Managing Tuberous Sclerosis Complex Across the Lifespan

A Resource for General Practitioners and Other Clinicians

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About this resource

TSA (Tuberous Sclerosis Australia) is the only patient organisation supporting people living with Tuberous Sclerosis Complex (TSC) in Australia. This resource is designed to help general practitioners (GPs) and other clinicians understand the common concerns of patients with TSC throughout their lives and how to collaborate with them to provide the highest standard of care.

Visit TSA's website tsa.org.au for information on understanding TSC and/or to download diagnostic criteria and surveillance guidelines.

This information resource is written for clinicians to help them understand their role in the care of patients with TSC and is NOT intended for patients. TSA publishes information resources specifically written for families of children diagnosed with TSC, adults diagnosed with TSC and information for a prenatal (or possible prenatal) diagnosis. Patient packs can be downloaded on TSA's website.

TSA also publishes separate information for health care professionals on patients who have a new or suspected TSC diagnosis.

You can connect with our TSA Nurse for recommendations of specialists with experience in TSC to refer your patient with TSC to.

TSA Tuberous Sclerosis Australia

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Overview of TSC

TSC is a rare autosomal dominant genetic condition caused by mutations in the *TSC1* or *TSC2* genes which disrupt the normal regulatory function of the hamartin and tuberin proteins. This loss of regulation leads to continuous activation of the mammalian target of rapamycin complex (mTORC), which promotes uncontrolled cellular growth and proliferation, contributing to the development of benign tumours in the brain and other vital organs such as the kidneys, heart, liver, eyes, lungs, and skin. The central nervous system is often affected, leading to TSC-Associated Neuropsychiatric Disorders (TAND), which include cognitive impairment, autism, behavioural disorders, and seizures.

TSC significantly impacts the personal lives of individuals living with TSC and their families. Patients can face setbacks in their education or career due to TSC, and caregivers state that TSC affects family life, social interactions, and working relationships. Well-coordinated TSC care is challenging to access.

Common concerns in TSC across the lifespan

TSC is a complex condition, and concerns and presentation change across the lifespan. Effective management involves continuous critical screening and coordinated care across various medical disciplines.

Prenatal

- **Detection of cardiac rhabdomyomas on ultrasound or echocardiology:** Prenatal consideration of TSC often arises from the detection of single or multiple cardiac rhabdomyomas. Nearly all babies with multiple, and about 70% with a single cardiac rhabdomyoma, have TSC. These can be detected on ultrasound/echocardiography.
- **Foetal MRI:** Can be used to look for specific features like cortical tubers, subependymal nodules (SEN), or subependymal giant cell astrocytomas (SEGA). The presence of one or more of these findings, along with cardiac rhabdomyoma(s), confirms a diagnosis of TSC. However, the absence of these findings does not rule out TSC.
- **Genetic counselling:** A consultation should be sought to discuss TSC and the option of genetic testing of *TSC1* and *TSC2*. The timing of the testing, either prenatally or after birth, usually depends on individual circumstances and is not routinely offered prenatally.

Prenatal – Care Considerations

- **Referrals for further testing and follow-up:** Confirm that the mother has been appropriately referred to a foetal medicine unit for consideration of further testing (foetal MRI, echocardiography) and to the appropriate specialists for follow-up.
- **Post-birth plan:** Ensure there is a plan in place for the infant to receive appropriate TSC screening and care after birth.
- **Support services:** If needed, consider referring to the TSA nurse service for support with a new diagnosis. Ensure awareness of TSA's website for up-to-date TSC information and support. Visit the TSA website to download patient information packs for new or suspected diagnosis of TSC.

Infancy

The most common initial presenting features of TSC in infancy are cardiac rhabdomyomas, hypomelanotic macules (ash-leaf spots), tubers/cortical dysplasia and subependymal nodules (SEN). In the first year of life, over 70% of infants develop epilepsy and adequate seizure control is associated with better developmental outcomes.

- **Infantile spasms:** Typically develop in the first 3-6 months of life, peaking between 4-6 months, but can start any time in the first two years. These are sudden, brief, bilateral, and symmetric contractions of the muscles of the neck, trunk, and extremities, and they occur in clusters.
  - > Immediate investigation is imperative as infantile spasms often indicate a significant underlying neurological disorder - refer to a paediatric neurologist urgently.
  - > Prompt diagnosis and treatment are critical to minimise developmental impacts. Referral to a paediatric epileptologist or neurologist is necessary due to the potential for drug-resistant epilepsy and serious developmental impacts of inadequately controlled epilepsy.
- **Cardiac rhabdomyomas:** Are usually asymptomatic and self-resolve in childhood. Monitoring is

recommended with echocardiograms/ECGs for newly diagnosed or suspected TSC, especially in children younger than 3 years. If the patient is already diagnosed with TSC, monitor every 1-3 years if asymptomatic rhabdomyomas are present and more frequently if symptomatic. If no rhabdomyomas are present, no regular monitoring is required. In major tertiary hospitals, this is usually managed by the treating team. In regional areas, refer to a cardiologist for review.

