Clinical Care in Turner Syndrome

A patient/lay version of the *Clinical Practice Guidelines For Girls And Women With Turner Syndrome, Their Parents, Caregivers And Families*

1. Introduction

This document summarizes the 2024 "Clinical Practice Guidelines for the Care of Girls and Women with Turner Syndrome [TS]." Building on the 2017 clinical practice guidelines, these new guidelines have been updated and expanded to include areas not previously addressed.

This summary, prepared for individuals with TS and their caregivers, is intended to improve patient care by encouraging communication between the individual with TS/parents/caregivers and their health-care provider(s). The information below can be used as a guide for visits with TS health care provider(s).

2. Diagnosis and Genetics of TS

2.1 Definition, genetic analysis, and indications for testing

- TS occurs in 25–50 per 100,000 females, affecting females with one intact X chromosome and complete or partial absence of the second sex chromosome in association with one or more clinical features (Table 1).
- The most frequent chromosome changes in TS are: 45,X (monosomy X), 45,X/46,XX (TS with mosaicism), and structural abnormality of the X chromosome. Other chromosomal arrangements are possible.
- The specific karyotype (genetic make-up of the chromosomes) does not always predict the health issues they will have. Someone with 45,X/46, XX mosaicism typically has milder signs and symptoms, including less severe heart problems, less high blood pressure, or fewer weight problems compared to someone with 45,X.
- TS is most often diagnosed during fetal life, in infancy, during late prepubescence (8-12 years), or in late adolescence/early adulthood.

Table 1. Indications for genetic testing to diagnose TS

As the only clinical feature:	If at least two of the following are present:
• Fluid collections in tissues and organs in fetus (hydrops)	• Kidney abnormality
• Short stature of unknown origin	• Misshapen forearm
• Left-sided heart defect [1]	• Neuropsychologic problems and/or psychiatric issues
• Unexplained delayed puberty/menstruation	• Multiple pigmented birthmarks
• Infertility	• Unusual shape of the nails
• Characteristic physical features [2]	• Certain other heart defects
	• Hearing impairment < 40 years together with short stature

1 Coarctation (narrow aorta arch), aortic valve narrowing, other left heart valve anomalies, and underdeveloped left heart.

2 Down-turning eyelids, low-set and prominent ears, small jaw, narrow palate, short broad/webbed neck.

2.2 Prenatal diagnosis

- Abnormal prenatal ultrasound results such as increased neck (nuchal) translucency or an abnormal blood ('triple') screen can suggest an increased likelihood of TS.
- A positive test result for TS in noninvasive prenatal testing should be interpreted with caution since there may be false positive results.
- TS can be confirmed prenatally by invasive testing like chorionic villous sampling, amniocentesis, or cordocentesis. Genetic counseling should always be provided before invasive testing.
- If TS is diagnosed prenatally, an ultrasound of the heart should be done during pregnancy and after the baby is born.
- Genetic (karyotype) testing for confirmation of TS after the baby has been delivered is essential.

2.3 Postnatal diagnosis

- All individuals with suspected TS should have a genetic test done called a karyotype.
- If TS is strongly suspected, but not demonstrated with a standard karyotype, additional genetic tests (for example on skin cells, cheek swab cells) should be done to confirm or rule out TS.

2.4 Improving early diagnosis of TS

- Missed and delayed diagnoses of TS remain a major problem.
- Early diagnosis allows for timely screening and intervention for problems such as abnormal alignment of the eyes, poor growth, hearing loss, heart and kidney abnormalities, underactive thyroid, gluten intolerance, and learning differences, improving quality of life. Fertility may also improve in certain individuals by allowing egg or ovarian tissue harvesting at a younger age.

3. Growth

3.1 Growth in TS

- Slowing of growth in TS starts before birth and worsens in the first years of life. Prompt treatment can prevent further loss of height potential.
- Goals of growth-promoting therapies, done with growth hormone (GH), are to help children reach a height that reduces physical and psychosocial limitations and allow puberty to begin at an age like that of peers.
- Growth outcomes vary but the goal is to reach an adult height close to or within the lower normal range for the general female population. Factors that predict a taller adult height after GH therapy include being tall before starting, having tall parents, starting GH at a younger age, being on GH longer (especially before puberty starts), and using a higher GH dose.

