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Psychiatric Impact of Tuberous Sclerosis Complex and Utilization of Mental Health Treatment

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PSYCHIATRIC IMPACT OF TUBEROUS SCLEROSIS COMPLEX AND
UTILIZATION OF MENTAL HEALTH TREATMENT

A

THESIS

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INTRODUCTION

Tuberous sclerosis complex (TSC) is a genetic disorder known to have a multi-system, neurocutaneous clinical presentation with an estimated incidence of 1 per 6,000 to 10,000 live births (1). The characteristic findings of TSC are skin lesions, seizures, hamartomas in the brain, kidneys, and heart in addition to a spectrum of neuropsychiatric conditions. The clinical manifestations of TSC show inter- and intra-familial variable expressivity and have the potential to fluctuate in severity over an affected individual's lifetime (2, 3). The pathophysiology of TSC arises from a heterozygous pathogenic variant in the tumor suppressor genes *TSC1* and *TSC2* that encode the instructions for the proteins hamartin and tuberin, respectively (4, 5). Consequently, the amount of functional protein is reduced, but the other copy provides enough products to effectively regulate cell growth. A second somatic pathogenic variant in *TSC1* or *TSC2* can lead to insufficient production of hamartin or tuberin and causes uncontrolled cell growth and division, resulting in hamartomas across multiple organ systems (6, 7). The pathohysiology of other clinical features associated with TSC is less well-understood.

At the 2012 International TSC Consensus Conference, the Neuropsychiatry Panel expressed concern regarding the 70% treatment gap and lack of uniformity in terminology regarding the non-physical manifestations associated with TSC (8). The term "treatment gap" refers to the difference between the portion of the population in need of services compared to the portion of the population actually receiving appropriate services (9). The members of the 2012 International TSC Consensus Conference showed support for the previously coined term, TAND, or TSC-Associated Neuropsychiatric Disorders, in order to collectively represent the various domains of neuropsychiatric manifestations within the continuum of TSC symptoms (8, 10). In order to address the treatment gap, the TAND checklist was developed and later

validated to serve as a screening tool for clinicians. The TAND checklist serves as a streamlined method to identify the concern for neuropsychiatric manifestations with the ultimate goal of prompt and precise diagnosis as well as effective management of symptoms (11, 12). Along with the development of the TAND checklist, the recommendation was made for all individuals with TSC to undergo annual neuropsychiatric screening (12). It has been previously determined that 90% of children and adults with TSC will experience symptoms associated with TAND at some point during their lifetime, but fewer than 20% them will ever receive an appropriate TAND assessment and/or treatment (12). The 70% treatment gap for neuropsychiatric conditions in the TSC community is similarly observed in global studies regarding utilization of mental health care treatment (13, 14). Poor physical health in addition to poor mental health can contribute to a lower quality of life. It is therefore important to address the TAND treatment gap in the TSC community and provide opportunities to improve quality of life through the utilization of mental health services.

Even though treatment for mental health conditions has been documented as effective, there remain significant attitudinal and structural barriers that individuals struggle to overcome to reach proper mental health care services (15, 16). Structural barriers, such as treatment availability, geographical access, and financial capability, continue to be important hurdles to obtaining mental health treatment. Attitudinal barriers, such as the negative connotation and stigma associated with undergoing mental health treatment, are more frequently reported in comparison to structural barriers as the cause behind lack of initiating as well as continuing treatment (17, 18). Unfortunately, the consequences of stigma lead to symptom denial and delay in treatment. Through education of the general public as well as healthcare providers, a reduction in negative beliefs and stigma of mental illnesses can contribute to elimination of barriers toward mental health treatment. The purpose of our study is to provide clinicians and

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members of the TSC community with a more intimate, first-hand look into the impact of neuropsychiatric manifestations of TSC. Through a multi-faceted survey, our study evaluated perception of disease severity, presence of anxiety and depression, as well as the barriers and utilization of mental health services among adults with a diagnosis of TSC.

