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Original Article

The Impact of Psychiatric Symptoms on Tuberous Sclerosis Complex and Utilization of Mental Health Treatment

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ABSTRACT

BACKGROUND: Tuberous sclerosis complex (TSC) is a multisystem, neurocutaneous disorder with a spectrum of TSC-associated neuropsychiatric disorders. The most common neuropsychiatric manifestations in the pediatric and adult populations are cognitive concerns, depression, and anxiety. Previous research suggests that while 90% of individuals with TSC have some TSC-associated neuropsychiatric disorders features, only 20% receive treatment, leading to a 70% treatment gap.

METHODS: This web-based study used validated measures in conjunction with researcher-designed questions to evaluate perception of disease severity, presence of anxiety and depression, and the utilization and barriers toward mental health services among adults with TSC.

RESULTS: The Beck Anxiety Inventory, Beck Depression Inventory-II, and Brief Illness Perception Questionnaire indicated that our overall study population had mild symptoms of anxiety, minimal depression, and a moderate perception of disease severity. Notably, the difference between the median depression score for men and women was statistically significant with men scoring higher than women ($P = 0.02$). Of 69 respondents, 57% ($n = 39$) reported receiving mental health treatment at some point over their lifetime. In both the mental health treatment group and the nonmental health treatment group, cost was more often indicated as a barrier to accessing mental health resources (treatment group: cost = 51% and stigma = 21%; nontreatment group: cost = 27% and stigma = 20%).

CONCLUSIONS: TSC 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.

Conflicts of interest: This study was completed in partial fulfillment of the requirements for the first author's Master of Science in genetic counseling from MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences. This work was conducted by Kate Mowrey, M.S. The authors thank the TS Alliance and all the Adult Regional Coordinators for their role in data collection. The authors appreciatively acknowledge the support of the Tuberous Sclerosis Alliance and the members of the TSC community who participated in this survey. The authors declare no conflict of interest or financial disclosures concerning the materials or methods used in this study or the findings specified in this article.

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Introduction

Tuberous sclerosis complex (TSC) is a genetic disorder known to have a multisystem, neurocutaneous clinical presentation with an estimated incidence of one per 6,000 to 10,000 live births.[1] The characteristic findings of TSC are skin lesions, seizures, and hamartomas in the brain, kidneys, and heart, in addition to a spectrum of neuropsychiatric conditions. The clinical manifestations of TSC show inter- and intrafamilial variable expressivity and have the potential to fluctuate in severity over an affected individual's lifetime.[2,3] The pathophysiology of TSC arises from heterozygous pathogenic variants 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* leads to insufficient production of hamartin or tuberin and causes uncontrolled cell growth and division, resulting in hamartomas across multiple organ systems.[6,7] The pathophysiology of other clinical features associated with TSC is less well understood.

Even though there are many non-neurological features of TSC, it is widely accepted that the central nervous system is the most prominently affected organ system and the largest contributor to mortality and morbidity associated with TSC.[8–11] It has been previously estimated that more than 90% of individuals with a diagnosis of TSC will have at least one neurological manifestation.[8,12,13] The major neurological manifestations of TSC include cortical dysplasias, subependymal nodules, subependymal giant cell astrocytoma, epilepsy, and TSC-Associated Neuropsychiatric Disorders (TAND). The presence for each of these manifestations varies amongst the TSC population. The incidence of cortical dysplasias is over 90% and subependymal nodules are found in over 80% of the TSC population.[8,14–16] Subependymal giant cell astrocytoma are observed in 10% to 20% of TSC patients, while epilepsy is found in over 80%.[8,12,14,15,17–19] Lastly, it has been previously estimated that 90% of individuals with TSC will experience one or more TANDs over their lifetime.[8,20,21] In the past, there has been significant amount of literature published regarding neurological findings associated with TSC with the exception of TAND. TAND, as well as its associated comorbidities and impact on quality of life, has gained attention within the TSC community in recent years.

