is to choose not to be interviewed. If you do not want to continue the interview once we have started, just let me know and we will stop. If you choose not to continue, we will not use any of the information we have collected unless you say it is OK to do so. The tape recording of your interview will be erased if you do not want us to use it.

Do you have any questions about the study? Do you want to continue with the study?

[If yes] Would you like me to mail you a copy of the informed consent that we just discussed?

I will now turn on the tape recorder so we can begin our interview.

WITH THE TAPE RECORDER ON: I am now recording the interview. Could I ask you to restate that we have your permission to tape record the interview?

AT THE BEGINNING OF EACH INTERVIEW:

As part of our research, we may want to re-contact some of our participants by phone so we can check and see if we are getting the gist of the interviews right, or if new questions come up during the interviews. We will keep all of our participants' personal information confidential and will delete all contact information within 5 months. Would it be OK if we kept you on a list to possibly call again within the next 5 months?

AT THE END OF EACH INTERVIEW:

If you want to talk to someone about this research because you think you have not been treated fairly, or because you have been hurt by joining the study, or if you have additional questions, you should call Dr. Ilyas Kamboh , Chair, Dept Human Genetics, (412) 624-3066. Would you like a minute to write that name and number down?

APPENDIX B: Interview Guide

Questions for Individuals with Bipolar Disorder

This interview includes questions about you and your family and bipolar disorder. You will also be asked to listen to some short stories and to provide your opinion about the information presented. If you have any questions or need anything repeated, please let me know.

1. Please tell me how you were diagnosed with bipolar disorder. When did the symptoms begin?
2. Does bipolar disorder affect your daily life? If so, how?
3. What is the worst thing about bipolar disorder for you? What is the worst thing for your family?
4. What is the best thing about bipolar disorder for you? What is the best thing for your family?
5. How many brothers and sisters do you have?
6. Do you have any children?

If yes- how many? Do you plan to have any more children?

If no- Do you plan to have children in the future?

7. Do you have other family members who have been diagnosed with bipolar disorder? Are there any family members who you think have bipolar disorder or any other mental illness but have not been diagnosed?

For each identified: how the participant is related to them; symptoms/diagnosis

8. What would you say caused your bipolar disorder? Do you think the same event causes bipolar disorder in everyone who is diagnosed?
9. Do you feel that you can control your own symptoms? If so, to what extent are you able to control your own symptoms?
10. To what extent can your family and friends control your symptoms?
11. Has anyone ever treated you differently because you have bipolar disorder? If so, has this affected your willingness to tell others about your diagnosis?
12. Do you feel that bipolar disorder runs in your family? If so, does this concern you?
13. If you were to compare yourself to another person who is similar to you with the exception that there is no bipolar disorder in his/her family, what is the likelihood that your children will have bipolar disorder?
14. Do you think anything can be done by you or your family members to affect the chance of one of your children developing a mental illness such as bipolar disorder?
15. Would you be interested in learning more about what factors cause bipolar disorder? If so, what type of information would you be interested in?
16. What comes to mind when I say genetics and bipolar disorder?
17. Has your diagnosis of bipolar disorder changed your plans to have children? If so, how? Have any of your family members expressed their opinion? If so, do they share the same opinion as you?

Now I'm going to read you a series of stories. The stories have a number of different pieces, so if you want me to repeat something, please let me know.

In these stories, Susan/Tom has a brother with bipolar disorder. She/He has questions about the cause of bipolar disorder and is concerned about it happening again in the family. Susan/Tom goes to see a genetic counselor. A genetic counselor is a health care professional who specializes in helping families who have concerns about conditions that can run in the family. After each story I'll ask you to tell me how the information that Susan/Tom learned could be useful or why you think that it is not useful.

1. Susan/Tom goes to a genetic counselor **to learn what causes bipolar disorder**. The genetic counselor tells Susan/Tom that bipolar disorder is caused by a mix of a person's genes and non-genetic things, like the environment that they live in. The genetic counselor explains that there are many genes involved that may be passed down from both sides of the family. Some things in a person's everyday environment, like being exposed to viruses, also may affect the chance of getting bipolar disorder. The genetic counselor says that, while good parenting helps all children's development, parenting style does not cause, or prevent, bipolar disorder. The genetic counselor and Susan/Tom discuss the importance of finding signs of bipolar disorder early and getting treatment right away.