3.2 Efficacy and safety of GH treatment

- GH treatment is associated with typical height gains of 5 to 8 cm (2 to 3 inches) over treatment periods ranging from 5.5 to 7.5 years in clinical trials; about 1 cm per year is expected.
- If children experience "catch-up" growth to the normal range within the first 2 years of treatment and maintain a good growth rate, an adult height of about 152 cm (60 inches = 5 feet) is possible.
- GH treatment is recommended at an early age to improve results. It may be offered as young as 2 years of age if there is poor growth, short stature, or likelihood of short stature. GH treatment also may be started at older ages if growth plates are still open. Treatment is continued until growth is complete.
- A starting GH dose of 0.32–0.35 mg/kg/week (equivalent to 45–50 µg/kg/day) is recommended and may be increased up to 0.47 mg/kg/week if response is poor. GH shots are given every day into the fat tissue under the skin. Response is monitored by tracking height every 4 to 6 months.

- In TS, safety of GH treatment has been reassuring. Studies indicate an increased risk of intracranial hypertension (pressure built-up in the head) and slipped capital femoral epiphysis (hip pain and limp) during GH treatment in TS compared to other children on GH therapy. These complications are rare but serious. Scoliosis (abnormal curvature of the back) is common in TS; curvature may increase during GH therapy. Talk to your doctor if you are concerned about these symptoms.

3.3 Other growth-promoting therapies

- At the time of this publication, long acting (weekly) GH injections are still awaiting approval in TS.
- Oxandrolone is not recommended and is not available in the US.

3.4 Sex-hormone replacement

- Most individuals with TS need hormonal replacement therapy (HRT) to start puberty, grow breasts, have menstrual periods, maintain female sex characteristics, develop and maintain strong bones, and normalize the size and overall health of the uterus.
- Estrogen treatment is usually administered through the skin (transdermal) or orally (by mouth). Transdermal estrogen is processed by the body like estrogen produced by the ovaries and is the preferred way to administer estrogen. Oral estrogen is used when transdermal estrogen cannot be administered.
- Giving estrogen via the vagina is not recommended for young girls but could be used in adults.
- Estrogen can also be given through an injection, but it is not usually preferred.
- The goals of estrogen treatment are to mimic the progression of puberty in an average girl and minimize risks. Table 2 shows the timing, route, and dose of estrogen replacement options.

Table 2. Recommended estrogen dose changes for puberty in girls with Turner syndrome

Initiation 11–12 years old	Timing for a late diagnosis and when growth is complete	Estrogen patch dose**	Oral Estrogen dose**
Year 1 (1-12 months)		7 µg (1/2 of 14 µg or ¼ of 25 µg patch)	0.25 mg/d
Year 2 (13-24 months)	Year 1 (1-4 months)	12.5–14 µg/d	0.5 mg/d
Year 3 (25-36 months)	Year 1 (4 – 12 months)	25–37.5 µg/d	1 mg/d
Year 4 (37-48 months)	Year 2 (13 -24 months)	50-200 µg/d	2 – 4 mg/d
Use this regimen for late diagnosis when growth is not complete		** Add progesterone if spontaneous bleeding AND more than 2 years on estrogen (E2)	

- Ovary function should be measured by checking luteinizing hormone (LH), follicle stimulating hormone (FSH), and anti-Mullerian hormone (AMH) at age 8-9 and then yearly as indicated.
- Treatment should begin at 11–12 years if labs show puberty will not start on its own (FSH is elevated twice). Girls with mosaicism are more likely to start puberty on their own, but they may not complete puberty on their own.
- If the puberty labs are normal for age, observation for spontaneous puberty is appropriate, with future HRT if the ovaries stop working.