At the 2012 International TSC Consensus Conference, the Neuropsychiatry Panel expressed concern regarding the 70% treatment gap and lack of uniformity in terminology for the nonphysical manifestations associated with TSC.[13,20,21] 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 receiving appropriate services.[22] The members of the 2012 International TSC Consensus Conference showed support for the previously coined term, TAND, in order to collectively represent the various domains of neuropsychiatric manifestations within the continuum of TSC symptoms.[13,23] 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.[20,24] Along with the development of the TAND checklist, the recommendation was made for all individuals with TSC to undergo annual neuropsychiatric screening.[20] 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. Of those with TAND, fewer than 20% of them will ever receive an appropriate TAND assessment and/or treatment.[20,21] The 70% treatment gap for neuropsychiatric conditions in the TSC community is similarly observed in global studies regarding utilization of mental health care treatment.[25,26] The impact of poor mental health, in addition to poor physical health, contributes to a reduced quality of life. Therefore, it is 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 being effective, there remain significant attitudinal and structural barriers that individuals with TSC struggle to overcome to reach proper mental health care services.[27,28] Structural barriers, such as treatment availability, geographical access, and financial capability, continue to be important hurdles to obtaining mental health treatment. In the general population, 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.[29,30] Unfortunately, the consequence of stigma as well as other barriers lead to symptom denial and delay in treatment. Through education of the general public and healthcare providers, a reduction in negative beliefs and stigma of mental illnesses can contribute to the elimination of barriers toward mental health treatment. The purpose of our study is to provide clinicians and members of the TSC community with a more intimate, first-hand look into the patient perception of the impact of neuropsychiatric manifestations of TSC. Through a multifaceted 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.

Materials 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 Institutional Review Board of University of Texas Health Science Center at Houston (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 option to provide a valid mailing address to receive a $5.00 gift card.

Study sample

The eligibility criteria for inclusion in this study were having a diagnosis of TSC, being 18 years or older, as well as having the ability to independently complete a 30-minute electronic survey. Participants were recruited via two sources: electronically using emails sent by the Tuberous Sclerosis (TS) Alliance and in-person at a TSC clinic. The TS Alliance is a national patient advocacy organization involved in education, research, and family networking among individuals and families with TSC. Adult Regional Coordinators provide support to individuals and families with TSC within their geographical communities. A hyperlink to the survey was embedded in an email that was sent out a minimum of three times during the study time frame by the Adult Regional Coordinators to all their members. The only criterion from this source was to have a subscription to the TS Alliance mailing list. The second source of participants was patients seen in a single multidisciplinary TSC clinic at McGovern Medical School at the University of Texas Health Science Center at Houston. They were provided information about the study and given a tablet on which they could self-administer the survey. All participants undertaking the survey were first directed to the consent page. Once electronic consent was obtained, screening questions were administered to determine eligibility based on the criteria above.

Survey components

The structure of the survey included four main parts: the demographics, clinical care, psychometric, and perception sections. The demographic section included questions on age, sex, ethnicity, years since TSC diagnosis, occupation, income, and type of insurance was collected for all participants. The psychometric section included screening instruments to measure their levels of symptoms of depression (BDI-II), anxiety (BAI), and their perception of disease severity (Brief-IPQ). Finally, the perception section inquired about the respondent's utilization of and perspectives on 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 dimensions.[31] 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.”[31] Permission to use the Brief-IPQ was obtained from the original authors. The BAI is the most widely used screening instrument to discriminate between anxious and nonanxious groups.[32,33] This 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.[34] The BDI-II is one of the more extensively used self-reported measures for depression.[35] It is comprised of 21–self-reported items with a Likert scale ranging from 0 to 3. The 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.”[35,36] The total score measures severity of the depression-related symptoms in the respondent. Permission to use and reproduce both the BAI and BDI-II was obtained through Pearson Education, publisher of these measures.

