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Diagnostic Journey for Tuberous Sclerosis Complex - Interviews from a Clinical Trial

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Corresponding Author:	Carly Hyde, M.S. University of California Los Angeles Los Angeles, CA UNITED STATES
First Author:	Carly Hyde, MS
Order of Authors:	Carly Hyde, MS
	Logan Shurtz, BA
	Nicole McDonald, PhD
	Maria Pizzano, PhD
	Connie Kasari, PhD
	Charles A Nelson, PhD
	Elizabeth Thiele, MD
	Shafali Jeste, MD
Manuscript Region of Origin:	UNITED STATES
Abstract:	Tuberous sclerosis complex (TSC) is a genetic condition characterized by both medical and neuropsychiatric diagnoses that emerge across the lifespan. As part of a clinical trial, caregivers of children with TSC were interviewed about their experiences navigating medical, school, and social services. Semi-structured interviews (N=20) with caregivers of children with TSC (27-60 months) were conducted upon exit from the study. The interviews covered topics related to experiences following diagnosis, interactions with providers, sources of information, and access to services and treatment. The main themes from the caregiver interviews included: 1) sources of information about TSC and treatment, 2) access to high-quality and expert medical care, 3) perception and diagnosis of TAND, 4) impact of epilepsy on daily life, intervention, and schooling, and 5) access to therapeutic services, compatible providers, and evaluations. Additionally, parents provided recommendations for other caregivers navigating their child's early treatment following diagnosis. These results reflect the importance of current research priorities for TSC stakeholders, including implementation of existing clinical guidelines, improved access to TSC expertise, and coordinated and integrated health care.

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Abstract:

Tuberous sclerosis complex (TSC) is a genetic condition characterized by both medical and neuropsychiatric diagnoses that emerge across the lifespan. As part of a clinical trial, caregivers of children with TSC were interviewed about their experiences navigating medical, school, and social services. Semi-structured interviews (*N*=20) with caregivers of children with TSC (27-60 months) were conducted upon exit from the study. The interviews covered topics related to experiences following diagnosis, interactions with providers, sources of information, and access to services and treatment. The main themes from the caregiver interviews included: 1) sources of information about TSC and treatment, 2) access to high-quality and expert medical care, 3) perception and diagnosis of TAND, 4) impact of epilepsy on daily life, intervention, and schooling, and 5) access to therapeutic services, compatible providers, and evaluations. Additionally, parents provided recommendations for other caregivers navigating their child's early treatment following diagnosis. These results reflect the importance of current research priorities for TSC stakeholders, including implementation of existing clinical guidelines, improved access to TSC expertise, and coordinated and integrated health care.

Key words: Tuberous sclerosis complex, diagnostic journey, access, qualitative, interview

Introduction:

Tuberous sclerosis complex (TSC) is a rare genetic disorder marked by the growth of benign tumors in critical organ systems, such as the heart, kidneys, and brain. The incidence is reported to be 1 in 17,785 live births annually (Ebrahimi-Fakhari et al., 2018). It affects about 1 in 5,000 individuals globally (Devlin et al., 2006; O'Callaghan et al., 1998; Osborne et al., 1991; Wiederholt et al., 1985; Zöllner et al., 2020), and there are about 50,000 people in the U.S. and approximately 1 million people worldwide living with TSC (Northrup et al., 2013; Stuart et al., 2021).

TSC may present with multiple co-occurring conditions, necessitating comprehensive management and often polypharmacy to address associated symptoms. TSC-Associated Neuropsychiatric Disorders (TAND) add complexity to managing TSC. TAND clusters include autism and autism-like profiles, dysregulated behavior, eating and sleeping concerns, neuropsychological and psychosocial difficulties, overactivity/impulsivity, and scholastic challenges (de Vries et al., 2023). These challenges significantly impact individuals with TSC and their families (Skrobanski et al., 2023). Management of TAND requires an interdisciplinary approach and evolves over a patient's lifetime, involving various medical and therapeutic disciplines for effective treatment.

The prevalence of TAND symptoms is high, with studies suggesting nearly all individuals with TSC experience TAND at some point in their lives (Müller et al., 2023; Zöllner et al., 2020). TAND symptoms can vary, especially between patients with and without epilepsy, as those with epilepsy may face more pronounced cognitive and behavioral challenges (Zöllner et al., 2020). The TAND Checklist is a screening tool used by both providers and patients, providing a shared

language to describe and evaluate TAND (de Vries et al., 2015). This framework can be a vital tool for screening and managing TAND, helping in early identification and facilitation of early intervention and personalized care plans (de Vries et al., 2015). Recent consensus recommendations underscore the importance of a nuanced approach to TAND in children with TSC, advocating for routine annual assessments and targeted interventions (de Vries et al., 2023). These guidelines highlight a biopsychosocial model of care that prioritizes a combination of medical, psychological, and social factors, aligning with the varied profiles of TSC manifestations in children. Emphasizing the critical role of early detection and personalized care, these recommendations also stress the need to address the broader impact of TAND on family well-being and quality of life.