- Using low estrogen doses is especially important for preserving height, regardless of GH treatment.
- Incremental dose increases of estrogen can occur every 6 - 12 months to mimic normal puberty until adult dosing is reached over a 2–4-year period (see Table 2)
  - Assessments of breast size, uterine growth, patient satisfaction, patient age, and growth potential are the primary determinants of the rate and amount of an estrogen dose increase.
  - If girls are noticeably short but still growing, they may remain on lower estrogen doses longer; if girls finished growing at puberty initiation, doses can be increased more quickly.
- Girls with TS typically have a normal uterus, so progesterone must be added to keep the uterus healthy. A doctor will add progesterone if menstrual bleeding or spotting occurs, or after 2 years of estrogen treatment and the uterus is mature. If spotting occurs prior to 18 months on estrogen - the dose may be increased, or progesterone may be added depending on uterus size based on an ultrasound evaluation.
  - Micronized crystalline progesterone (e.g., Prometrium® 100–200 mg) is preferred.
  - Medroxyprogesterone acetate is no longer the first choice if the micronized form is available.
  - Progesterone is added for 10-12 days each month to induce menstrual bleeding. Estrogen is continued during those days. In young girls, monthly dosing is recommended to avoid abnormal uterine bleeding. In older women, the progesterone regimen may be altered to reduce the frequency of menstrual periods.
  - Intrauterine progesterone (an IUD, an intrauterine device) can also be used.
- Once growth is complete, people may prefer a combined estrogen and progesterone pill or oral contraceptive pill (OCP). While transdermal estrogen is best, it is important to use a treatment that you/your child can agree to take. The OCPs are better than no treatment. Once adult replacement doses of estrogen are reached, treatment is continued until the average age of menopause.
- Screen for blood clot risk in girls starting oral estrogen if there is a personal or family history of blood clots.
- An estrogen patch can be cut into smaller parts to give lower doses. Although pharmacists do not recommend this, endocrinologists do. This is successful and okay.
- Conjugated equine estrogens are not preferred because of heart and stroke risks.
- A test for bone health (DXA scan) is recommended once an individual reaches adult doses of estrogen, if estrogen treatment is delayed, or when transitioning to adult care.

4. Fertility in Women with Turner Syndrome

- Due to early ovarian insufficiency (where the ovaries stop working correctly), most women with TS cannot become pregnant on their own.
- At a young age, it is important to discuss different ways of creating a family (assisted fertility, surrogacy, adoption, egg donation, choice not to have children) and that women with TS may not be able to become pregnant naturally or at all.
- Problems with fertility may cause mental health and romantic relationship challenges. Psychological support is recommended.

4.1 Natural pregnancy (able to become pregnant without medical help)

- Natural pregnancies are rare, occurring in less than 10% of women with TS, usually seen in women with mosaic TS (45,X/46,XX). The risk of losing the baby before birth (miscarriage) or having a baby with a birth defect is higher.
- Women with certain heart conditions may be at a higher risk for serious heart complications during pregnancy and may be advised not to become pregnant. Women with TS who become pregnant are also at a higher risk for pre-eclampsia (blood pressure issues) and the need for a cesarean section (delivery by surgery rather than natural childbirth).

4.2 Fertility preservation using autologous oocytes (woman's own eggs) and ovarian tissue cryopreservation.

- Since women with TS have a rapidly decreasing number of eggs from a very young age, offering fertility treatment should be considered at an early age. This should be done in centers with expertise and psychological support.
- Cryopreservation (freezing in a lab) of eggs is an option for females who have periods on their own and can understand the procedure. Spontaneous periods occur in about 15% of girls with TS. This is more common with mosaic TS but can occur in those with classic 45,X. The frozen eggs can be fertilized with sperm in a lab, also known as in-vitro fertilization (IVF).
- The success rate of pregnancy using cryopreserved eggs is unknown. The optimal number of eggs required for a successful live birth in TS is also unknown. A patient's own eggs have an increased risk of carrying X chromosome abnormalities.
- There is currently ongoing research on ovarian tissue cryopreservation (where the ovary is surgically removed and frozen to use later) in individuals with TS.

4.3 Becoming pregnant using another woman's egg (egg donation)

- For most women with TS, egg donation is the only way to become pregnant.
- Women with TS who become pregnant are at a higher risk for complications than the general population with the pregnancy (blood pressure problems, cesarean section, needing to deliver the baby early) and for having babies born small in size.
- For safety, women with TS undergoing IVF should only have one embryo transferred at a time.