Statistical analysis

All data were extracted from Qualtrics and data analysis was performed using Stata (v. 14, College Station, TX, USA). 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 were 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 test (for comparisons between more than two groups). To analyze the impact of stigma and cost as barriers 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 stigma as a barrier, which assigned respondents an overall positive (cost a bigger barrier than stigma), negative (stigma a bigger barrier than cost), or zero (both cost and stigma are equal with respect to their magnitude as a barrier) 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 in Table 1 and illustrated in Figure 1. The average age of the study participants was 43.7 years (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)

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%

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 individual 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 to 3) compared to respondents receiving care in a non–multidisciplinary clinic (median: 1; IQR: 0 to 3) ($P = 0.007$). Additionally, these same multidisciplinary clinic patients made significantly fewer clinic visits in the last year (median: 1; IQR: 0 to 2) compared to the non–multidisciplinary clinic patients (median: 2; IQR: 1 to 4) ($P = 0.009$).

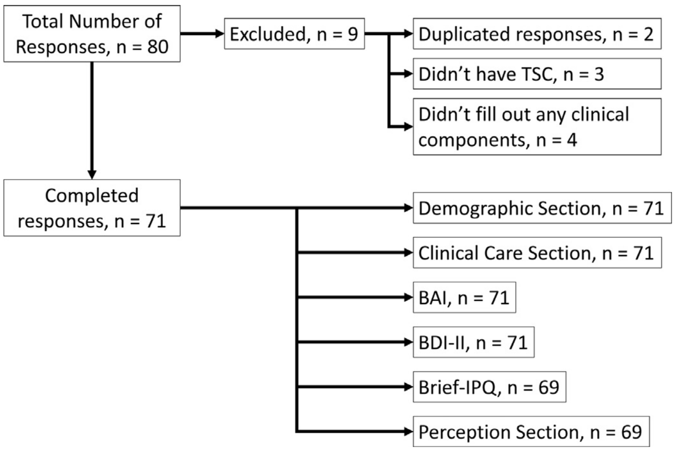


FIGURE 1. Breakdown of survey responses.