MATERIAL AND METHODS

Our study used a cross-sectional, web-based approach to survey adults with TSC. The electronic survey was designed using the Qualtrics online software (Qualtrics, Provo, UT). The survey components and recruitment strategy were developed by the authors and approved by the University of Texas Health Science Center at Houston Institutional Review Board (HSC-MS-17-0599). Data collection was performed from November 2017 through February 2018. Each participant provided consent electronically before completing the 30-minute survey. All survey responses were anonymous. To compensate for their time, participants who completed the survey were given the opportunity to provide a valid mailing address to receive a $5.00 gift card. The survey responses were kept separately from the mailing addresses.

Study sample

Participants were recruited via email through the Tuberous Sclerosis (TS) Alliance. The TS Alliance Adult Regional Coordinators sent the survey to their constituents a minimum of three times over the previously mentioned time frame. Additionally, the researchers approached eligible participants in the TSC clinic at University of Texas Health Science Center at Houston. If they agreed to participate, then they were given an iPad to use in clinic to complete the survey. The eligibility criteria for both electronic and clinical participants included having a diagnosis of TSC, being 18 years or older, as well as having the ability to independently complete a 30-minute electronic survey. Eligible participants were first directed to the consent page. Once electronic consent was obtained, participants proceeded with the survey.

Survey components

The structure of the survey included questions to determine the participant's clinical care setting, evaluate their perception of disease severity, measure levels of depression and

anxiety, as well as their use and perspectives on mental health care services. Demographic information including age, sex, ethnicity, years since TSC diagnosis, occupation, income, and type of insurance was collected for all participants. The survey design set out to assess the influence of a person's perception of disease severity on mental health and utilization of mental health care services.

The standardized and validated measures used in the survey included the Brief-Illness Perceptions Questionnaire (Brief-IPQ), Beck Anxiety Inventory (BAI), and Beck Depression Inventory-II (BDI-II). The Brief- IPQ was designed to provide a quick assessment of illness perceptions through single item questions on a scale from 0 to 10 to assess the severity of eight different dimension (19). The dimensions included "perceived consequences of their illness, timeline, perceived personal control, treatment control, identity, concern about the illness, coherence of illness, and emotional representation" (19). Permission to use the Brief-IPQ was obtained from the original authors. The BAI is the most widely used diagnostic instrument to discriminate between anxious and non-anxious groups (20, 21). The tool consists of 21-self reported items that assess for common symptoms of anxiety that have occurred during the past week including "numbness, feeling hot, nervousness, unsteadiness, dizziness, heart racing, fear of losing control, feeling scared, difficulty breathing, feeling faint, inability to relax and discomfort in the abdomen." Each item is answered on a Likert scale ranging from 0 to 3 and the total score of all the items indicates whether the respondent has a low, moderate, or severe level of anxiety (22). The Beck Depression Inventory-II, or BDI-II, is one of the more extensively used self-reported measures for depression (23). It is comprised of 21-self reported items with a Likert scale ranging from 0 to 3. The Beck Depression Inventory-II (BDI-II) is a 21-item, self-rated scale that evaluates key symptoms of depression having occurred during the past two weeks including "sadness, pessimism, past failure, loss of pleasure, guilty feelings,

punishment feelings, self-dislike, self-criticalness, suicidal thoughts or wishes, crying, agitation, loss of interest in activities, indecisiveness, worthlessness, loss of energy, change in sleeping pattern, irritability, changes in appetite, difficulty in concentration, tiredness, and loss of interest in sex" (23, 24). The total score indicates the presence as well as the severity of the depression in the respondent. Permission to use and reproduce both the BAI and BDI-II was obtained through Pearson Education.

Statistical analysis

All data was extracted from Qualtrics and analysis was performed using Stata (v. 14, College Station, TX). Categorical variables were described using frequencies (with percentages). Medians (with interquartile range, IQR) and means (with standard deviation, sd) were used to describe continuous data that was not normally and normally distributed, respectively. Categorical variables were compared across groups using contingency tests (Fisher exact or Chi-square). Distributions of continuous variables were compared across groups using a Mann-Whitney test (for comparisons between two groups) or a Kruskal-Wallis test with post-hoc Dunn's test (for comparisons between more than two groups). To analyze the impact of stigma and cost as a barrier to the utilization of mental health resources, values were assigned to each response with 5 representing strongly agree and 1 representing strongly disagree. Then, for each participant the response value for cost as a barrier was subtracted from their response value for is stigma a barrier, which assigned respondents an overall positive, negative, or zero response value. Spearman's correlation coefficients were utilized to assess relationships between BDI-II, BAI and Brief-IPQ scores. Statistical significance was assumed at a Type I error rate of 5%.