- **Hypomelanotic macules**: Best visualised with a Wood Lamp. The presence of 3 or more macules at least 5mm in diameter is a major diagnostic feature of TSC. If suspected, refer for dermatology input.

Infancy - Care Considerations

- **Seizure activity:** Epilepsy affects 75-90% of people with TSC. Question parents/carers about seizure activity during routine consults, and ensure they are receiving adequate specialist care, follow-up and support to manage seizures.
  - > Parents/carers should be taught to recognise infantile spasms and encouraged to video record any possible occurrences. Advise parents/carers to present to the emergency department for investigation, especially at the first suspected occurrence of infantile spasms.
- **Neurology involvement:** Ensure the infant has been referred appropriately for neurology involvement, EEG/VEEG and MRI brain. Paediatric neurology involvement may require a referral from a paediatrician.
- **Cardiology involvement:** Ensure infant has had an echocardiogram, especially if rhabdomyomas identified prenatally or they are newly diagnosed. Refer to cardiologist for further intervention if needed.
- **Dermatology involvement:** Perform a thorough skin examination and refer to dermatologist if needed.
- **Vigabatrin:** The first-line treatment for infantile spasms in TSC is usually vigabatrin. Check with parents/carers whether they have been offered ophthalmologic screening due to the risk of visual field loss associated with vigabatrin.
- **Research participation:** Consider the possibility of clinical trial participation linked to major tertiary hospitals. Research is ongoing into the use of preventative anti-seizure medication and the benefits of commencing treatment prior to seizure onset.
- **Developmental monitoring:** Monitor infant developmental milestones and refer to a paediatrician for further surveillance and early intervention. All children with TSC should be monitored by a paediatrician due to risk of developmental delays.
- **Genetic counselling:** Consider referral to a genetics service, especially if parents are having more children.
- **Vaccinations:** Ensure vaccinations are up-to-date, especially if the infant is on an mTOR inhibitor medication (usually everolimus in Australia). **NOTE:** Live vaccines should be avoided in patients taking everolimus - liaise with the prescribing specialist if needed regarding vaccination schedule.
- **Surveillance:** Ensure regular surveillance is being completed in line with TSC surveillance guidelines (see Table 2).

Childhood/Adolescence

The main TSC concerns in childhood centre around epilepsy, developmental concerns and commencing school, as well as TSC Associated Neuropsychiatric Disorders (TAND), and the development of kidney angiomyolipomas (AMLs) and facial angiofibromas. In adolescence, the concerns are similar. Other concerns may include: commencing secondary schooling/tertiary education, transitioning from paediatric to adult care, mental health, menstrual cycle management, lung involvement - lymphangioleiomyomatosis (LAM) (particularly in females), contraception, and sex and sexuality.

- **Epilepsy management:** The most common type of seizures that occur in TSC are focal seizures, although multiple seizure types can be experienced. Polypharmacy, and complex and drug-resistant epilepsy are common and seizure activity can be difficult to control.
- **Facial angiofibromas:** Facial angiofibromas can appear in early childhood and are found in most patients with TSC over 5 years of age. At first, angiofibromas can cause a rosy appearance in the cheeks due to increased vascularity of the skin and turn into small spots and bumps due to increasing amounts of fibrous tissue.
- **Kidney anigomyolipomas (AMLs):** AMLs are benign kidney tumours made up of blood vessels (angio), muscle (myo), and fat (lipo). The presence of fat in

AMLs allows them to be distinguished from other kidney tumours by MRI, CT scan, or ultrasound imaging. AMLs can begin to develop in childhood and their growth can be rapid and unpredictable. It is estimated that 80% of people with TSC will develop AMLs during their lifetime.

- **TAND:** TAND includes behavioural, psychiatric, intellectual, academic, neuropsychological, and psychosocial manifestations. It affects up to 90% of individuals with TSC and has a significant carer burden.
- **Pneumothorax/lymphangioleiomyomatosis:** About 30% of women with TSC will develop cystic lung disease or lymphangioleiomyomatosis (LAM) of the lungs, which may present with a collapsed lung or pneumothorax. This can be detected by CT scanning of the lungs. Screening for LAM should be considered in girls after puberty because treatment with an mTOR inhibitor may prevent complications of LAM in later life.