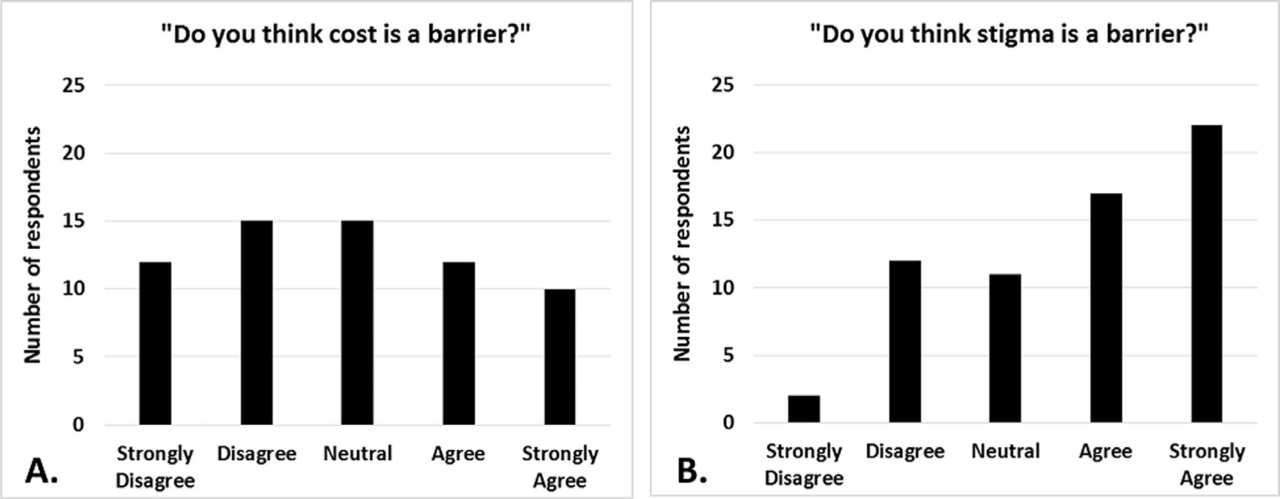
BAI results

The overall median score for BAI was 8 (IQR 3 to 14) with no statistically significant differences between the median score of men and women (Table 2). The BAI scores were stratified by disease severity and the presence or absence of intellectual disability (Fig 2). The median BAI score showed a statistically significant increase in the severity of anxiety and depression-related symptoms amongst individuals with self-reported higher levels of TSC disease severity as well as in individuals with intellectual disabilities. Furthermore, individual BAI items were compared across three demographic factors, including intellectual disability, education level, and TSC disease severity. The *P* values for the previously mentioned BAI stratifications were not controlled for Type I errors and are presented in Supplementary Material 1. The majority of the BAI items (13/21; 62%), excluding unsteadiness, hand trembling, feelings of choking, and face flushed, showed a statistically significant relationship demonstrating more severe symptoms of anxiety in individuals who characterized their disease severity as moderate or severe. The overall BAI scores were significantly higher in patients that

TABLE 2. BAI, BDII-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)

* The difference between the median BDI-II score for men and women was statistically significant with men scoring higher than the females ($p < 0.05$).



		Do you think STIGMA is a barrier?				
		Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
Do you think COST is a barrier	Strongly Disagree	2	-	2	3	5
	Disagree	-	7	3	3	2
	Neutral	-	4	5	4	1
	Agree	-	1	-	6	5
	Strongly Agree	-	-	-	1	8

C.

FIGURE 2. Stratifications of BAI and BDI-II items across demographic factors.

categorized their TSC symptoms as moderate or severe (median: 11; IQR: 6 to 23) compared to those with mild TSC symptoms (median: 5; IQR: 2 to 10) ($P < 0.001$) (Fig 2). Similarly, nearly all of BAI components (16/21; 76%), with the exception of feeling hot, feelings of choking, hands trembling, face flushed, and sweating (not due to heat), showed a statistically significant trend with individuals affected by intellectual disabilities indicating more severe anxiety related symptoms. Furthermore, the overall BAI scores were significantly higher in patients with intellectual disability (median: 15.5; IQR: 8 to 28.5) compared to those without (median: 6; IQR: 2 to 10) ($P < 0.001$) (Fig 2). Conversely, only two of the 21 BAI items shows a significant difference in distribution between patients with a low level of education (high school or less) compared to those with at least some level of college or trade school education. The overall BAI scores were not statistically different based on the respondent's level of education. Similarly, the overall BAI scores did not demonstrate a statistically significant difference based on clinical care setting ($P = 0.51$).

BDI-II results

The overall median score for BDI-II was 8 (IQR 2 to 20.5; Table 2). The difference between the median BDI-II score for men and women was statistically significant with men scoring higher than women ($P = 0.02$; Table 2). The BDI-II scores were stratified by disease severity and the presence or absence of intellectual disability (Fig 2). The median BDI-II score showed a statistically significant increase in severity of anxiety and depression-related symptoms amongst individuals with self-reported higher levels of TSC disease severity as well as in individuals with intellectual disabilities. Similar to the BAI, the individual BDI-II items were compared across the same three demographic factors. The P values for the following BDI-II stratifications were controlled for type I errors and are presented in Supplementary Material 1. Just over a third of the BDI-II items (8/21; 38%), 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 characterized their TSC disease severity as moderate or severe. The overall BDI-II scores were significantly higher in patients that categorized their TSC symptoms as moderate or severe (median: 14; IQR: 8 to 24) compared to those without (median: 6; IQR: 2 to 16) ($P = 0.02$) (Fig 2). Similarly, individuals with a diagnosis of intellectual disability reported 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. The overall BDI-II scores were significantly higher in patients with intellectual disability (median: 12; IQR: 7 to 25) compared to those without (median: 6; IQR: 2 to 17) ($P = 0.02$) (Fig 2). Conversely, there was no statistically significant difference in any of the BDI-II items between patients with a low level of education (less than or equal to high school) compared to those with higher levels of education. The overall BDI-II scores were not statistically different based on the respondent's level of education. Similarly, the overall BDI-II scores did not demonstrate a statistically significant difference based on clinical care setting ($P = 0.48$).