4.4 Recommendations for follow-up during pregnancy

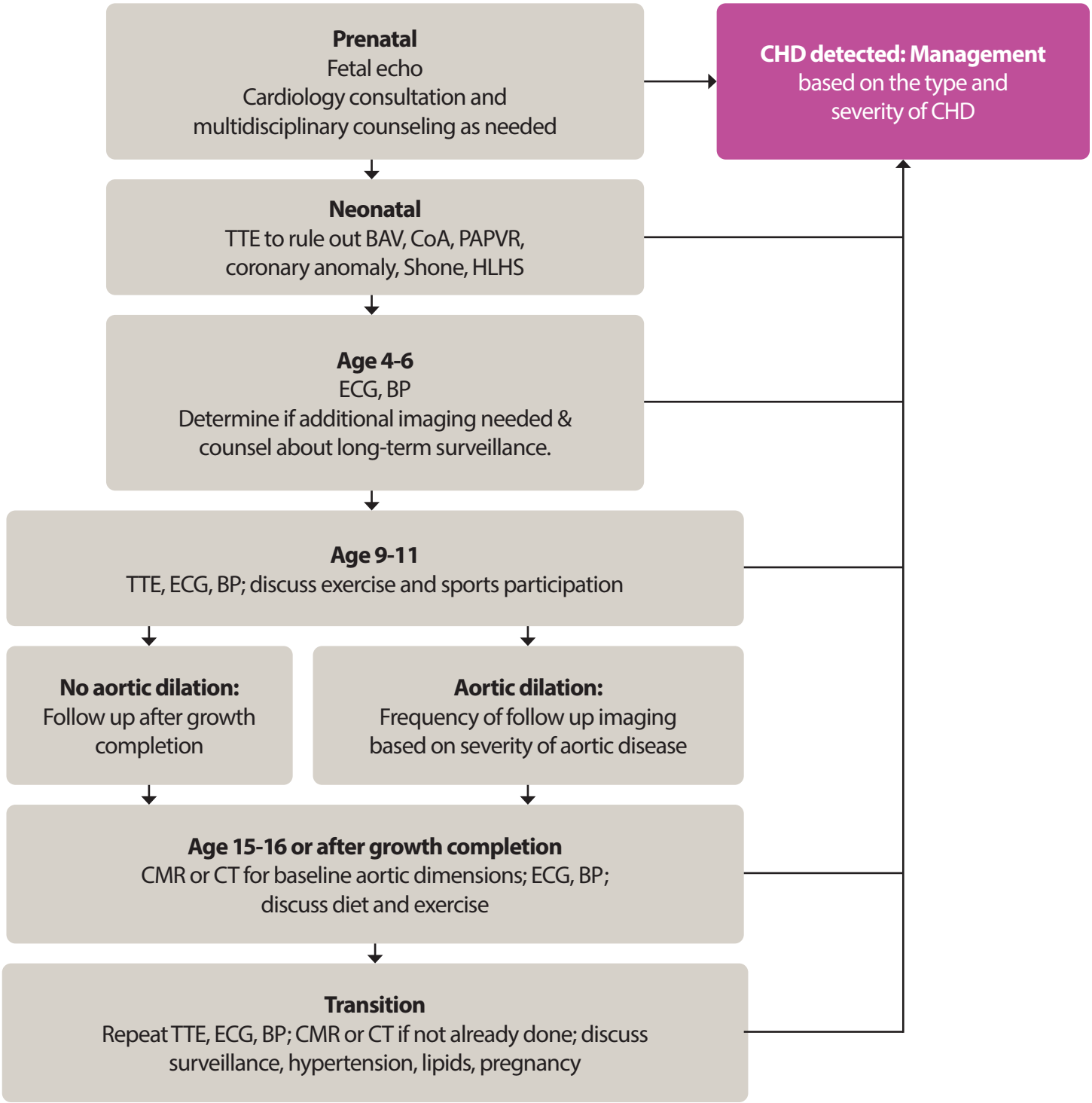
- Safe monitoring of pregnancy in women with TS and delivery of the baby should be done by a team of specialists including maternal-fetal medicine (increased pregnancy risk) specialists, cardiologists with expertise in TS and behavioral health support.