Childhood/Adolescence - Care Considerations

- **Regular surveillance and monitoring:** Continue to ensure regular surveillance and monitoring are being completed as per surveillance guidelines.
- **Seizure management:** Question carers/parents about seizure activity and ensure that appropriate monitoring is being carried out. Ensure all medications are documented and seizure management/action plans are up to date.
  - > For patients with refractory epilepsy who are surgical candidates, surgical intervention may be considered. This is mainly performed in tertiary paediatric public hospitals in Melbourne, Sydney, and Brisbane.
- **Vaccinations:** Ensure vaccinations are up-to-date. **NOTE:** Live vaccines cannot be given in patients taking mTOR inhibitors - liaise with the prescribing clinician to ensure vaccinations are given at the appropriate intervals.
- **Chronic disease management plan:** Consider implementing a chronic disease management plan to coordinate care and track surveillance requirements.
- **Dental:** Ensure regular 6 monthly dental checkups are being completed and the patient is being monitored for dental enamel pits and oral fibromas. Dental enamel pits increase the risk of oral cavities.
- **Facial angiofibromas:** Recognise the negative psychosocial impact of facial angiofibromas, especially in school-age children and adolescents. Facial angiofibromas can be treated with rapamycin cream (topical sirolimus) and laser. Consider referral to a dermatologist for assessment and management.
- **Monitoring for AMLs:** Ensure regular renal monitoring is being undertaken and refer to a nephrologist for follow-up. Renal monitoring is essential for early detection and management of AMLs. (For newly diagnosed TSC: abdominal MRI◆, blood pressure check, blood test for kidney function/GFR, urine test for blood and protein/ACR/PCR. In existing TSC: Abdominal MRI every 1-3 years, annual kidney function/GFR test). ◆Abdominal MRI is funded on the MBS for people with clinically diagnosed TSC.
- **TAND management:** TAND can include behavioural, psychiatric, intellectual, academic, neuropsychological, and psychosocial manifestations. It affects up to 90% of individuals with TSC and has a significant carer burden, but is often overlooked and under-researched, leading to inadequate assessment and treatment. Regular screening using the TAND Checklist and referral to multidisciplinary health care professionals are important for improving patient outcomes.
  - > **Autism spectrum disorder (ASD):** TSC is one of the most commonly occurring single-gene disorders associated with ASD, therefore monitoring, early intervention and referral to the appropriate specialists is essential. Consider proactive referral due to extensive wait times for access to paediatricians, behavioural supports and allied health professionals.
  - > **Intellectual disability:** TSC can cause mild to severe intellectual disability, with some patients having high and complex needs. Regularly check in with patients and carers/family about psychosocial needs and refer to supports as appropriate.
  - > **Consider annual Comprehensive Health Assessment Program (CHAP) assessment (12-18 years):** The CHAP is a Medicare funded, evidence based tool for conducting annual health assessments for people with intellectual disability in Australia.
- **Administrative tasks:** Provide medication charts etc for schools/school excursions and medical information for government services such as Centrelink and NDIS.

- **Transitioning from paediatric to adult care:** In major capital cities with tertiary paediatric hospitals, paediatric care for TSC is often coordinated from these centres. Once adolescents are no longer eligible for these services the burden of coordinating care often falls on parents. Primary care clinicians should ensure familiarity with surveillance guidelines to assist with the transition to adult health services. Contact TSA for transition services and key contacts around Australia.
- **LAM:** This rare lung disease almost exclusively affects women, and usually occurs between the onset of puberty and menopause. Surveillance is crucial to monitor for and manage LAM.
  - > **Symptom evaluation:** Assess for unexplained cough, chest pain, and breathing difficulties at each clinical visit. Refer to respiratory physician if needed.
  - > **High-resolution chest CT (HRCT):** Females aged 18+ should have a high-resolution chest CT scan for signs of LAM. LAM is exceedingly rare in males, so include adult males only if symptomatic. If lung cysts are detected, repeat HRCT every 2-3 years; otherwise, every 5-10 years. Refer to a respiratory physician for specialist management.
  - > **No one with LAM should smoke or vape:** Educate adolescents with TSC about the risks and harm of vaping and smoking, especially in the context of LAM.

Adults

Like many of the concerns listed for adolescents, TSC-related concerns in the adult population are commonly TAND, the monitoring and management of AMLs, LAM (particularly in females), contraception/pregnancy planning and menopause. Sclerotic bone lesions are reported as a frequent finding in the imaging of adults with TSC but are usually benign. While less common than kidney AMLs, hepatic AMLs and pancreatic AMLs, cysts and other benign lesions can also occur in adults with TSC.

Adults - Care Considerations

- **Regular surveillance and monitoring:** Continue to ensure regular TSC surveillance and monitoring are being completed as per surveillance guidelines and use RACGP Red Book recommendations in conjunction to guide general screening. Ensure diligence in meeting general screening requirements and currency of vaccinations.
- **Sclerotic bone lesions:** It is important to be aware of the occurrence of these lesions to avoid misdiagnosis as osteoblastic metastases.
- **Monitor for hepatic and pancreatic AMLs/ lesions/cysts:** These usually occur without clinical symptoms or complications, but continued surveillance is important. Seek specialist input for management of TSC related hepatic/pancreatic AMLs, lesions and cysts.
- **Monitoring for AMLs:** Ensure regular renal monitoring is being undertaken and refer to a nephrologist for follow up. Renal monitoring is essential for early detection and management of AMLs. (For newly diagnosed TSC: abdominal MRI◆, blood pressure check, bloods for kidney function/GFR, urine test for blood and protein/ ACR/PCR. In existing TSC: Abdominal MRI every 1-3 years, annual kidney function/GFR test). ◆Abdominal MRI is funded on the MBS for people with clinically diagnosed TSC.
- **TAND management:** TAND can include behavioural, psychiatric, intellectual, academic, neuropsychological, and psychosocial manifestations. It affects up to 90% of individuals with TSC and has a significant carer burden, but is often overlooked and under-researched, leading to inadequate assessment and treatment. Regular screening using the TAND Checklist and referral to multidisciplinary health care professionals are important for improving patient outcomes.
  - > **Autism spectrum disorder (ASD):** TSC is one of the most commonly occurring single-gene disorders associated with ASD, therefore monitoring, early intervention and referral to the appropriate specialists is essential.
  - > **Intellectual disability:** TSC can cause mild to severe intellectual disability, with some patients having high and complex needs. Refer to supports as appropriate. The psychosocial impact on the patient and their carers/family should not be underestimated; regularly check in with patients and carers/ family about mental health needs and implement mental health plans/supports as needed.