When implemented appropriately, these guidelines may be able to reduce the physical, emotional, financial, and social burden experienced by many families of individuals with TSC (Jansen et al., 2020). Caregivers have reported feelings of loneliness, disorientation, anxiety, and abandonment from the healthcare system following their child's diagnosis (Graffigna et al., 2013). This may be due in part to the insufficient and uncoordinated medical, home, and social service support that makes navigating the complex medical and therapeutic landscapes immensely difficult.

There is a lack of research on how caregivers of children with TSC navigate the healthcare, therapeutic, and educational landscapes after their child's diagnosis to achieve high-quality, comprehensive, and coordinated care. This study aims to address this gap by exploring the experiences of caregivers of young children with TSC, including their access to early intervention services and information about TAND, communication with healthcare

providers, and their perception of services for their children's unique developmental needs. Through post-clinical trial interviews with caregivers, this study seeks to better characterize their journeys and potential areas to improve systems of care.

Methods:

Participant Recruitment

Children with a TSC diagnosis aged 12 to 36 months and their primary caregivers were recruited for a randomized waitlist-control design clinical trial of early behavioral intervention testing a social communication-focused intervention. Participant recruitment was completed through a variety of outreach mechanisms, including referrals from TSC specialty clinics and a national patient advocacy group (TSC Alliance), online social media postings, and institution-specific medical record queries to mail recruitment materials to eligible participants. Children were required to have a confirmed clinical diagnosis of TSC and be between 12 and 36 months of age at the time of their enrollment. Participants were excluded if they had a planned epilepsy surgery during the trial period or a developmental level below 6 months.

Clinical Trial Design

Participation in the study last 15-21 months and took place at two research sites. Before participation, caregivers completed the informed consent process in-person, during which they were provided with the opportunity to review the consent form and ask questions, following a review of the study protocol with the trained research coordinator. The study included four assessment visits at baseline, 3-months, 6-months, and 1-year follow-up. Initially, assessment

visits were designed to be in-person at the research sites. However, due to the COVID-19 pandemic, this requirement was reduced to only one in-person assessment visit at baseline and all remaining assessments could be completed either in-person or remotely. In the active treatment condition, intervention began after the baseline assessment. In the wait-list control condition, intervention began after the 6-month follow-up assessment visit (after 6 months of "standard care" in the community).

Parent surveys and assessment

A demographics questionnaire was collected at the baseline visit. The TAND Checklist and a follow-up parent survey collected updated seizure information at each assessment visit. These multiple sources aided in the cross-verification of participant data. Additionally, the Vineland Adaptive Behavior Scales (3rd Edition) (VABS-3) was administered as a comprehensive parent interview to gather data on functional skills at each assessment visit (Pepperdine & McCrimmon, 2018). All TAND Checklist, seizure, and VABS-3 data is reported from the final 1-year follow-up assessment.

Behavioral Intervention

During the 12-week intervention period, caregivers completed 12 weekly behavioral intervention sessions with their child and a site-trained interventionist. The intervention program focused on building child social communication, play, and engagement skills through evidence-based strategies in a caregiver-mediated model (Kasari, et al., 2015, Gulsrud, et al., 2024). Up to four of these weekly intervention sessions could be completed in-person, and the

remainder took place remotely using video conferencing. During these 12 weeks, caregivers were asked to record a weekly video practicing the intervention skills. These videos were reviewed by the interventionist and feedback was provided to each caregiver via a weekly 45-minute session using Zoom Video Communications, an online conferencing platform. The study team consulted with the institution's Security Compliance Office to identify secure and HIPAA-compliant platforms for intervention delivery, resulting in an Institutional Review Board (IRB) approved protocol.

Reflexivity and Positionality

The corresponding author (A1) is the study coordinator and a graduate student with training and prior work in qualitative methods. A1 conducted interviews, ongoing and final thematic data analysis, and writing. A2, a graduate student in clinical psychology, was involved in data coding, final thematic analysis, and writing. The remaining authors, ranging from junior to senior investigators, contributed to the direction of the interview guide, determined saturation for the interviews, interpreted findings, and edited the manuscript. We acknowledge that our backgrounds, experiences, and professional roles may have influenced the research process and interpretations.

Interview

Following completion of the final 1-year follow up assessment visit, participant caregivers semi-structured interviews led by study site personnel. The interview guide was formulated based on the [REDACTED FOR REVIEW]. These questions covered topics related to

personal experiences following diagnosis, interactions with providers, sources of information, navigating TAND, and access to services and treatment. A1 piloted the interview guide with two study participants and slight adaptations to question phrasing were made to improve question clarity. The complete interview guide is available by request.

These semi-structured interviews were conducted between January 2020 and July 2021. Interviews lasted approximately 45 minutes and were completed over Zoom. The sampling method for the study involved sequential interviews with caregivers at the study's conclusion until theme saturation was reached (*N*=20). No caregivers declined the interview opportunity, though the sample was limited to those who completed the study; caregivers who withdrew before the final visit were not interviewed. Early withdrawals were most commonly the result of caregiver time constraints.