RESULTS

Demographics and Clinical Experience

The data collection process and demographic information of the 71 participants is listed Table 1 and illustrated in Figure 1. The average age of the study participants was 43.7 years old (sd 13.2). The majority of respondents were Caucasian (88%, n = 62), female (73%, n = 52), and received their initial clinical diagnosis of TSC over 10 years ago (86%, n = 61). Of the 71 respondents, over a quarter (28%, n = 20) reported receiving a diagnosis of intellectual disability. In regards to clinical experience, 39% (n = 28) reported receiving care in a multidisciplinary setting, while 61% (n = 43) reported a non-multidisciplinary clinical care setting. In our study, a multidisciplinary clinical care setting was defined as seeing multiple doctors from different specialties in a single clinic visit. A non-multidisciplinary clinic was defined as seeing a single specialty or multiple specialties in independent clinic visits. Out of the 43 individuals who reported receiving care in a non-multidisciplinary clinical setting, just over a quarter (28%, n = 12) reported not having any medical provider for their TSC diagnosis. From the 28 respondents who reported receiving care in a multidisciplinary clinic, the most frequently seen specialties were neurology and nephrology at 35% and 28%, respectively. The least commonly seen specialties in a multidisciplinary setting were psychiatry and endocrinology at 2% each. The most frequently reported specialties seen in a non-multidisciplinary setting (n = 31) were neurology and nephrology at 25% and 18%, respectively. The least commonly seen specialty in a non-multidisciplinary clinic setting was genetics at 2%. Respondents who reported receiving care in a multidisciplinary setting also reported being seen by more physicians in the past year (median: 2; IQR: 1-3) compared to respondents receiving care in a non-multidisciplinary clinic (median: 1; IQR: 0-3) (p=0.007). Additionally, these same multidisciplinary clinic patients made significantly fewer clinic visits

in the last year (median: 1; IQR: 0-2) compared to the non-multidisciplinary clinic patients

(median: 2; IQR: 1-4) (p=0.009).