- **Consider annual Comprehensive Health Assessment Program (CHAP) assessment (Adults):** The CHAP is a Medicare funded, evidence based tool for conducting annual health assessments for people with intellectual disability in Australia.

- **LAM:** Almost exclusively affects women, and tends to stabilise after menopause, however, regular screening is still necessary. LAM can be worsened by pregnancy. Therefore, referral for specialist advice regarding pregnancy is advised. Some women with LAM may also have microscopic multifocal pneumocyte hyperplasia (MMPH), which is a benign condition and improved by mTOR inhibition. Surveillance is crucial to monitor for and manage LAM. Educate on the risks of smoking and vaping. No one with LAM should smoke or vape.
  - **Symptom evaluation:** Assess for unexplained cough, chest pain, and breathing difficulties at each clinical visit. Refer to a respiratory physician if needed.
  - **High-resolution chest CT (HRCT):** Females aged 18+ should have a high-resolution chest CT scan for signs of LAM. Adult males should be included only if symptomatic. If lung cysts are detected, repeat HRCT every 2-3 years; otherwise, every 5-10 years.
  - **Vaccinations:** Offer annual flu vaccine and pneumococcal vaccine (PBS listed for chronic lung disease).
- **Dental:** Ensure regular (6 monthly) dental checkups are being completed and the patient is being monitored for dental enamel pits and oral fibromas.

Pregnancy and menopause

- **Pre-pregnancy planning:** Refer patients with TSC to a clinical geneticist for genetic counselling prior to conception to discuss genetic risks and options for prenatal or preimplantation genetic testing.
  - **Folic acid:** Ensure adequate folic acid supplementation of at least 0.4mg/day and consider higher doses (up to 5mg/day) in conjunction with neurologist/obstetrician input if the patient has epilepsy and is taking AED.
  - **Medication:** Perform a thorough medication review and seek specialist advice, particularly if the patient is taking mTOR inhibitors.
  - **Renal evaluation:** Consider referral to a nephrologist for pre-pregnancy evaluation as pregnancy can cause bleeding, growth and rupture of renal AMLs.
  - **LAM screening:** Ensure LAM screening is up to date prior to conception. LAM can be worsened by pregnancy and therefore referral for specialist advice regarding pregnancy is advised.
- **Pregnancy:** TSC can adversely affect maternal and foetal outcomes. There are no established best practice guidelines on managing maternal TSC so refer any woman with TSC considering pregnancy to appropriate specialists (particularly neurology and nephrology if epilepsy and AMLs are present) and/or the foetal medicine unit of a tertiary hospital for monitoring. Consideration of the following factors is important:
  - **Medications:** Polypharmacy in TSC is common. Everolimus, an mTOR inhibitor commonly prescribed for the management of AMLs, CNS lesions and LAM in TSC, is a category C drug in pregnancy.
  - **Neurological complications:** Intractable epilepsy, status epilepticus, and SEGA with hydrocephalus are the leading causes of mortality and morbidity in mothers with TSC.
  - **Renal complications:** Renal issues (exponential growth, bleeding and rupture of AMLs), are the next most common cause of morbidity and mortality in TSC pregnancies. Renal involvement is a crucial prognostic factor, highlighting the importance of renal evaluation for patients seeking prenatal counselling. Ideally, renal evaluation should happen in the pre-pregnancy planning stage, but refer for nephrologist input as soon as possible otherwise.
  - **LAM:** LAM can be worsened by pregnancy and therefore referral for specialist advice regarding pregnancy is advised.
  - **Genetic counselling:** Early referral to a clinical geneticist for genetic counselling is imperative if preimplantation genetic testing was not performed, for a discussion of genetic risks and counselling regarding genetic testing.
  - **Folic acid:** Ensure adequate folic acid supplementation of at least 0.4mg/day and consider higher doses (up to 5mg/day) in conjunction with neurology/obstetrics input if the patient has epilepsy and is taking AED.
  - **Vaccination:** Encourage patient to have influenza, pertussis and RSV vaccines at the appropriate times during pregnancy.
- **Contraception:** Research suggests that oestrogen may be involved in the pathogenesis of LAM, so the current recommendation is to avoid the use of oestrogen-containing contraceptives in women with

TSC and preferentially use long acting reversible and progesterone-only contraceptives. Contraception is recommended if the patient is taking mTOR inhibitors. See contraception section for more information.