5. Cardiovascular Health Issues in TS

5.1 Background and Surveillance

- Individuals with TS have a lifelong risk of congenital (present at birth) or acquired heart and blood vessel disease.
- Congenital heart disease (CHD) occurs in about 50% of girls, most commonly an abnormally shaped (bicuspid) aortic valve in the heart, coarctation of the aorta (a narrowing of the main chest artery, the aorta), and a widened aorta that can rarely lead to tearing, with potentially catastrophic consequences.
- Some of these blood vessel issues are difficult to see with ultrasound, so other imaging, such as MRI (magnetic resonance imaging), is required.
- Blood vessel problems such as high blood pressure, ischemic/coronary heart disease, and cerebrovascular disease (stroke) are other possible issues.
- An MRI of the heart is still recommended, but if the ultrasound is normal, then the MRI can wait until the patient can lay still for the scan without being put to sleep, usually in early teen years.
- A heart MRI should be performed at age 13 and over at diagnosis.

Figure 1. Suggested monitoring protocol for girls with TS



TTE: transthoracic echocardiogram; BAV: bicuspid aortic valve; CoA: aortic coarctation; PAPVR: partial anomalous pulmonary venous return; HLHS: hypoplastic left heart syndrome; ECG: electrocardiogram; BP: blood pressure; CMR: cardiovascular magnetic resonance; CT: computed tomography.

5.2 Medical and operative management of aortic enlargement and aneurysm

- Enlargement and tearing of the aorta occur more often in TS than in the general population; those with bicuspid aortic valve, coarctation of the aorta or high blood pressure are at higher risk for tearing of the aorta and may need to see the heart doctor more often.
- Tearing of the aorta can occur at younger ages and with less severe aortic changes in TS (30-35 years) compared to the general population.
- When measuring the aorta size in an individual with TS, this should not be compared to others of the same age but should be compared to one's body size (generally, using a z-score, aortic height index or aortic size index). Aortic height index tends to be a better marker of risk for tearing of the aorta in TS.
- Treating high blood pressure earlier than in the general population can help prevent aortic tearing.
- Patients should discuss surgery on the aorta to prevent tearing if there is a rapid increase in aortic size, uncontrolled high blood pressure, history of other heart problems, or an already moderately increased aortic size.

5.3 Congenital heart disease

- Those with 45,X karyotype or webbed neck are more likely to have heart or blood vessel problems.
- If TS is found prior to birth, a fetal echocardiogram should be done and, if abnormalities are found, the family should meet with a pediatric heart doctor prior to birth.
- Even if the heart imaging done before birth is normal, if a baby has TS, an ultrasound of the heart should be done at 2-3 days of age or sooner.
- A heart ultrasound should be done at the time of diagnosis in everyone with TS.
- 25% of individual with TS have an abnormal heart valve; treatment is the same as for other individuals with this problem who do not have TS.
- Heart issues can cause chest pain, pain with breathing or passing out. A doctor should be seen regardless of prior evaluation if these symptoms occur.

5.4 Electrocardiogram (ECG)

- An ECG is a recording of the electrical activity of the heart. Electrodes are placed on the skin of the chest and connected to a machine that measures the heart's electrical activity.
- An ECG should be done at the time of diagnosis to look for any abnormality with the heart that cannot be seen on ultrasound.
- Previously, it was thought that individuals with TS were at higher risk of QTc prolongation (one of the things looked at on ECG). This is no longer thought to be true.
- Even if normal, an EKG should be repeated when starting medications that change QTc.

5.5 Sports participation and exercise

- Those with TS who don't have blood vessel or heart abnormalities should be allowed to participate in all sports.
- The guidelines have specific recommendations regarding sports participation for those with aortic widening, but weightlifting should be avoided.

5.6 Hypertension or high blood pressure

- High blood pressure occurs in 20-40% of girls and up to 60% of adults with TS.
- Early on, high blood pressure can occur overnight and can be normal during the day, so ambulatory blood pressure monitoring (24-hour blood pressure monitoring) is recommended starting around 10 years of age.
- If someone with TS has high blood pressure, other causes for elevated blood pressure, such as heart, kidney and blood vessel issues should be checked.
- Treatment for high blood pressure in TS is like that of the general population and includes making healthy lifestyle choices, weight management, and/or medication.

5.7 Blood clots and bleeding

- TS does not increase the risk for blood clots or bleeding, and no routine evaluation is needed prior to starting estrogen therapy unless otherwise indicated.