Brief-IPQ results and Spearman's correlation

The overall median for the Brief-IPQ was 45.5 (IQR 35.5 to 53.5) with no statistically significant differences between men and women (Table 2). The Brief-IPQ and the BDI-II demonstrates a moderate correlation with each other (Spearman's rho = 0.42, $P < 0.001$). Similarly, the Brief-IPQ and BAI as well as the BAI and BDI-II exhibit good to strong correlations to each other (Spearman's rho = 0.59, $P < 0.001$; Spearman's rho = 0.76, $P < 0.001$, respectively). Furthermore, the overall Brief-IPQ scores did not demonstrate a statistically significant difference based on clinical care setting ($P = 0.78$).

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% (n = 7) of them felt they had symptoms that could be addressed by a mental health specialist and 67% (n = 20) of them either “strongly agreed” or “agreed” that they would feel comfortable asking their primary provider about mental health services. Figure 3A and B illustrate the number of respondents in each category, thus, representing their level of agreement or disagreement with how cost or stigma affects their ability to access mental health services. Figure 3C highlights that our respondents felt that cost was a more significant barrier to accessing mental health services in comparison to stigma. 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 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 as a barrier and socioeconomic status or between cost as a barrier and socioeconomic status as a function of income, occupation, or education.

Discussion

We evaluated the perception of disease severity as well as presence of anxiety and depression within the

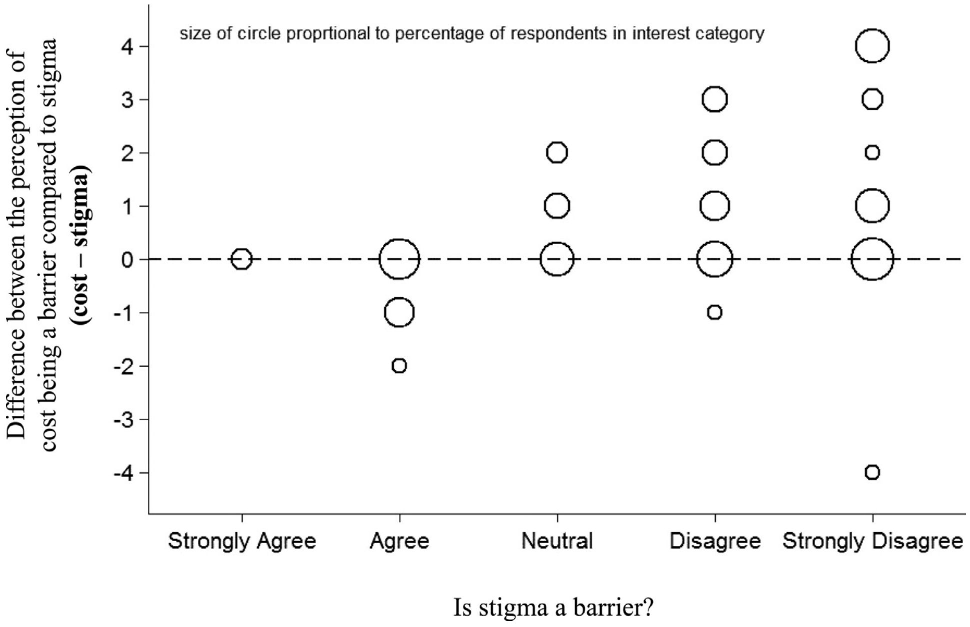


FIGURE 3. Cost versus stigma as barriers to accessing mental health services.

adult TSC population. Overall, men and women both indicated a perception of moderate disease severity. There was a significant difference in the median BDI-II score between men and women with men having a higher BDI-II score. Unlike BDI-II, 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. Lastly, the 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 had significant associations in our study.