Do you think this information would be useful to Susan/Tom? Why or why not?

2. Susan/Tom goes to the genetic counselor **to learn about the chance that bipolar disorder could happen again** in the family. The genetic counselor takes a careful family history, and asks Susan/Tom questions about the mental health of family members. The genetic counselor also asks about Susan/Tom's own mental health. The genetic counselor uses the family history information to estimate that there is about a 20% chance, which is the same as a 1 in 5 chance, that bipolar disorder could happen again in a young person in Tom's/Susan's family. The genetic counselor says that this chance might not be exactly right, but is probably close. She hopes the information can give Susan/Tom an idea of how likely it is that others in her/his family may get bipolar disorder.

Do you think this information would be useful to Susan/Tom? Why or why not?

The next three stories are about genetic testing. Right now there is no genetic test that can tell someone their chance of getting bipolar disorder, but there may be a test like that

in the future. I am going to ask you to think about different kinds of tests that could be available one day.

Each story is a little bit different. If the differences aren't clear, please ask me to say the stories again. In each story, Susan/Tom is interested in genetic testing to learn more about the chance that young people in her/his family will get bipolar disorder.

3. Here is the first story about genetic testing. Susan/Tom goes to a genetic counselor to learn about testing for bipolar disorder. The genetic counselor explains that the test looks for a change in **one gene** that will raise someone's chance of getting bipolar disorder. If the genetic test finds that change in a person's gene, then that person will have a **60% chance, or more than a 1 in 2 chance**, of getting bipolar disorder during their life.

Do you think this information would be useful to Susan/Tom? Why or why not?

4. Now I'm going to tell you a second story about genetic testing. In this one, Susan/Tom goes to the genetic counselor to learn about a **different** genetic test for bipolar disorder. The genetic counselor explains that this test looks at changes in **six different genes**. **Each of these changes** plays a small role in the chance of getting bipolar disorder. If the genetic test shows that a person has changes in all six genes, then that person has a **20% chance**, which is the same as a **1 in 5 chance**, of getting bipolar disorder during their life.

Does this information seem more useful, less useful, or about the same as in the previous story? Why?

5. What if the genetic counselor could give Susan/Tom more information? Say the genetic counselor uses the results from the genetic test **together** with information from Susan/Tom's **family history**. If a person has changes in all six genes and has at least one family member with bipolar disorder, then that person has a 60% chance, or a more than 1 in 2 chance, of getting bipolar disorder during their life.

Does this information seem more useful, less useful, or about the same as in the previous stories? Why?

Say that we were able to prevent bipolar disorder in people who have a high chance of getting the disease. Would that change the way you thought about any of the stories we just discussed? How?

If you could write the best possible story about how genetics could help Bob/Jan in the future, what would it be? I'll start it and you finish it. "Bob/Jan goes to the genetic counselor, and finds out that..." and you finish it.

Now I'll end by asking a few questions about you.

How old are you?

What state do you live in?

What racial or ethnic category do you belong to?

American Indian/Alaska Native

Asian

Native Hawaiian or other Pacific Islander

Black or African American

White

Do you consider yourself to be Hispanic or Latino?

This is the end of my questions. Are there other things that you've thought of as we've talked about bipolar disorder and genetics that you'd like to tell me?

Debriefing:

Once tape is off: I'd like you to keep in mind that the stories you heard were made up. Right now there is no genetic testing that can tell risk for bipolar disorder. The chances given to the person in the story for bipolar to happen again in that family are also made up. The chance depends on many things that are specific to each family.

Thank you for participating in this study. Do you have any questions or comments for me?

Questions for Siblings of Individuals with Bipolar Disorder

This interview includes questions about you and your family and bipolar disorder. You will also be asked to listen to some short stories and to provide your opinion about the information presented. If you have any questions or need anything repeated, please let me know.

First, I am going to ask you questions about your brother or sister, then I'll ask you for your thoughts and experiences.