Figure 1: Breakdown of Survey Responses


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┌─────────────────────────┐
│  Total Number Surveys   │
│       Returned:         │
└─────────────────────────┘
                                    ┌──────────────────────────────────┐
                                    │      Duplicated Surveys          │
                                    │       Didn't have TSC            │
                                    │ Completed Demographic Information │
                                    │             Only:                │
                                    └──────────────────────────────────┘
┌─────────────────────────┐
│ Completed Demographics: │
│        n = 71           │
└─────────────────────────┘
                                    ┌──────────────────────────────────┐
                                    │   Completed Clinical Experience: │
                                    │             n = 71               │
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                                    ┌──────────────────────────────────┐
                                    │  Completed Beck Anxiety Inventory:│
                                    │             n = 71               │
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                                    │ Completed Beck Depression        │
                                    │ Inventory-II:                    │
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                                    │ Completed Brief-Illness Perception│
                                    │          Questionnaire:          │
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                                    │ Completed Utilization of Mental   │
                                    │         Health Services:         │
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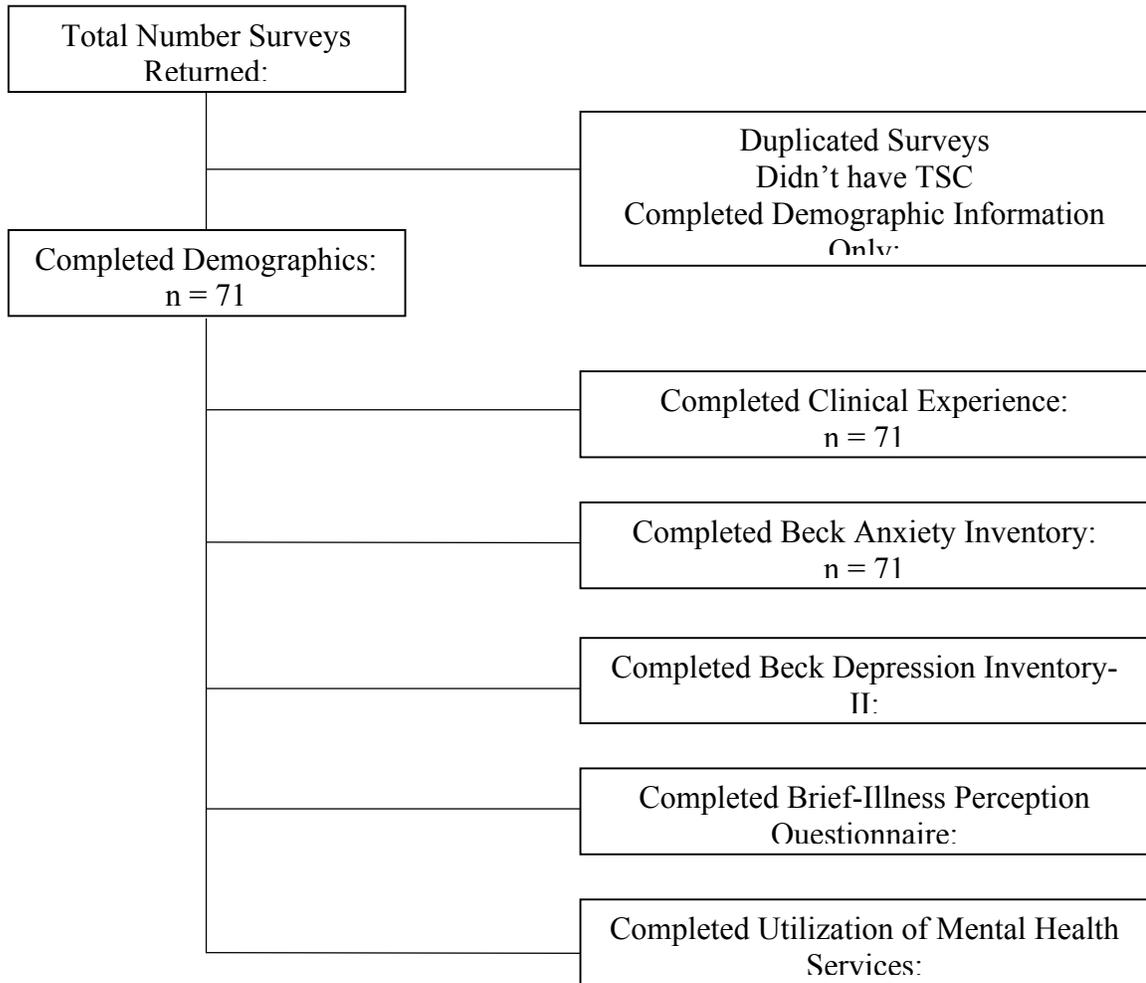
Figure 1 shows the breakdown of responses by highlighting the number of surveys returned, respondents who did not meet inclusion criteria, as well as the total sample size for each of the six components of the survey.

Table 1: Participant Demographics	
Age	Percent (%)
Mean (SD)	43.7 (13.2)
18-24	10%
25-34	14%
35-44	32%
45-54	13%
55 +	31%
Years since TSC Diagnosis	
1-10	14%
11-20	27%
>20	59%
Diagnosis of Intellectual Disability	
Yes	28%
No	72%
Sex	
Female	73%
Male	25%
Non-Binary	2%
Race	
Asian	3%
African American	1%
Caucasian	88%
Native American	1%
Pacific Islander	1%
Other	6%
Annual Household Income	
< $24,999	27%
$25,000 - $49,999	18%
$50,000 - $74,999	16%
$75,000 - $99,999	3%
> $100,000	18%
Prefer to not respond	18%
Country of Residence	
United States	98%
Canada	1%
Other	1%
Education Level	
High School/GED Less	22%
Trade School	6%
Some College	23%
Bachelor's Degree	32%
Graduate Degree	17%