All interviews were conducted by A1, who used probing techniques to clarify, elaborate, and illustrate caregiver responses to open-ended questions. Responses were recorded, transcribed, and de-identified. After transcription, the interview recordings were erased to ensure participant confidentiality. Ongoing thematic analysis was conducted, and the interviews were concluded when no new themes emerged after three sequential interviews, indicating saturation.

Analyses

Following saturation, thematic analyses was completed using Dedoose (Version 9.0.62), a web-based qualitative coding system. Analysis was guided by constructivist/interpretivist theory, relying on subjective interpretation of the caregivers' experiences (Patton, 2002). Two

coders read a subset of three transcripts and independently assigned initial codes to the data, then discussed any discrepancies until the codebook was finalized. A1 then coded all transcripts and A2 reviewed codes and identified any missing or discrepant codes, which were discussed until consensus was reached. Identified themes were refined by both coders and discussed with the full study team. A transparent audit trail was maintained through data collection and analysis. Final themes were reviewed by the study team, who further aided in interpretation.

Results:

Participants

Caregivers (N = 20) were interviewed following their completion of the study. All caregivers interviewed were the participants' biological (n=18) or adoptive (n=2) mothers. Two biological fathers joined their co-parents in the interview. These participants were predominately White (n=12), from families whose yearly income was above $90,000 (n=15), and highly educated, with most of the mothers completing some form of education after high school (n=17). Participants represented eleven states. Further caregiver demographic information is presented in **Table 1**.

Table 1. Demographics of interviewed caregivers

Demographic	N	Percent	Demographic	N	Percent
Income			**State**		
$30,000-60,000	3	15%	California	6	30%
$60,000-90,000	2	10%	Nevada	3	15%
>$90,000	15	75%	Arizona	2	10%
Race/Ethnicity			New York	2	10%
White	10	50%	Arkansas	1	5%
Asian	4	20%	Massachusetts	1	5%
Hispanic	4	20%	Florida	1	5%
More than one race	2	10%	Illinois	1	5%
Mother education			Washington	1	5%
High School	3	15%	Kansas	1	5%
Associate's Degree	3	15%	Maryland	1	5%
4-Year College	5	25%			
Some Graduate	3	15%			
Graduate school	6	30%			

Children ranged from 33 to 60 months old at the time of the interview, with an average age of 49.0 months (SD = 11.2). The age of TSC diagnosis ranged from 0 to 9 months, with an average diagnosis age of 4.0 months (SD = 3.4). All children had a diagnosis of epilepsy, with the age of onset ranging from 0 to 18 months and average onset 5.8 months (SD = 5.0). The number of anti-epileptic medications ranged from 1 to 6, with an average of 2.4 (SD = 1.4). By the conclusion of the study, 40% of children had received a medical autism diagnosis (n=8). The most common TAND symptoms reported were absent/delayed onset of language (65%), temper tantrums (50%), and difficulty concentrating (50%). Further child characteristics are presented in **Table 2**. Scores on the Adaptive Behavior Composite Standard Score for the VABS-3 ranged from 56 to 117, with an average of 76.5 (SD = 13.2).

Table 2. Child epilepsy and TAND

	Current		Ever	
Seizure type	**N**	**Percent**	**N**	**Percent**
Infantile spasms	2	10%	11	55%
Complex partial	6	30%	11	55%
Generalized	0	0%	3	15%
Drop seizure	1	5%	3	15%
Other	0	0%	4	20%
TAND Symptom	**N**	**%**		
Absent/delayed language onset	13	65%		
Difficulty paying attention or concentrating	10	50%		
Temper tantrums	10	50%		
Repeating words or phrases	9	45%		
Difficulties with eating	8	40%		
Overactivity/hyperactivity	8	40%		
Restlessness or fidgetiness	8	40%		
Impulsivity	6	30%		
Self-injury	6	30%		
Aggressive outbursts	5	25%		
Anxiety	5	25%		
Difficulties getting on with other people	4	20%		
Mood swings	4	20%		
Poor eye contact	4	20%		
Repetitive behaviors	4	20%		
Sleep difficulties	4	20%		
Very rigid or inflexible	3	15%		
Depressed mood	1	5%		
Extreme shyness	1	5%		

Interview Codes and Themes

The final coding tree for this study consisted of the following codes and subcodes: "Medical Treatment," including physician interactions, TAND and autism evaluations, and initial TSC diagnosis responses; "Factors Contributing to Care and Services," including provider knowledge, insurance coverage, geographic location, time commitment, continuity and quality of care, COVID-19 impact, and service coordination; "Parent Education/Knowledge," including

parent recommendations, information about services, medical information, education of providers, future concerns, information adequacy, information about autism and TAND, and sources of information such as publications, online sources, and other parents; "Services," including referrals, interactions with therapists and educators, IEP/special education, and therapies like ABA; and "Parent Advocacy," highlighting parent advocacy actions.