1. Please tell me how your brother/sister was diagnosed with bipolar disorder. When did the symptoms begin?
2. Do you think bipolar disorder affects your brother/sister's daily life? If so, how?
3. What is the worst thing about bipolar disorder for your brother/sister? What is the worst thing for your family?
4. What is the best thing about bipolar disorder for your brother/sister? What is the best thing for your family?
5. How many brothers and sisters do you have?
6. Do you have any children?

If yes- how many? Do you plan to have any more children?

If no- Do you plan to have children in the future?

7. Do you have other family members who have been diagnosed with bipolar disorder? Are there any family members who you think have bipolar disorder or any other mental illness but have not been diagnosed?

For each identified: how the participant is related to them; symptoms/diagnosis

8. What would you say caused your brother/sister's bipolar disorder? Do you think the same event causes bipolar disorder in everyone who is diagnosed?

9. Do you feel that your brother/sister can control his/her own symptoms? If so, to what extent is he/she able to control his/her own symptoms?
10. Do you feel that you are able to affect your brother/sister's symptoms? If so, to what extent?
11. Has anyone ever treated you differently because you have bipolar disorder in your family? If so, has this affected your willingness to tell others about your brother/sister's diagnosis?
12. Do you feel that bipolar disorder runs in your family? If so, does this concern you?
13. If you were to compare yourself to another person who is similar to you with the exception that there is no bipolar disorder in his/her family, what is the likelihood that your children will have bipolar disorder?
14. Do you think anything can be done by you or your family members to affect the chance of one of your children developing a mental illness such as bipolar disorder?
15. Would you be interested in learning more about what factors cause bipolar disorder? If so, what type of information would interest you?
16. What comes to mind when I say genetics and bipolar disorder?
17. Has your brother/sister's diagnosis of bipolar disorder changed your plans to have children? If so, how? Have any of your family members expressed their opinion? If so, do they share the same opinion as you?

Now I'm going to read you a series of stories. The stories have a number of different pieces, so if you want me to repeat something, please let me know.

In these stories, Susan/Tom has a brother with bipolar disorder. She/He has questions about the cause of bipolar disorder and is concerned about it happening again in the family. Susan/Tom goes to see a genetic counselor. A genetic counselor is a health care professional

who specializes in helping families who have concerns about conditions that can run in the family. After each story I'll ask you to tell me how the information that Susan/Tom learned could be useful or why you think that it is not useful.

1. Susan/Tom goes to a genetic counselor **to learn what causes bipolar disorder**. The genetic counselor tells Susan/Tom that bipolar disorder is caused by a mix of a person's genes and non-genetic things, like the environment that they live in. The genetic counselor explains that there are many genes involved that may be passed down from both sides of the family. Some things in a person's everyday environment, like being exposed to viruses, also may affect the chance of getting bipolar disorder. The genetic counselor says that, while good parenting helps all children's development, parenting style does not cause, or prevent, bipolar disorder. The genetic counselor and Susan/Tom discuss the importance of finding signs of bipolar disorder early and getting treatment right away.

Do you think this information would be useful to Susan/Tom? Why or why not?

2. Susan/Tom goes to the genetic counselor **to learn about the chance that bipolar disorder could happen again** in the family. The genetic counselor takes a careful family history, and asks Susan/Tom questions about the mental health of family members. The genetic counselor also asks about Susan/Tom's own mental health. The genetic counselor uses the family history information to estimate that there is about a 20% chance, which is the same as a 1 in 5 chance, that bipolar disorder could happen again in a young person in Tom's/Susan's family. The genetic counselor says that this chance might not be exactly right, but is probably close. She hopes the information can give Susan/Tom an idea of how likely it is that others in her/his family may get bipolar disorder.

Do you think this information would be useful to Susan/Tom? Why or why not?

The next three stories are about genetic testing. Right now there is no genetic test that can tell someone their chance of getting bipolar disorder, but there may be a test like that in the future. I am going to ask you to think about different kinds of tests that could be available one day.

Each story is a little bit different. If the differences aren't clear, please ask me to say the stories again. In each story, Susan/Tom is interested in genetic testing to learn more about the chance that young people in her/his family will get bipolar disorder.

3. Here is the first story about genetic testing. Susan/Tom goes to a genetic counselor to learn about testing for bipolar disorder. The genetic counselor explains that the test looks for a change in **one gene** that will raise someone's chance of getting bipolar disorder. If the genetic test finds that change in a person's gene, then that person will have a **60% chance, or more than a 1 in 2 chance**, of getting bipolar disorder during their life.