BAI Results

       The overall median score for BAI was 8 (IQR 3-14) with no statistical significant differences between the median score between men and women (Table 2). Comparisons of the BAI scores for the individual BAI items and compared across stratifications by intellectual disability, education, and TSC disease severity. The p-values were controlled for Type I errors and are presented in Table 3A. Nearly all of the BAI items, excluding unsteadiness, hands trembling, feelings of choking, and face flushed, showed a statistically significant relationship demonstrating more severe symptoms of anxiety in individuals who self-reported higher levels of TSC disease severity. Similarly, the majority of BAI components, with the exception of feeling hot, feelings of choking, hands trembling, face flushed, and sweating (not due to heat), showed a statistically significant trend in which individuals with intellectual disabilities who have TSC indicated more severe anxiety related symptoms. Additionally, respondents with some level of higher education indicated a statistically significant increase in severity of anxiety related symptoms including feelings of choking, terrified, fear of losing control, feeling faint, wobbliness, feeling dizzy or lightheaded, and difficulty breathing. There was no significant correlation between intellectual disability and education level.

Table 2: BAI, BDI-II, and Brief-IPQ Scores	
	Median (25th-75th)
BAI	8 (3 – 14)
Women	7 (3 – 11)
Men	10.5 (4 – 17)
BDI-II	8 (2 – 20.5)
Women	7 (2 – 16)*
Men	22 (6 – 26)*
Brief-IPQ	45.5 (35.5 – 53.5)
Women	45 (35 – 54)
Men	47 (40 – 53)

Table 3A: BAI Item Analysis	Intellectual Disability	Education Level	Disease Severity
Numbness or tingling	**0.001**	0.552	**0.017**
Feeling Hot	0.302	0.496	**0.015**
Wobbliness in legs	**0.001**	**0.036**	**0.005**
Unable to relax	**0.021**	0.192	**0.016**
Fear of the worst happening	**0.002**	0.187	**0.005**
Dizzy or lightheaded	**0.001**	**0.049**	**0.013**
Heart Pounding or racing	**0.022**	0.120	0.237
Unsteady	**0.000**	0.099	**0.002**
Terrified	**0.004**	**0.009**	**0.002**
Nervous	**0.001**	0.169	**0.000**
Feelings of choking	0.228	0.088	0.140
Hands trembling	0.260	0.323	0.506
Shaky	**0.000**	0.687	**0.002**
Fear of losing control	**0.001**	**0.013**	**0.003**
Difficulty breathing	**0.007**	**0.036**	**0.000**
Fear of dying	**0.001**	0.301	**0.001**
Scared	**0.003**	0.062	**0.000**
Indigestion/discomfort in abdomen	**0.025**	0.127	**0.003**
Faint	**0.000**	**0.036**	**0.000**
Face flushed	0.074	0.190	0.213
Sweating (not due to heat)	0.274	0.193	**0.007**

BDI-II and Brief-IPQ Results

   The overall median score for BDI-II was 8 (IQR 2-20.5; Table 2). The difference

between the median BDI-II score for men and women was statistically significant with men

scoring higher than the females ($p = 0.023$; Table 2). Comparisons of the BDI-II scores for the

individual BDI-II items were compared across stratifications by intellectual disability,

education, and TSC disease severity. The p-values were controlled for Type I errors and

presented in Table 3B. Slightly fewer than half of the BDI-II items (9 out of 21), including

sadness, pessimism, suicidal thoughts or wishes, indecisiveness, worthlessness, change in

appetite, difficulty concentrating, and loss of interest in sex, showed a statistically significant

relationship demonstrating more severe symptoms in individuals who self-reported higher

levels of TSC disease severity. Individuals with a diagnosis of intellectual disability

demonstrated a statistically significant increase in severity of depression symptoms, including

the BDI-II items of sadness, pessimism, indecisiveness, loss of energy, change in appetite,

difficulty concentrating, and tiredness. Similarly, respondents with some level of higher

education illustrated a statistically significant increase in the BDI-II items of self-dislike and

worthlessness. There was no significant correlation between intellectual disability and

education level. The overall median for the Brief-IPQ was 45.5 (IQR 35.5 - 53.5) with no

statistically significant differences between men and women (Table 2).