Qualitative thematic analyses revealed five primary themes: 1) sources of information about TSC and treatment, 2) access to high-quality and expert medical care, 3) perception and diagnosis of TAND, 4) impact of epilepsy on daily life, intervention, and schooling, and 5) access to therapeutic services, compatible providers, and evaluations. Additionally, parents provided recommendations for other caregivers navigating their child's early treatment following diagnosis. These themes are explored in greater detail below.

Theme 1: Sources of information about TSC and treatment

While some caregivers reported receiving information from their physician about TSC at the time of their child's diagnosis, all caregivers described receiving most information from their own efforts online. In particular, parents cited sources like the TSC Alliance website, Google, peer-reviewed publications, and hospital or university clinic pages about TSC. One parent expressed their initial hesitation to browse online without confirming the trustworthiness of sources with their child's physician. YouTube was perceived by another caregiver to be unhelpful and inaccurate. The TSC Alliance was endorsed universally as the most helpful, comprehensive, and well-organized source of resources and information about TSC. Facebook was described by over half of the caregivers as an important source of information

and support as connections established with other parents online (sometimes through TSC Alliance liaisons) helped them feel less isolated and understand their child's prognosis.

Caregivers described mixed experiences with their physicians at the time of their child's initial diagnosis. Generally, helpful information from physicians included an overview of TSC, a description of organ systems potentially affected, a summary of challenges that might arise in the future (i.e., TAND), and actions they could take now (such as enrolling in early intervention, meeting with specialists or TSC clinics, and connecting with the TSC Alliance or other family resources). Several families described negative interactions with physicians at the time of their child's diagnosis. Multiple caregivers reported that the physician who initially provided their diagnosis acknowledged that they were not familiar with TSC. In these cases, caregivers described immediately going online to learn about the diagnosis. Receiving insufficient information at the time of diagnosis was generally perceived as memorable but neutral. In contrast, caregivers expressed dissatisfaction or anger when they received incorrect, contradictory, or even damaging information about TSC. Some parents reported that their physician had provided them with the "worst case scenario," which upon later reflection seemed outdated or misinformed. Several caregivers expressed frustration with feeling as if they had been passed from one physician to the next without gaining additional information about TSC. "…we left with more questions than answers because the doctors were like 'we really don't know, you have to talk to [another] doctor'...At that point in time, it was very frustrating because we weren't able to get any of the answers that we needed to find out what we could actually do." (Mother from Maryland, 36-month-old child)

Notably, a few caregivers described that a physician, social worker, or nurse had connected them to early intervention quickly after their child's diagnosis or even helped them complete and submit the required paperwork. Those who had not received referrals until months later or who had found early intervention on their own expressed wishing they had been connected to services sooner regardless of their child's current degree of developmental delay. Only one parent received ongoing coordination from their physicians' office. Several caregivers did receive some coordination support through service agencies. Care coordinators provided parents with ongoing emotional support, advocacy information, specific parenting and developmental strategies, and overall direction for accessing services and planning for transitions. Parents sometimes highlighted care coordinators' previous experience as special education teachers, therapists, or caregivers of other children with neurodevelopmental challenges. One parent described monthly meetings with her care coordinator, who acted as a sounding board for her developmental concerns. "We get plenty of information, sometimes too much. What I really needed and wanted was guidance… somebody to tell me 'This is developmentally appropriate' or 'Yes, this is concerning'." (Mother from Washington, 42-month-old child)

Theme 2: Access to high-quality and expert medical care

Nearly all parents found connecting with a TSC expert or TSC clinic to be a critical component of their diagnostic journey. Several reported a gap of over a year before connecting with a TSC expert. In all of these cases, parents perceived that their child had experienced prolonged and adverse health consequences related to misdiagnosed seizures, incorrect

medications, or unnecessary surgeries. One parent said, “It almost makes me angry that we lost a year of development… If we would have known in the beginning he had infantile spasms, his life would have been different. I think his developmental delay would have been shorter.” (Mother from Nevada, 64-month-old child) Some parents described the value of getting second opinions early in their diagnostic journey when permitted by insurance coverage and provider accessibility.

Many caregivers described challenges communicating and coordinating with physicians, particularly when their child was seen by multiple specialists across disciplines. Caregivers frequently experienced long waitlists and needed to explain TSC to specialists. One family described medication changes or increased seizure activity repeatedly taking them to the emergency room when they were unable to reach their neurologist through limited communication portals.

When options were available, caregivers described switching between multiple physicians before finding one they preferred. Selection was based on ease of communication, level of responsiveness, perceived effectiveness of treatment, knowledge, trust, and proactive/preventative efforts. One parent described a particularly positive relationship with her child’s “medical home”, a team of coordinated providers with whom she communicated regularly about medical, therapeutic, and schooling decisions. Alternatively, one caregiver described feeling that her concerns about her child had been dismissed by their physician, so she stopped making appointments and instead looked to her friends and family for advice and support.