- **Menopause:** Currently, no protocols exist for the treatment of menopause-related symptoms in TSC or in women with LAM. No contraindications exist for the use of local treatments for genitourinary symptoms of menopause. Low dose hormone-replacement-therapy is often required in menopause and generally safe, however refer to the LAM guidelines from the American Thoracic Society and consult with a respiratory physician prior to commencing hormone replacement therapy.

Contraception

- **Menstrual management:** Menstruation can pose significant challenges for people with TSC, particularly those with ASD and intellectual disabilities, due to sensory sensitivities related to bleeding and difficulties in communicating pain, as well as challenges in undergoing diagnostic procedures like ultrasounds. Cyclical hormonal changes can worsen behavioural issues, and catamenial epilepsy may occur. Pregnancy, cyclical hormonal changes, and breastfeeding can impact seizure frequency and severity, and patients often require specialist gynaecological management.
- **Contraceptives:** Limited research suggests that oestrogen may be involved in the pathogenesis of LAM, so the current recommendation is to avoid the use of oestrogen-containing contraceptives in women with TSC, and preferentially use progesterone-containing contraceptives. Menstrual management in TSC can be complex so consider referral to a gynaecologist for review.
- **TSC/Epilepsy contraceptive considerations:** Enzyme inducing antiepileptic drugs (AED) can make contraceptives less effective and increase the risk of unplanned pregnancy.
  - > **First line:** Hormonal IUD (Mirena or Kyleena).
  - > **Second line:** Copper IUD or Depo-Provera (consider AED can reduce bone density and Depo-Provera can contribute to bone density loss).
  - > **Not recommended concomitantly with AED, as AED can reduce efficacy:** Progesterone only pills and progesterone implants (Implanon), combined hormonal contraceptives **(combined hormonal contraceptives not recommended generally in TSC due to association between LAM and oestrogen- containing contraceptives).**
  - > **Emergency contraception: Note:** consider recommendations regarding the use of oestrogen-containing contraceptives in TSC and seek specialist input if emergency contraception required. Efficacy of emergency contraceptive pills with levonorgestrel and ulipristal acetate are affected by enzyme-inducing AEDs. Consider double dosing or Copper IUD.
  - > **TSC and mTOR inhibitors:** mTOR inhibitors are category C in pregnancy, long-acting reversible contraception is recommended in patients taking mTOR inhibitors.

Everolimus (Afinitor): mTOR inhibitor

Everolimus is the most commonly prescribed mTOR inhibitor in Australia. It is prescribed by specialist clinicians for various manifestations of TSC. It is a potent immunosuppressive medication. Common side effects include stomatitis, infections, pneumonitis, hyperglycaemia and hyperlipidaemia. Serious side effects may include renal failure, impaired wound healing, and increased risk of infections. For any patients on this medication:

- Annually monitor renal and liver function and perform diabetes screening. Patients on this medication have a significantly increased metabolic risk.
- Monitor urine ACR and PCR at least 6 monthly once established on everolimus as mTOR inhibitors can cause proteinuria.
- Regular blood tests should be performed to monitor everolimus levels and ensure they remain within therapeutic range (this is usually organised by the prescribing clinician, but confirm that the patient has monitoring arrangements in place).
- Exercise caution in patients with active infections due to immunosuppressive effects.
- Monitor patients with mobility issues due to risk of impaired healing, educate parents and carers regarding pressure injury risks in this cohort and ensure that adequate pressure injury management strategies are in place.
- Ensure vaccinations are up to date prior to commencing mTOR inhibitors as live vaccines should be avoided in these patients.

- Exercise caution when reviewing or prescribing other medications when the patient is taking everolimus, as it has many common drug-drug interactions (CYP3A4 + P-glycoprotein).
- Ensure adequate contraceptive measures in patients using everolimus, as it is a category C pregnancy drug with limited evidence of use in pregnancy.

TSC clinics

NSW

Westmead: The only multidisciplinary TSC clinic for adults in Australia is through Westmead Hospital's Comprehensive Epilepsy Service. Patients can be referred via fax: (02) 8890 5756 or email: WSLHD-Epilepsy@health.nsw.gov.au

Sydney Children's Hospital, Randwick (SCH): SCH runs a multidisciplinary rare disease clinic through the Randwick Campus that caters for paediatric patients with TSC. Refer patients directly to the clinic or via consultmed (preferred): the clinic is listed as Paediatric Neurology - Tuberous Sclerosis Clinic or email schn-sch-tsclinic@health.nsw.gov.au. Upon referral, provide an explanation of why the patient is being referred and ensure that the patient has an up to date MRI brain and abdominal MRI/renal ultrasound upon referral if possible.

Macquarie University Hospital LAM Clinic: Macquarie University Hospital runs an outpatient LAM clinic and offers expert advice on TSC and its respiratory issues by dedicated respiratory physicians. A referral from a GP is required. Links towards research are part of this clinic.