Table 3B: BDI-II Item Analysis	Intellectual Disability	Education Level	Disease Severity
Sadness	**0.001**	0.269	**0.002**
Pessimism	**0.043**	0.342	**0.004**
Past Failure	0.361	0.131	0.295
Loss of Pleasure	0.178	0.134	0.284
Guilty Feelings	0.086	0.824	0.128
Punishment	0.986	0.190	0.493
Self-Dislike	0.148	**0.026**	0.465
Self-Criticalness	0.332	0.103	0.405
Suicidal Thoughts or Wishes	0.313	0.424	**0.005**
Crying	0.551	0.409	0.135
Agitation	0.112	0.129	**0.032**
Lost of Interest	0.659	0.387	0.147
Indecisiveness	**0.004**	0.533	**0.001**
Worthlessness	0.127	**0.047**	**0.021**
Loss of Energy	**0.038**	0.164	0.064
Change in Sleeping Pattern	0.085	0.436	0.211
Irritability	0.187	0.189	0.056
Change in Appetite	**0.014**	0.495	**0.003**
Difficulty in Concentrating	**0.033**	0.408	**0.008**
Tiredness or Fatigue	**0.002**	0.471	0.073
Loss of Interest in Sex	0.110	0.769	**0.015**

Barriers and Utilization of Mental Health Services

Out of 69 respondents, 57% (n = 39) reported receiving mental health treatment at some point over their lifetime. Of the group of individuals with a history of receiving mental health treatment, approximately 31% (n = 12) of them had not seen a mental health specialist in the past year. In contrast, 56% (n = 22) of respondents from the treatment group reported seeing a mental health specialist on a regular basis. Of these respondents who were receiving mental health services, the majority of respondents either "strongly agreed" or "agreed" that mental health treatment was meeting their needs (65%, n = 25) as well as improving their overall mental health (74%, n = 29). From the group of individuals who had never previously received mental health treatment (n = 30), 23% of them felt they had symptoms that could be addressed by a mental health specialist and 67% of them either "strongly agreed" or "agreed"

that they would feel comfortable asking their primary provider about mental health services. The treatment group and the non-treatment group's responses to stigma and cost as being barriers to accessing mental health resources are shown in Figure 2. In regards to barriers to accessing mental health services, about half of the individuals from the mental health treatment group (n = 39, 51%) felt that cost would prevent continued use of services while only a fifth (n=33, 21%) of the individuals from that group felt that stigma would prevent continued use of services. Of the group of individuals with no previous use of mental health services, 27% (n = 8) of individuals felt cost would prevent initiating mental health treatment while 20% (n = 6) of individuals felt that stigma would prevent initiating mental health treatment. There was no statistically significant relationship between stigma and socioeconomic status (SES) as well as cost and SES as a function of income, occupation or education.

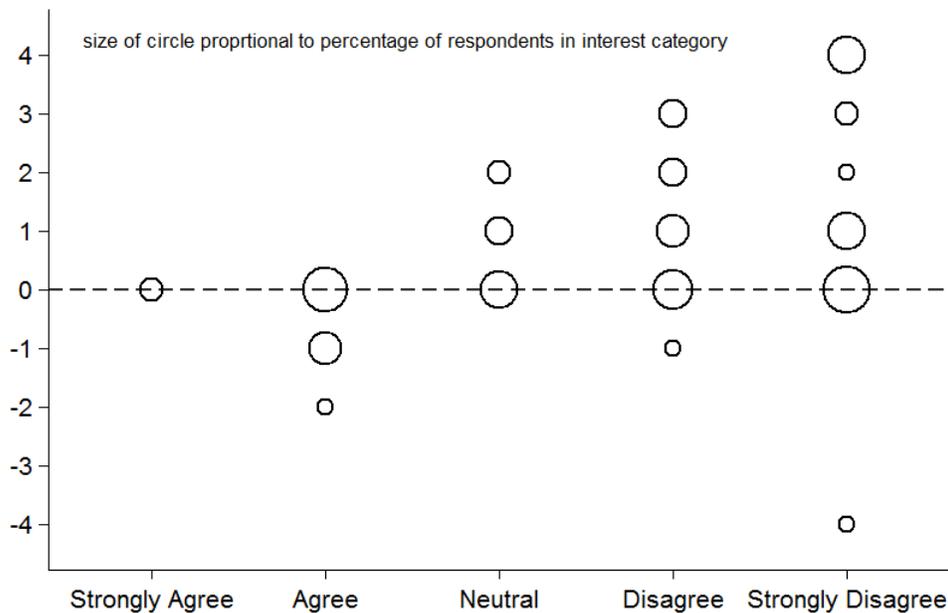Figure 2: Cost versus Stigma as Barriers to Accessing Mental Health Services