Geography was a common theme surrounding access to high-quality and expert care. Several caregivers expressed feeling that they lived "in the wrong state for medical care" due to limited local expertise. A few families incurred substantial out-of-pocket costs from traveling to TSC clinics around the country. One family described the challenge of relaying information back to their local physician after visiting an out-of-state TSC clinic, which resulted in disjointed care and inconsistent medications. Another family reported that their distant medical team was not familiar with local resources, which made specific referrals and recommendations difficult. One caregiver described that a planned move to another state had been prohibited by the 90-day residency requirement for the state's Medicaid program, along with long new-patient waitlists for specialists and limited access to prescription refills.

Theme 3: Perception and diagnosis of TAND

A common theme in the interviews was confusion about autism and other TAND diagnoses. Almost half of caregivers described that their medical and therapeutic providers attributed concerning delays and behaviors to TSC or tuber placement, and therefore delayed referrals for evaluation or intervention. In describing their journey towards an autism diagnosis, one parent said "...our answers always were 'we'll just cross that bridge when we need to'. They were walking on eggshells because they didn't want to open the can of worms." (Mother from Maryland, 36-month-old child) Multiple caregivers described frustration when they felt their neurodevelopmental concerns were dismissed or delayed by providers. Instead, caregivers expressed wanting specific information about what they could look out for, as well as strategies to help intervene. Several caregivers described their frustration in learning about the high

prevalence of TAND in TSC; they felt that their child should have been tested earlier and automatically.

Multiple caregivers described that providers, and even developmental experts, had repeatedly dismissed autism concerns due to their child's eye contact and social engagement, but that they still had elevated scores on diagnostic tests for autism. Caregivers also described surprise from providers and therapists following diagnosis; some caregivers perceived that access to evaluation, diagnosis, and intervention for autism had been delayed by misconceptions that autistic children cannot be socially engaged. Several caregivers of autistic children emphasized the helpfulness of evidence-based autism interventions. "Ever since we added ABA (applied behavior analysis) therapy into the mix (when he was about 5 years old), his language has flourished. He was able to tell us way more objects than we thought he knew and tell us his feelings better." (Mother from California, 62-month-old child) Several parents described some uncertainty about whether their child has "real autism," but expressed certainty about the importance of autism-specific services in advancing their child's development. After a year of ABA, one caregiver was uncertain whether her child would still qualify as autistic on an evaluation.

Theme 4: Impact of Epilepsy on Daily Life, Intervention, and School Readiness

The onset of seizures was nearly always the initial sign that led to the evaluation and diagnosis of TSC. For children whose epilepsy was uncontrolled or unpredictable, seizures were the caregivers' top concern. Those who had a TSC diagnosis in utero prioritized the early detection and management of seizures. In some cases where TSC was diagnosed before any

seizures occurred, parents felt confused and poorly informed on how to recognize the initial seizures. A significant worry among parents was the impact of seizures on their child's development, and this was a frequently cited source of concern following the TSC diagnosis. Parents also highlighted the usefulness of epilepsy specialists and neurologists in providing information about TSC soon after diagnosis.

Additionally, caregivers described epilepsy medications affecting their child's balance, attention, and cognitive functioning, with the readiness for interventions fluctuating based on the medication regimen. Gains or regressions in development were sometimes observed when medications were changed. The control of epilepsy was linked to caregivers' perception of their child's readiness for interventions, as uncontrolled seizures were observed to result in fatigue, lethargy, or irritability in children.

Furthermore, parents reported the challenges of missed therapy sessions or school days due to medication and seizure effects. Ensuring safety and supervision at school was challenging, especially in managing the child's tendency to elope and addressing seizures. Some children were not enrolled in any school or preschool programs because of their behavioral issues and complex medical needs. Caregivers also expressed concerns regarding emerging ADHD and how potential treatments might interact with seizure medications.

Theme 5: Access to therapeutic services, compatible providers, and evaluations

Parents often described difficulties accessing the types of services they wanted due to both availability and eligibility. Parents described hearing about interesting services that were not available in their area, such as music therapy. Some discussed how telehealth services were

not ideal for their family due to their child's attention or vision challenges, while others described wanting access to more telehealth services. Specifically, a few parents described wanting access to more parent training to deliver higher quantities of services to their child at home, including when their services were disrupted due to travel, parent or child health issues, insurance coverage, or COVID-19.

Another parent was unable to find a local physical therapist with pediatric experience. Waitlists for services were common for both diagnosis and interventions; when faced with a multiple-year waitlist for ABA therapy, one parent became a licensed ABA provider to deliver her daughter's therapy. Several parents described needing an autism diagnosis to access special education services and autism intervention, which they could not access through their child's TSC diagnosis alone. One family reported a concerning gap in their insurance coverage through which their child's genetic diagnosis overruled mandated coverage for autism services. Some parents paid out-of-pocket to get faster access to diagnoses and ABA therapies.

Another theme was the importance of the perceived quality and fit of therapists. Several parents spoke about specific providers that their child loved, through which they perceived that their child made substantial gains in development. Parents spoke about specific qualities that they found important in their child's therapist, such as patience or authority. Two parents spoke with frustration about their inability to switch providers given constraints with insurance or availability.