5.8 High cholesterol

- If high cholesterol is found, it is important to check for other causes, such as underactive thyroid or familial forms of elevated cholesterol, and work on healthy eating and regular exercise.
- The use of statins to treat high cholesterol may increase the risk of diabetes, but further research is needed.

5.9 Cardiovascular risks during pregnancy

- Women with TS are at increased risk for cardiovascular complications from pregnancy, including tearing of the aorta and high blood pressure associated problems.
- Prior to a planned pregnancy, an MRI of the heart should be performed, and a heart doctor and a maternal-fetal medicine specialist should provide individualized counseling regarding the safety of pregnancy. High blood pressure treatment includes blood pressure lowering medicine to prevent (further) aortic dilatation and to keep blood pressure under 130/80.
- Aspirin can be considered to prevent high blood pressure starting around week twelve of pregnancy.
- Even if there is minimal risk, a heart ultrasound of the mother should be done around 20 weeks of pregnancy and further testing should be done if an aortic enlargement is found.
- A team consisting of at least an obstetrician, cardiologist (heart doctor), and anesthesiologist with knowledge of maternal heart and aortic disease should create a delivery plan.
- It is recommended to counsel someone with TS not to become pregnant if she is symptomatic with severe obstructive heart disease (aortic stenosis) or asymptomatic patients with impaired heart function (left ventricular function) or has an abnormal exercise test.

5.10 Transition and Adulthood

- Adults with TS who do not have heart issues should continue to see a heart doctor every 5-10 years.

6. Co-morbidity in TS: monitoring for associated health issues

- Problems in Newborns and infants: increased risk for low birth weight, congenital heart problems, feeding difficulties, and low blood sugar.
- Eye problems: There is an increased risk of eye problems like refractive errors (such as nearsightedness), strabismus (out-of-line eye), amblyopia (weak eye), ptosis (eyelid drooping), cataract (clouding of eye lens), glaucoma (increased pressure in eye) and unusual eyelid folds.

- Ear and hearing problems: Hearing loss and frequent ear infections are common in TS. Regular hearing screens are recommended (See Tables 3,4,5).
- Dental (teeth) problems: Individuals with TS may have a wide range of dental issues. Treatment of poorly aligned teeth is recommended to prevent tooth deformities, teeth crowding, trismus (jaw-muscle spasm), chewing difficulties, breathing obstruction, and disturbed digestion.
- Skin and lymphatics: Accumulation of fluid under the skin (lymphedema) is common in TS, ranging from severe swelling in the fetus to swelling of hands and feet or webbing of the neck. Hand and foot swelling may improve by 2 years of age without therapy, but professional edema therapy may be necessary if the fingernails, toenails, and/or skin are severely affected. Individuals with TS are more likely to have various skin rashes and markings, keloid scarring (hard and thick scars), and more pigmented nevi (brown spots on the skin).
- Cardiometabolic disorders: The risk of type 1 and type 2 diabetes is increased in individuals with TS, along with higher rates of being overweight and obese. A healthy diet and regular exercise are recommended.
- Kidney problems: Structural kidney abnormalities affect 18-60% of individuals with TS. A renal ultrasound is recommended at diagnosis to detect abnormalities. Urinary tract infections are more frequent in some individuals with TS
- Gastrointestinal and liver problems: Inflammatory bowel disease (Crohn's disease), celiac disease (gluten sensitivity), and liver function abnormalities occur more often in individuals with TS. Those with abnormal liver function tests are more likely to develop liver problems.
- Bone problems: There is an increased risk for fractures (broken bones) and low bone density (weak bones) in TS. Estrogen therapy helps improve bone strength and optimal calcium and vitamin D intake is recommended to improve bone health.
- Autoimmunity: Individuals with TS are at increased risk for autoimmune diseases, including underactive thyroid and celiac disease.
- Musculoskeletal problems: Musculoskeletal problems are more common in TS and individuals should be evaluated if they have back, wrist, elbow, knee, or ankle/foot pain.

7. Health surveillance for co-morbidity (associated health issues) through life

7.1 The TS clinic

- It is recommended that girls and women with TS attend specialist interdisciplinary or multidisciplinary clinics for health surveillance in addition to their primary care provider.

7.2 Sexual function in adults

- Women with TS should see a gynecologist experienced in ovarian insufficiency.