QLD

Queensland Children's Hospital (QCH): QCH runs a multidisciplinary paediatric and adolescent TSC clinic through the QCH Neurosciences Unit. Patients can be referred to the service via referral software, to the QCH Neurosciences Unit. The service is available to children and young people living in QLD and northern NSW.

WA

Rare Care Centre, WA: While not a TSC clinic, the Rare Care Centre in WA is the first of its kind in Australia. It comprises a multidisciplinary team, including a genetics counsellor, a liaison from the Department of Communities (providing child protection, housing, and disability support), an NDIS coordinator, a paediatric nurse leading care coordination, welfare support, an Aboriginal health practitioner, a GP, a mental health clinician, a teacher for school support, and a consultant paediatrician for medical case management. The centre provides cross-sector care coordination for children in WA with rare and undiagnosed diseases. Patients can be referred to the centre by a paediatrician.

Other states and territories

The major tertiary hospitals in other states and territories do not run clinics but there are clinicians that are experienced with TSC Australia-wide. TSA has a database of health care professionals in Australia who are experienced in managing TSC. Contact the TSA Nurse for details of health care professionals who are experienced in managing TSC.

TSA (Tuberous Sclerosis Australia)

TSA: TSA is the only charity in Australia supporting people living with TSC. By providing knowledge, support and connections, we aim to create a better life and a more hopeful future for everyone in Australia affected by TSC. TSA supports individuals and families affected by TSC, fostering a community for shared experiences and learning. We connect people to expert health care professionals and services. Collaborating with our Medical Advisory Panel and global researchers, we seek new treatments, screening options, and ultimately, a cure for TSC.

We raise awareness, advocate for better health care access and partner with TSC International, Rare Voices Australia and Tuberous Sclerosis Complex New Zealand. TSA is the trusted go-to resource for information, advice and support for everyone in Australia affected by TSC.

TSA Website: Visit our website for up-to-date information about TSC, including resources for families and patients, links to videos, materials for health care professionals, and details on joining our TSC health care professionals network.

TSA Nurse Service: TSA operates a telehealth nurse service staffed by a Registered Nurse to provide information and support to people living with TSC or a possible diagnosis of TSC and their families and carers. The service also assists clinicians caring for people with TSC. Health care professionals can contact the nurse for TSC-specific advice and recommendations on clinicians and specialists experienced with TSC across Australia. You can book a call with the TSA nurse, call 1300 733 435 (Australia only) or email nurse@tsa.org.au

Surveillance and management guidelines for TSC: Regular surveillance and screening are crucial for anyone living with TSC, as symptoms often change over time.

Other useful services and resources

Carer Gateway: An Australian Government website providing free and practical services and support for carers.

Disability Gateway: An Australian Government website providing information and services to help people with disability, their families, friends, and carers, to find the support they need in Australia.

Epilepsy Action: Epilepsy Action provides general support and information nationwide for those affected by epilepsy. The site has a nurse-led telehealth line and provides assistance, advice, education and training related to epilepsy.

Kiind WA: Kiind is a family-led, independent peer support organization in Western Australia, supporting families raising children with disabilities, developmental delays, autism, and other conditions. With nearly 40 years of experience, Kiind offers practical assistance, emotional support, and connections to other families. They serve over 6,600 families, providing all services free of charge.

Living With LAM: Provides information and peer support to women living with LAM. They also provide information for health care professionals caring for women with LAM.

Trapeze/Transition Care Service: Trapeze offers support and care plans to young people aged 14-25 with chronic conditions as they transition from paediatric to adult care through the Sydney Children's Hospital Network (SCHN). The Transition Care Service assists young people across NSW and ACT who have not been part of SCHN.

More organisations and useful contacts can be found on TSA's website.

Appendix: TSC diagnosis and surveillance tables

Diagnosing TSC

- Most patients are diagnosed using clinical diagnostic criteria. Genetic testing, although increasingly done, is not usually required for a diagnosis.
- The symptoms of TSC can vary depending on the organs affected and the stage of life at which symptoms present, making it a difficult condition to diagnose.

Definitive diagnosis versus possible diagnosis

- A definitive diagnosis of TSC requires the presence of 2 major diagnostic criteria, or 1 major with 2 or more minor features.
- A combination of the 2 major clinical features, LAM and AML, without any other features doesn't meet the criteria for a definite diagnosis because they can occur together in sporadic disease that is not TSC.
- A possible diagnosis of TSC can be made with 1 major feature or 2 or more minor features.
- Genetic testing can confirm a possible diagnosis if a pathogenic variant in *TSC1* or *TSC2* is identified, which is typically the case in 80-90% of TSC cases.

Table 1: How is TSC diagnosed?