Figure 2 illustrates that cost was overall a more significant barrier to accessing mental health resources in comparison to stigma. Positive values were indicative of cost being a more prominent barrier than stigma and negative values were indicative of stigma being a more prominent barrier than cost. The value of zero represents that the respondent felt stigma and cost were equal barriers.

DISCUSSION

The study described here set out to evaluate perception of disease severity within the adult TSC population. Overall, men and women both indicated a perception of moderate disease severity. The Brief-IPQ outcome supports the medical community's understanding of the clinical features of TSC. The implication of a moderate level of disease severity stems from the spectrum of symptoms and life-long nature of the condition that contributes to feelings of little personal control over the disease. The results of our study bring attention to the individual's daily experiences with their disease, regardless of the medical provider's perception of their patient's disease severity. Medical providers, as well as members of the TSC community, could benefit from studies that develop evidence-based care guidelines regarding the psychosocial impact of TSC in an effort to tailor and improve overall clinical care.

Our study results showed a moderate association between one's perception of disease severity and self-reported depression and anxiety. There was a strong correlation between BAI and BDI-II scores. Even though these tools were designed with the intent of discriminant validity, previous studies have also indicated moderate to strong correlations between the BAI and BDI-II (21, 25). Suggested explanations for this phenomenon include that depression and anxiety often co-occur or that depression and anxiety are simply different points on the same spectrum (26, 27). The correlation seen in our study further supports their interrelated nature given that the BAI and BDI-II tools were developed to be complementary to each other. The overall BAI and BDI-II scores of our study population correspond and build upon previous neuropsychiatric co-morbidity studies that indicate that the chronic illness populations have increased incidences of anxiety and depression (28-33).

The analysis of each validated measure indicated a significant difference in the median BDI-II score between men and women. Our results do not align with the previously established trend of women typically having higher BDI-II scores in comparison to men, as well as the general consensus that women are twice as likely to experience depression (34, 35). The increased incidence of depression within the TSC community compared to the general population is well known, but there has not been any previous evidence of men with TSC more frequently experiencing depression than women with TSC. It is possible that the men in our study feel more disenfranchised by their diagnosis and severity of TSC in comparison to the women leading to heightened levels of depression. The literature regarding depression in men has been growing in recent years. Current theories thought to contribute to depression in men include difficulty in fulfilling gender roles, biological factors, and/or coping styles (36). Furthermore, it has been determined that men demonstrate a wider range of depressive symptoms that stray from the traditionally known symptoms; therefore, typical methods used to diagnose depression could lead to under-diagnosis (37). Given the moderate level of depression among the men in our study, it would be beneficial to further delve into the etiology and risk factors that contribute to depression in men with TSC as well as in men with other chronic illnesses.

There was no significant difference between the median BAI scores for men and women with both sexes falling in the minimal to mild range of anxiety. Despite the lack of significance, the trend of women scoring on average four points higher on the scale (as outlined in the BAI manual) was not observed in our study population (22). Comparisons of BAI and BDI-II items across stratifications, including intellectual disability, educational level, and self-reported perception of disease severity, shed light on specific dimensions that showed significant associations in our study. Given the exploratory nature, our results on these

variables should primarily offer guidance and tailoring options during clinical interactions with patients. Further analysis of these variables on a larger scale would be needed to elucidate a more definitive relationship between individual dimensions from the BAI and BDI-II and demographic information. Any studies that can provide the medical community insight about the complex impact of psychiatric conditions in individuals with a chronic illnesses will augment quality of care in the clinical setting.