Do you think this information would be useful to Susan/Tom? Why or why not?

4. Now I'm going to tell you a second story about genetic testing. In this one, Susan/Tom goes to the genetic counselor to learn about a **different** genetic test for bipolar disorder. The genetic counselor explains that this test looks at changes in **six different genes**. **Each of these changes** plays a small role in the chance of getting bipolar disorder. If the genetic test shows that a person has changes in all six genes, then that person has a **20% chance**, which is the same as a **1 in 5 chance**, of getting bipolar disorder during their life.

Does this information seem more useful, less useful, or about the same as in the previous story? Why?

5. What if the genetic counselor could give Susan/Tom more information? Say the genetic counselor uses the results from the genetic test **together** with information from Susan/Tom's **family history**. If a person has changes in all six genes and has at least one family member with bipolar disorder, then that person has a 60% chance, or a more than 1 in 2 chance, of getting bipolar disorder during their life.

Does this information seem more useful, less useful, or about the same as in the previous story? Why?

Say that we were able to prevent bipolar disorder in people who have a high chance of getting the disease. Would that change the way you thought about any of the stories we just discussed? How?

If you could write the best possible story about how genetics could help Bob/Jan in the future, what would it be? I'll start it and you finish it. "Bob/Jan goes to the genetic counselor, and finds out that..." and you finish it.

Now I'll end by asking a few questions about you.

How old are you?

What state do you live in?

What racial or ethnic category do you belong to?

American Indian/Alaska Native

Asian

Native Hawaiian or other Pacific Islander

Black or African American

White

Do you consider yourself to be Hispanic or Latino?

This is the end of my questions. Are there other things that you've thought of as we've talked about bipolar disorder and genetics that you'd like to tell me?

Debriefing:

Once tape is off: I'd like you to keep in mind that the stories you heard were made up. Right now there is no genetic testing that can tell risk for bipolar disorder. The chances given to the person in the story for bipolar to happen again in that family are also made up. The chance depends on many things that are specific to each family.

Thank you for participating in this study. Do you have any questions or comments for me?

APPENDIX C: Recruitment Flyer

PERSPECTIVES OF INDIVIDUALS WITH BIPOLAR DISORDER AND SIBLINGS OF INDIVIDUALS WITH BIPOLAR DISORDER: A TELEPHONE or PERSONAL INTERVIEW STUDY

We invite you to participate in a research study sponsored by the University of Pittsburgh. Through this study we hope to learn more about what people with bipolar disorder and siblings of people with bipolar disorder think about the cause of bipolar disorder and the possibility that it can occur again in the family.

Who are we asking to take part in the study?

- 1. People who have bipolar disorder, OR*
- 2. brothers or sisters of people with bipolar disorder.*

We would like to find people who are willing to share what they think about the causes of bipolar disorder, their experiences with this illness, their concerns about the disorder happening again in their family, and their feelings about discussing these issues with health care professionals.

What is involved in the study?

We will ask people to complete a telephone interview that will take about 60 minutes. All interviews will be confidential.

Will I receive any compensation?

Participants who complete the survey will receive a \$25 gift certificate in return for their time.

How do I take part?

Contact the Principal Investigator, Elizabeth Gettig, by phone at 412-624-3066 or by email at bgettig@pitt.edu to learn more.

APPENDIX D: Diagnostic Criteria Details for Bipolar I and II

THE CRITERIA FOR A MANIC EPISODE (ASSOCIATION, 2000)

“1.) A distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least one week (or any duration if hospitalization is necessary).

2.) During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree: 1. Inflated self-esteem or grandiosity, potentially including grandiose delusions, 2. Decreased need for sleep (e.g., feels rested after only 3 hours of sleep) or persistent difficulty falling asleep, 3. More talkative than usual or pressure to keep talking, 4. Flight of ideas or subjective experience that thoughts are racing, 5. Distractibility (i.e., attention too easily drawn to unimportant or irrelevant stimuli), 6. Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation, 7. Excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

3.) The symptoms do not meet criteria for a mixed episode.

4.)The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.

5.) The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatment) or a general medical condition (e.g., hyperthyroidism).