BODY SYSTEM	MAJOR FEATURES	MINOR FEATURES
Brain	• Multiple cortical tubers and/or radial migration lines • Subependymal nodules (SEN) (≥2) • Subependymal giant cell astrocytoma (SEGA)	
Nails and Teeth	• Ungual fibromas (≥2)	• Dental enamel pits (>3) • Intraoral fibromas (≥2)
Eyes	• Multiple retinal hamartomas	• Retinal achromic patch
Renal System	• Angiomyolipomas (renal AML) (≥2)	• Multiple renal cysts
Skin	• Angiofibromas (≥3) or fibrous cephalic plaque • Hypomelanotic macules/ash leaf patches (≥3, at least 5mm) • Shagreen patch	• "Confetti" skin lesions
Cardiac System	• Cardiac rhabdomyoma	
Respiratory System	• Lymphangioleiomyomatosis (LAM)	
Other		• Non-renal hamartomas • Sclerotic bone lesions

Table 2: TSC Surveillance Guidelines

MANIFESTATION	TEST	NEW DIAGNOSIS OR SUSPICION OF TSC	EXISTING TSC
BRAIN The benign tumours associated with TSC include cortical tubers and subependymal nodules (SENs). Subependymal giant cell astrocytomas (SEGAs) can develop and grow. Approximately 80-90% of patients will develop seizures.	MRI brain +/- gadolinium to look for possible tubers, subependymal nodules (SENs) and subependymal giant cell astrocytomas (SEGAs).	Yes.	Every 1-3 years up to 25 years old. Periodically in adults with childhood SEGAs.
EPILEPSY Early identification and treatment of seizures with anticonvulsants like vigabatrin have the potential to lessen epilepsy's impact and possibly enhance developmental outcomes. Recent research also indicates that mTOR inhibitors may improve both seizure control and developmental progress. The potential benefits of using vigabatrin preventatively are currently under investigation. Overall, it is anticipated that infants born with TSC today will have superior neurodevelopmental outcomes compared to previous generations.	EEG Obtain a baseline routine EEG; if the EEG is abnormal, and particularly if features of TAND (see below) are present, follow with a 24-hour video EEG to look for subtle seizure activity. Refer the patient to a neurologist with experience in epilepsy associated with TSC. Counsel parents of infants about seizures and infantile spasms.	Yes. If abnormal, 24-hour video EEG. Educate parents to recognise focal seizures and infantile spasms and what to do if they suspect the child is having seizures. Visit the TSA website for more information on epilepsy.	Routine EEG is suggested every 6 weeks in asymptomatic infants <12 months old and every 3 months in infants 12-24 months of age. Video EEG if seizure occurrence is unclear or new behavioural or neurological symptoms are present.

Table 2 cont'd

MANIFESTATION	TEST	NEW DIAGNOSIS OR SUSPICION OF TSC	EXISTING TSC
TSC-ASSOCIATED NEUROPSYCHIATRIC DISORDERS (TAND) A significant portion of cases experience some level of developmental disability, including autism. The neurodevelopmental prognosis is closely tied to the age at which seizures begin and their severity.	Comprehensive evaluation for TAND. TAND encompass a range of behavioural, psychiatric, intellectual, academic, neuropsychological and psychosocial issues. Despite impacting up to 90% of individuals with TSC at some stage, TAND is frequently neglected and lacks sufficient research, resulting in suboptimal assessment and management. Consistent screening for TAND and prompt referral to a multidisciplinary team of health care professionals, including psychiatrists, psychologists, occupational therapists, speech pathologists, and others, when there is suspicion, are crucial for enhancing patient outcomes.	If the TAND checklist indicates clinical need. This is a validated screening tool for the interrelated behavioural, intellectual, and neuropsychiatric features common in TSC, designed to be used by clinicians. Family members, parents or other caregivers may also need psychological and social support.	At key developmental stages/ages: 0-3 years, 3-6 years, 6-9 years, 12-16 years, 28-35 years and as needed thereafter.
EYES Hamartomas can develop in the retina but do not usually affect vision.	Referral to an ophthalmologist for a comprehensive eye exam with dilated fundoscopy. Regular ophthalmological screening is required if the patient is taking vigabatrin due to the risk of vigabatrin-associated visual field loss.	Yes.	Annually if lesions/ symptoms at baseline.
SKIN/TEETH	Detailed skin exam.	Yes.	Annually.
	Detailed dental exam.	Yes.	6 monthly.
	Panoramic radiographs of teeth.	Age 7 or older.	At age 7 if not done previously.
HEART	Foetal echocardiography.	If cardiac rhabdomyomas identified by prenatal ultrasound.	
	Echocardiogram.	Yes, especially in children under 3 years old.	Every 1-3 years if rhabdomyoma present and more frequently if symptomatic.
	Electrocardiogram.	Yes.	Every 3-5 years and more frequently if symptomatic.