Multiple parents discussed that the evaluations performed by their service providers or school district to determine eligibility for special education seemed insufficient. They described assessments that lasted less than five minutes, did not include the child, or were done when

the child was uncooperative. Some parents thought the assessment had underestimated their child's skills, but others felt the evaluation had overestimated their child's ability and diminished their eligibility for services. One mother described a successful routine of getting her child re-evaluated every 3-6 months to determine whether any services should be added, removed, or changed. Through ongoing evaluation, providers identified a plateau in the child's development, which was reinvigorated by switching to a different therapy module. The parent did express dismay that her child was not able to stay in a helpful short-term intensive intervention longer despite perceived effectiveness.

Substantial gaps in their child's service delivery after the age of three years were described by several parents. Uncertainty about their child's needs and options led to delayed care or missed opportunities for services. In contrast, some parents described a seamless transition between early intervention and the school system, which was facilitated by care coordinators, early planning, knowledge about their legal rights and available resources, and state-level system coordination. Despite this, the majority of parents anticipated and often dreaded ongoing challenges in the future as they continued to advocate for their children's needs.

Parent recommendations

Caregivers provided insightful information for other parents of children newly diagnosed with TSC, which is summarized in **Figure 1**.

[Figure 1 Attached]

Conclusion:

Key findings from this study indicate that caregivers of children with TSC heavily rely on the TSC Alliance for information, face mixed experiences with healthcare providers, and confront systemic barriers to accessing expert care. The uncertainty surrounding the TAND diagnosis and access to related services, coupled with the significant impact of epilepsy on educational and intervention services, underscores the systemic challenges within the current care framework. These themes validate the importance of current research priorities for TSC stakeholders, including implementation of existing clinical guidelines, improved access to TSC expertise, and establishment of coordinated and integrated health care (Stuart et al., 2021).

Several themes point to the importance of increasing access to specialists and expanding physician knowledge of TSC. Telehealth clinics and hub-and-spoke structures like the Extension for Community Health Outcomes (ECHO) model can facilitate communication between specialists, local providers, and patients despite geographical, financial, and medical barriers (Arora et al., 2011). ECHO projects currently exist for autism and pediatric genetic conditions, and effectively connect specialists with local healthcare providers through tele-mentoring. This model allows for the dissemination of specialized knowledge and management strategies for complex conditions to a broader range of practitioners. These proven and sustainable techniques can help specialty TSC clinics communicate care plans back to local physicians and pediatricians. Both specialty clinics and local physicians can utilize clear and specific international clinical guidelines published to inform treatment and medication management, particularly for consideration of the interplay between medications and physical

manifestations of TSC (de Vries et al., 2023). Other strategies to enhance the dissemination of clinical guidelines to physicians include leveraging professional societies and organizations, conducting educational seminars and workshops, developing online learning platforms, and collaborating with health systems, insurance providers, and patient advocacy groups.

There also is a critical need for families of children with TSC to receive care coordination, which can reduce caregiver burden, improve transition planning, and promote comprehensive care and positive health outcomes (Akobirshoev et al., 2019). “Medical homes,” which establish patient-centered coordinated care, are particularly helpful across complex disorders requiring multidisciplinary care and can help prevent emergency room visits, reduce caregiver burden, and expand inter-provider communication (Gall et al., 2022). Recent guidance on Medicaid health home benefits may increase the availability of patient-centered medical homes (Affairs (ASPA), 2022). One potential benefit of this guidance may be the increased ability for children to receive care across state lines, which would particularly aid families of children with rare and complex disorders like TSC. The American Pediatric Association provides tool kits and guidelines for establishing coordinated care teams for complex medical conditions (*Tools and Resources for Medical Home Implementation*, n.d.).

Autism-specific services were reported by caregivers to be helpful for children with TSC and autism, as further demonstrated by pilot behavioral intervention studies (McDonald et al., 2020). The autism evaluation and diagnosis process delayed treatment for some families, despite the high rate of autism diagnosis for children and adolescents with TSC (40-50%). For this reason, all children with TSC and any autism-like manifestations should receive a comprehensive evaluation for communication disorders starting in early infancy, along with

other continued screening and monitoring for other TAND manifestations (de Vries et al., 2023). International guidelines advise annual screening and monitoring using the TAND Checklist to determine if any new neurodevelopmental disorders have emerged (de Vries et al., 2023). Further, clinical guidelines developed outside of TSC are relevant for identifying and intervening for autism in TSC, including the use of evidence-based Naturalistic Developmental Behavioral Interventions (NDBIs) (de Vries et al., 2023). Policies that allow services to start before the acquisition of a medical diagnosis could decrease the time, stress, cost, and persistence required to access beneficial services. It is also important to better understand the autism phenotype in TSC and educate TSC providers about the wide-ranging autism presentations in these children.

While the perceived quality and availability of early intervention varied across geographic locations, public services were available in some capacity for children under the age of three years due to federal funding and legislation through the Individuals with Disabilities Education Act (IDEA) Part C (CDC, 2018). The knowledge and advocacy skills parents acquire during these early years may support them in successfully transitioning into school- and insurance-based services when their child is no longer eligible for Part C public services after the age of three. It is advisable to introduce families to the complex network of services immediately following their diagnosis, regardless of their level of delay. However, the quality and availability of Part C services reportedly varied widely across states, an issue that warrants more investigation.