Regardless of the medical provider's perception of their patient's disease severity, 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 and brings attention to the individual's daily experiences with their disease. The increased incidence of depression within the TSC community is well known, but there has not been any previous evidence of men with TSC more frequently experiencing depression than women with TSC.[14,20,37] 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. Despite the lack of significance between BAI, 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.[34]

It should be recognized that TSC is a systemic and complex condition with great variability of expression in clinical phenotype. Given that this study was a nonmandatory anonymous online survey, we did not inquire about specific clinical manifestations and diagnoses among our participants, including onset of psychiatric symptoms, and clinical expression was assessed via questions about the type and number of medical specialists followed by our respondents. Future studies should incorporate comprehensive data on neurological, psychiatric, and other comorbidities in these patients to fully assess their correlations with anxiety and depression symptoms. There are several limitations to our study design and the results. There is likely a selection bias given that our study sample was derived from English-speaking individuals on the TS Alliance e-mail distribution list 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, which inherently discourages individuals with more severe phenotypes from participating in our survey. Given this as well as the low response rate and sample size, we acknowledge that our sample population may not be representative of the TSC population at large.

In regards to the past utilization of mental health services from our respondents, our results largely indicate that we still need to improve the accessibility of mental health services within the TSC community. Since we did not obtain diagnostic TAND information, we cannot report an absolute treatment gap comparable to Leclezio et al. 2015. Our data does support previous studies that have found individuals who receive mental health treatment report feeling that it does improves their overall mental health.[27,28,38] 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] In order to support individuals with TSC in reaching and maintaining optimal quality of life, medical providers, such as pediatric neurologists, must continually assess their patient's mental health in addition to their physical health starting in childhood and throughout adolescence into adulthood. Through consistent mental health screening starting during early childhood, providing appropriate referrals, and encouraging utilization of mental health treatment, children and adults can obtain services that can lessen disease burden, and in turn, improve quality of life. The burden of mental health illnesses accounts for 7.4% of disability-adjusted life years (DALYs[1]) worldwide.[40] 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, which aligns with the most commonly reported neuropsychiatric manifestations in the pediatric and adult TSC population.[41,42] Furthermore, our results indicate that the majority of individuals with TSC would feel comfortable asking their primary provider about mental health services; therefore, TSC patients would welcome integrating routine mental health evaluations in each clinical interaction.

Given the general complexity of accessing mental health services, a major goal of our study was to identify potential barriers to access specifically in the TSC community. 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.[43] Moreover, the view of mental health illnesses has evolved in recent years to be analogous with physical illness.[43] 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.[44–46]

Conclusions

Overall, the disease severity had a moderate and low-moderate association with symptoms of anxiety and depression, respectively. Irregardless of past utilization of mental health services, respondents had a positive

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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]

outlook toward the use of mental health services with the major barrier being cost. All healthcare providers, starting with pediatricians and pediatric neurologists, seeing patients with TSC should routinely screen their patients using the TAND checklist, available for download (at no cost) at: http://www.tscinternational.org/documents/TAND_checklist%202014.pdf). Patients whose profiles on the TAND Checklist are suggestive of neuropsychiatric concerns should be referred for appropriate comprehensive follow-up.

In summary, the primary goal of this study was to raise awareness among all clinicians caring for children, adolescents, and adults with TSC in order to communicate prognosis and provide anticipatory guidance to the parents, caregivers, and affected individuals about the neuropsychiatric manifestations associated with TSC. By educating caregivers and affected individuals about these concerns, proper preventative care can be established shortly after diagnosis and/or earlier treatment made when neuropsychiatric disorders onset. Appropriate and timely care regarding neuropsychiatric conditions is known to enhance quality of life and optimize clinical outcomes.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.pediatrneurol.2018.10.011.

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