THE CRITERIA FOR A MIXED EPISODE(ASSOCIATION, 2000)

1.) The criteria are met both for a Manic Episode and for a Major Depressive Episode (except for duration) nearly every day during at least a 1-week period.

2.) The mood disturbance is sufficiently severe enough to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.

3.) The symptoms are not due to the direct physiological effects of a substance (e.g., an illicit drug, a medication, or other treatment) or a general medical condition (e.g., hyperthyroidism).

CRITERIA FOR A MAJOR DEPRESSIVE EPISODE (ASSOCIATION, 2000)

1.) Five (or more) of the following symptoms have been present during the same two-week period and represent a change from previous functioning; at least one of the symptoms is either (1) or (2). 1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful).

Note: in children and adolescents, can be irritable mood. 2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others), 3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. Note: in children, consider failure to make expected weight gains. 4. Insomnia or hypersomnia nearly every day, 5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down), 6, fatigue or loss of energy nearly every day, 7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick), 8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others, 9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

2.) The symptoms do not meet criteria for a Mixed Episode.

3.) The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

4.) The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

5.) The symptoms are not better accounted for by bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

CRITERIA FOR A HYPOMANIC EPISODE(ASSOCIATION, 2000)

1.) A distinct period of persistently elevated, expansive, or irritable mood, lasting throughout at least 4 days, that is clearly different from the usual non depressed mood.

2.) During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree: 1. Inflated self-esteem or grandiosity, 2. Decreased need for sleep (e.g., feels rested after only 3 hours of sleep), 3. More talkative than usual or pressure to keep talking, 4. Flight of ideas or subjective experience that thoughts are racing, 5. Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli), 6. Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation, 7. Excessive involvement in pleasurable activities that have a high potential for negative consequences (e.g., the person engages in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

3.) The episode is associated with an unequivocal change in functioning that is uncharacteristic of the person when not symptomatic.

4.) The disturbance in mood and the change in functioning are observable by others.

5.) The episode is not severe enough to cause marked impairment in social or occupational functioning, or to necessitate hospitalization, and there are no psychotic features.

6.) The symptoms are not due to the direct physiological effects of substance (e.g., a drug of abuse, a medication, or other treatment) or a general medical condition (e.g., hyperthyroidism).

APPENDIX E: IRB Approval Letter



University of Pittsburgh Institutional Review Board

3500 Fifth Avenue
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)
<http://www.irb.pitt.edu>

Memorandum

To: Elizabeth Gettig, MS, CGC
From: Sue Beers, PhD, Vice Chair
Date: 9/23/2009
IRB#: [PRO09070167](#)
Subject: Perceptions of Genetic Counseling from Adults with Bipolar Disorder

The University of Pittsburgh Institutional Review Board reviewed and approved the above referenced study by the expedited review procedure authorized under 45 CFR 46.110 and 21 CFR 56.110. Your research study was approved under:

45 CFR 46.110.(7) characteristics/behaviors

The IRB has determined the risk to be minimal risk.

Please note that the waiver for the requirement to obtain a written informed consent has been approved.

Please note that the advertisement that was submitted for review has been approved as written. As a reminder, any changes to the wording of the approved advertisement would require IRB approval prior to distribution.

Approval Date: 9/23/2009
Expiration Date: 9/22/2010

For studies being conducted in UPMC facilities, no clinical activities can be undertaken by investigators until they have received approval from the UPMC Fiscal Review Office.

Please note that it is the investigator's responsibility to report to the IRB any unanticipated problems involving risks to subjects or others [see 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)]. The IRB Reference Manual (Chapter 3, Section 3.3) describes the reporting requirements for unanticipated problems which include, but are not limited to, adverse events. If you have any questions about this process, please contact the Adverse Events Coordinator at 412-383-1480.

The protocol and consent forms, along with a brief progress report must be resubmitted at least one month prior to the renewal date noted above as required by FWA00006790 (University of Pittsburgh), FWA00006735 (University of Pittsburgh Medical Center), FWA00000600 (Children's Hospital of Pittsburgh), FWA00003567 (Magee-Womens Health Corporation), FWA00003338 (University of Pittsburgh

Medical Center Cancer Institute).

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

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