This study promotes the importance of partnering with patient advocacy groups, heeding caregiver perspectives, and utilizing qualitative research, which generates insightful

and detailed accounts of barriers, challenges, and priorities for urgent needs and future research. Collaboration between caregivers, providers, researchers, and government organizations has advanced knowledge and treatment for TSC, including the development of international consensus clinical guidelines for TSC (de Vries et al., 2023). Overall, this qualitative study emphasizes many of these recommendations for service providers, including physicians and early educators, as described in **Figure 2**.

[Figure 2 Attached]

This study interviewed only caregivers who completed the preceding clinical trial, omitting insights from those who withdrew early. Additionally, this study exclusively included children with epilepsy, potentially skewing the results toward those more heavily affected by the neurological impacts of TSC. While this study included children at a range of developmental levels, it may not fully represent the wider spectrum of TSC experiences, particularly those of individuals with less severe manifestations of the condition. This research is further limited by its inclusion of only English-speaking caregivers and the high rates of inclusion of White, educated, and high-income families. Non-English speakers, non-White caregivers, and families with low socioeconomic status likely have different, and often more complex, experiences navigating the medical and service landscape, and inclusion of these perspectives would further enhance understanding of barriers. Additionally, only caregivers within the United States were interviewed, while TSC is a global disorder with an internationally engaged community. Families from other countries might have vastly different experiences accessing information, services, and research. The study has begun to include international and Spanish-speaking participants to include more diverse perspectives in future research. However, more work must be done to

enhance representative recruitment in TSC research studies, including increasing genetic testing in low-resourced communities, connecting families with the TSC Alliance, and disseminating accessible research information.

The study's findings highlight the critical need for further research into the management of Tuberous Sclerosis Complex (TSC). Future research should aim to improve telehealth services possibly through the implementation of the ECHO model or a similar structure, broaden the scope of early intervention programs, and refine TSC-specific treatment protocols. A key goal of these endeavors is to enhance family-centered care and alleviate caregiver burden, ensuring comprehensive support for those impacted by TSC. Additionally, future investigations are encouraged to explore the various interventions that families utilize, particularly focusing on modular and eclectic strategies and considering the full lifespan of individuals with TSC, a priority within the TSC community (Vanclooster et al., 2022). Tracking educational progress, transitional phases, and the evolution of TAND in study participants could yield valuable longitudinal data.

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Diagnostic Interview

June 2019

Education around diagnosis

When was your child diagnosed with TSC? What led to concern? Who diagnosed? Has your child received genetic testing? If you can recall, what was your biggest concern at the time of diagnosis?

What information did you receive about TSC at the time of the initial diagnosis? What source of information was the most helpful to you in obtaining information about your child's diagnosis? What were the top two sources of information? Was your doctor a helpful source of information?

Do you feel that all of the information you were provided was correct? Do you feel that your child's treatment and medication is correct, and for how long?

Has your child ever been seen by a TSC specialist? How soon after diagnosis? Did you have any trouble getting into clinics?

At the time of first diagnosis, did you receive information about neurodevelopmental disorders associated with TSC? Did you receive information about autism? About GDD? If not, **when** did you first receive information about the increased risk for autism and GDD? **Who** gave you this information?

Has anyone told you they are concerned about autism/GDD in your child? Who? If so, what was your reaction to this? Were you ever told not to be concerned?

> Have you received a formal diagnosis of autism/GDD? When? Was it expected? How did you feel about receiving the diagnosis?

How did your understanding of autism change following enrollment in this study?

Education around services

What services did you receive information about, and when? How did you pay for these services? Which (additional) services would you have liked to have access to, or sooner? Which services have most benefited your child?

For children over 3: Does your child have an IEP? *For everybody*: Has anyone told you about IEPs or how to get one? What is your child's IEP eligibility criteria?

What barriers did you encounter when trying to access early intervention or special education services for your child?

How did your access to services change following enrollment in this study? Have you used the JETS reports to obtain services?

Next steps

Do you feel like you have the right team of providers in place to manage your child's educational and developmental needs? Do you feel like you have a good idea of next steps to take in this journey? What are your biggest concerns moving forward? What are you looking forward to?

If you were to give advice to another family with an infant recently diagnosed with TSC, what would you recommend? Based on your enrollment in the study, is there something that you now know to advocate for that you previously had not been aware of?

What were the biggest challenges to being a part of this study? What modifications would have improved your experience? Overall, how would you summarize your experience in the study?

If you had the option, would you prefer to have done JASPER fully remotely? Would you have preferred more or less in-person sessions? If in-person intervention was available locally, would you prefer more sessions?

Do you use JASPER skills now? Have you received other types of parent-mediated intervention?

Are there any areas of research you think should be further studied? What are your research priorities?