There are several limitations to our study design and the results. The response rate and sample size were low, making it difficult to generalize the conclusions from the study to the entire TSC community. There is likely a selection bias given that our study sample was derived from English-speaking individuals on the TS Alliance listserv with Internet access or those who receive their medical care at the University of Texas Health Science Center at Houston. Another selection bias is the inclusion criteria requiring that the individual with TSC must independently complete the survey. The independence required to complete the survey inherently discourages individuals that are cognitively impaired or have more severe phenotypes from participating in our survey. Lastly, our survey was conducted through an anonymous online survey; therefore, any clinical information gathered during data collection was unable to be confirmed by the researchers. Future research regarding how to appropriately address the neuropsychiatric phenotype in the clinical setting should be conducted in order to effectively change clinical management for these patients. Research opportunities, such as evaluating the efficiency and usefulness of an annual visit with a genetic counselor to discuss the TAND, will provide the evidence needed to improve the clinical outcomes for patients with TSC.

Our study results further supports the mental health treatment gap seen in previous studies in the TSC community (12, 38). In a recent quality of life study, adults and children

with TSC were identified to have significantly reduced quality of life in comparison to the general population (39). Regardless of clinical care setting, our data suggest that the majority of participants visited at least one medical provider each year. It is imperative for all medical disciplines to routinely inquire about physical health changes in addition to changes in the patient's mental health during each clinical evaluation through the use of the TAND checklist. In 2004 and 2005, the World Health Organization (WHO) published reports expressing that mental health is intricately linked to physical health and is integral to one's overall well-being (40, 41). Specifically, quality of life consists of one's well-being and life-satisfaction as well as the ability to sufficiently function within society (42). Therefore, in order to support individuals with TSC in reaching and maintaining optimal quality of life, providers must continually assess their mental health from childhood to adulthood. Through appropriate referrals and utilization of mental health treatment, individuals can obtain services that can lessen disease burden, and in turn, improve quality of life. The burden of mental health illnesses was further supported by the 2010 Global Burden Disease Study that highlighted the worldwide impact of mental and substance use disorders, as they account for 7.4% of disability-adjusted life years (DALYs[1]) worldwide (43). Within mental and substance use disorders, depressive disorders and anxiety disorders accounted for over half of DALYs making them the most prominent mental health illnesses worldwide (44). Likewise, the most commonly reported neuropsychiatric manifestations in the pediatric and adult TSC population are cognitive concerns, depression, and anxiety (38). Our data support previous studies that have found individuals who receive mental health treatment report feeling that it does

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[1] Disability-adjusted life years (DALYs) reflect the overall burden of disease, which corresponds to the number of years lost to disability, illness, or premature death. The loss of the equivalent of one year of full health equates one DALY (42).

improves their overall mental health (15, 16, 45). Furthermore, our results indicate that the majority of individuals with TSC would feel comfortable asking their primary provider about mental health resources and services; therefore, TSC patients would welcome integrating routine mental health evaluations in each clinical interaction.

Given the general complexity of accessing mental health services, our study set out to identify potential barriers to access specifically in the TSC community. The stigma of mental health illnesses and cost of services are commonly known as attitudinal and structural barriers to accessing mental health treatment. Interestingly, our study results indicated that stigma was not considered a significant barrier to initiating or continuing to access mental health resources. Our results relate and build upon a recent study conducted by Whitley et al, 2014. The results of their study identified that individuals with mental health illnesses frequently employ behavioral and psychological strategies to prevent or reduce problems associated with stigma (46). Moreover, the view of mental health illnesses has evolved to be analogous with physical illness (46). If society's view of mental health continues to shift in a more accepting and supportive direction, then stigma will diminish further and will progressively become less of a barrier to mental health services (47). In regards to cost, the results of our study align with the notion that cost is a persistent and increasing barrier among these individuals. With increasing use of mental health services in conjunction with limited solutions to the issue of cost or insurance coverage, individuals will continue to face barriers during utilization of these resources (48-50).

In conclusion, disease severity had a moderate and low-moderate association with anxiety and depression, respectively. Regardless of past utilization, respondents had a positive outlook towards the use of mental health services with the major barrier being cost. All healthcare providers seeing patients with TSC should use the readily available TAND

checklist. Specifically, the evaluation for neurobehavioral changes falls within the clinical genetic counselor's scope of practice. For the benefit of the TSC community, a genetic counselor could undertake the responsibility of consistently assessing patients with TSC for changes or new developments within the spectrum of TAND and subsequently refer any patients in need of mental health services.

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