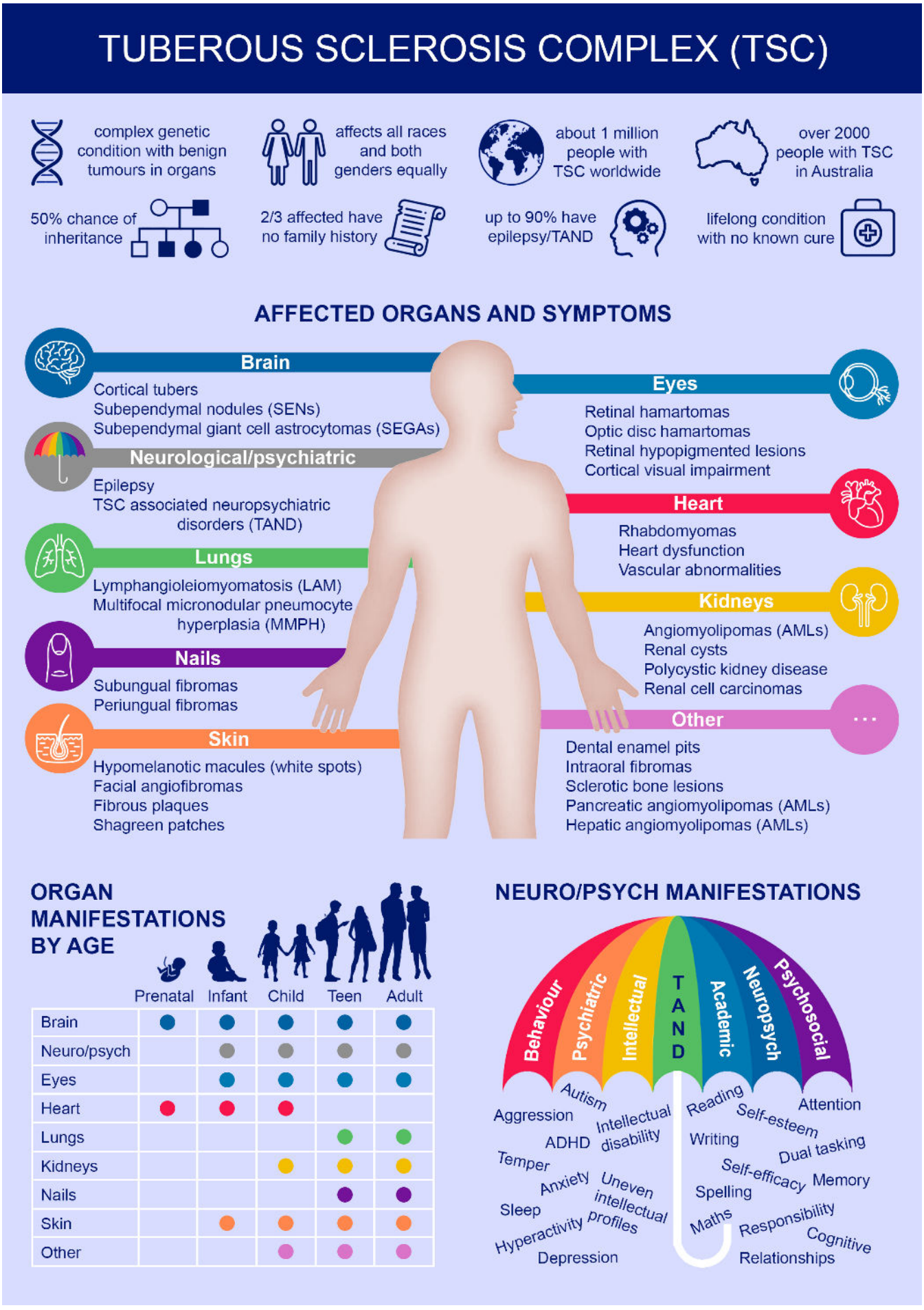
Table 2 cont'd

MANIFESTATION	TEST	NEW DIAGNOSIS OR SUSPICION OF TSC	EXISTING TSC
KIDNEYS	Blood pressure.	Yes.	Annually.
	Abdominal MRI (in Australia ultrasound of the kidneys was traditionally the common practice due to lack of MBS funding). *From 1 July 2024, Abdominal MRI is now funded under the MBS for TSC patients so this service can be bulk billed.	Yes.	Every 1-3 years.
LUNGS	Clinical screening for LAM symptoms (evaluate for chronic cough, chest pain, breathing difficulty).	Yes.	At each clinic visit.
	Pulmonary function test including diffusion capacity.	In females 18 years or older; in adult males if symptomatic.	Annually if lung cysts are detected by high resolution computed tomography (HCRT).
	High resolution computed tomography (HCRT) of chest.	In females 18 years or older; in adult males if symptomatic.	Every 2-3 years if lung cysts are detected, otherwise every 5-10 years.
	Counsel on risks of smoking, oestrogen use and pregnancy.	In adolescent and adult females.	At each clinic visit for individuals at risk of LAM.
GENETICS	Genetics consult.	Obtain 3 generation family history.	For individuals of reproductive age, refer to a geneticist for genetic testing for TSC and counselling, if it was not done previously.

Table 3: Common clinical presentations by age group

PRENATAL	INFANCY/ CHILDHOOD	PUBERTY/ ADOLESCENT	ADULT
Cardiac rhabdomyomas, cortical tubers.	Infantile spasms, seizures, hypopigmented macules, developmental delay, facial angiofibromas, cardiac rhadomyomas, retinal hamartoma. TAND.	Ungual fibromas, facial angiofibromas, new onset seizures, AML, TAND.	LAM, AML, bone lesions, skin lesions.

Diagram 1: TSC infographic



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