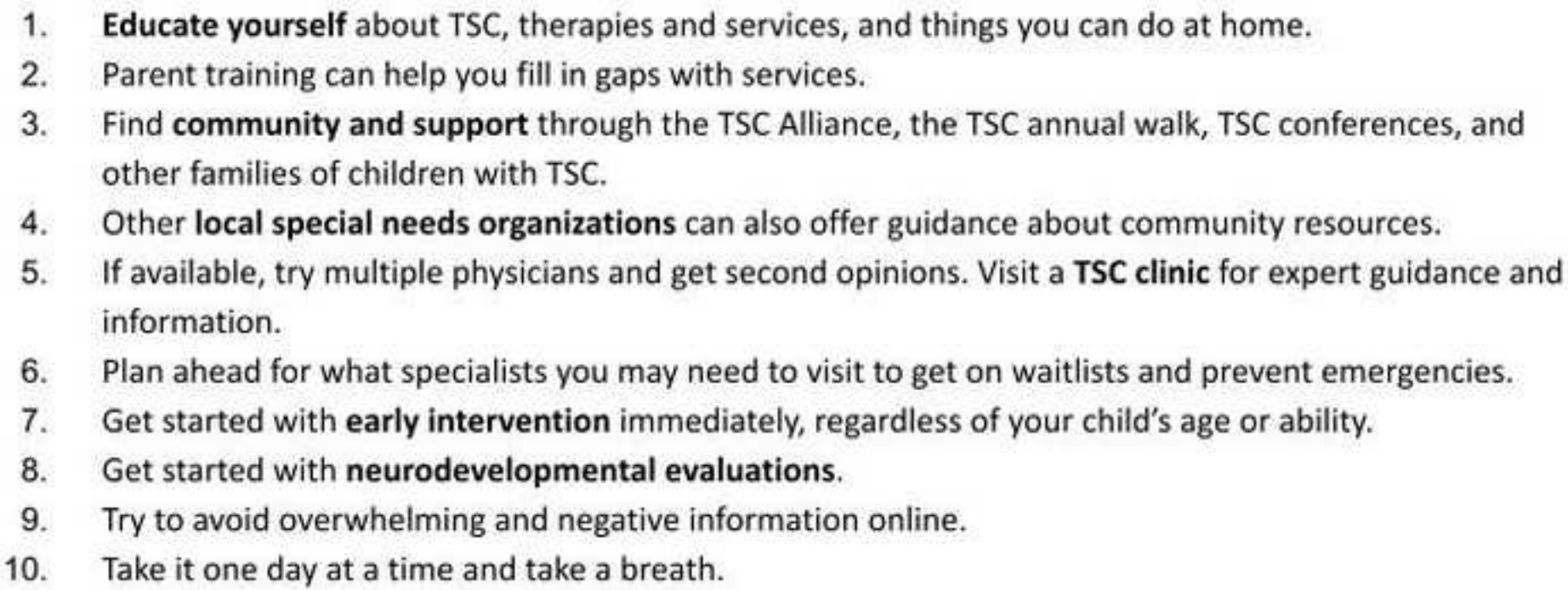

Figure 1. Caregiver recommendations for newly diagnosed families.

1. Train providers (i.e., pediatricians, geneticists, neurologists) on delivering **clear, accurate information** post-diagnosis and on referring families to **supportive resources** like the TSC Alliance.[1]
2. Facilitate **access to TSC experts and specialized TSC Clinics**, ensuring families receive the most informed and current care strategies.[2]
3. Implement **coordinated care** through multi-disciplinary teams or dedicated care coordinators to improve quality of life and reduce healthcare costs.[3]
4. Employ the TAND Checklist for **early identification and consistent monitoring** of TSC-specific neuropsychiatric issues. Physical and digital versions of the TAND Checklist can be integrated into routine check-ups, and can also be utilized by any clinician or caregiver of a person with TSC.[4, 5]
5. **Assess and treat emerging concerns** as they arise with evidence-based approaches applicable to all children, while also ensuring alignment with the latest TSC-specific clinical guidelines for a comprehensive and tailored treatment strategy.[6]
6. Aid families in **understanding and accessing the healthcare and educational services** available for early intervention and ongoing support. Early intervention through Part C services can be critical for all children with TSC, regardless of observed developmental delays.
7. **Consider the unique TAND profile of each child** when planning educational transitions and access to educational services, which may require support through the development and implementation of tailored Individualized Education Plans (IEP) in collaboration with caregivers, educators, therapists, physicians, and case managers.[6]
8. Systematically **assess the well-being of individuals with TSC and their families**, focusing on psychological health, family dynamics, and social connectivity. Offer targeted support to families, including psychological support and practical help to enhance family resilience and reduce stress.[6]

1. Get Support Now. *TSC Alliance* https://www.tscalliance.org/newly-diagnosed/get-support-now/.
2. TSC Clinics. *TSC Alliance* https://www.tscalliance.org/individuals-families/tsc-clinics/.
3. Tools and Resources for Medical Home Implementation. https://www.aap.org/en/practice-management/medical-home/tools-and-resources-for-medical-home-implementation/.
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Figure 2. Recommendations for providers.