7.3 Cancer surveillance

- Risk of breast cancer in women with TS is lower than the general population, but following national screening recommendations are advised.
- Individuals with Y chromosome material have a greater risk of growths in their ovaries. Therefore, it is important to determine if/when surgical removal of the ovaries should occur while considering the impact of surgery on potential fertility.

Table 3. Recommendations for TS screenings for infants through 9 years of age

Screening at Diagnosis	Further screening
Weight, height, weight for height, body mass index	Every visit
Blood pressure	Annual
Ear exam and hearing evaluation	Annual
Eye exam (6-12 months of age or older)	Once, then as needed
Dental evaluation	Every 6 -12 months
Thyroid function	Annual
Liver function	Once
Fertility evaluation (Anti Mullerian hormone)	Consider Annually
Puberty hormones (Follicle stimulating hormone, estradiol)	At 4-12 weeks and at age 9
Celiac screen (Gluten sensitivity) (starting at age 2)	Every 2-5 years
Electrocardiogram (rhythm of heart)	At diagnosis and follow up as recommended
Echocardiogram (an ultrasound of the heart)	At diagnosis and follow up as recommended
Kidney ultrasound	At diagnosis, then as needed
Back exam-scoliosis evaluation (curvature of the spine)	Every 1-2 years
Hip dislocation evaluation (less than 6 months of age)	At every pediatrician visit in infancy
Skin exam	Annual
Developmental screening by pediatrician	Every 3 months in infancy and then annual
Neuropsychological evaluation (starting at 5-11 years of age)	At least once as clinically indicated
Genetic counseling	As needed
Fertility counseling (with family)	At diagnosis

Table 4. Recommendations for TS screenings for those 10-17 years of age

Screening at Diagnosis	Further screening
Weight, height, weight for height, body mass index	Every visit
Blood pressure	Annual
Ear exam and hearing evaluation	Annual
Eye exam	As needed
Dental evaluation	Every 6-12 months
Thyroid function	Every 1-2 years
Liver function	Every 1-2 years
Celiac disease (Gluten sensitivity)	Every 2-5 years
Diabetes screen	Annual
Blood counts (anemia screen)	Annual
Vitamin D levels	Every 2-3 years
Fertility evaluation (Anti Mullerian hormone)	As determined by a physician
Puberty hormones (Follicle stimulating hormone, estradiol)	Annual
Electrocardiogram (rhythm of heart)	At least once, follow up as recommended.
Echocardiogram (an ultrasound of the heart)	At least once, follow up as recommended.
Kidney ultrasound	At diagnosis, then as needed
Ultrasound of the pelvis at age 12	After 12 years as needed
Breast exam for development	Every 6-12 months
Back exam-scoliosis evaluation (curvature of the spine)	Annual
Skin exam	Annual
Academic screening	Annual
Neuropsychological evaluation	Once as clinically indicated
Genetic counseling	As needed
Fertility counseling	As needed
Preconception /Contraception counseling	As needed

Table 5. Recommendations for TS screenings in adults

Screening at Diagnosis	Further screening
Weight, height, weight for height, Body mass index	Annual
Blood pressure	Annual
Ear exam and Hearing evaluation	As needed
Eye exam	As needed
Dental evaluation	Every 6-12 months
Thyroid function	Every 1-2 years /with new symptoms
Liver function	Every 1-2 years
Celiac disease (Gluten sensitivity)	Every 2-5 years /with new symptoms
Diabetes screen	Every 1-2 years/with new symptoms
Blood counts (anemia screen)	Every 1-2 years
Vitamin D levels	Every 2-3 years
Lipid (cholesterol) levels	Every 3 years
Electrocardiogram (rhythm of heart)	Every 5-10 years and follow up as recommended
Echocardiogram (an ultrasound of the heart)	Every 5-10 years and follow up as recommended
Kidney Ultrasound	As needed
Ultrasound pelvis	As needed
Skin exam	Annual
Bone density scan	Every 5-10 years
Psychosocial screening	Annual
Genetic counseling	As needed
Fertility counseling	As needed
Preconception /Contraception counseling	As needed

8. Transition from pediatric to adult care

- Every patient should have an individualized pathway to transition to adult care. Discussions with the individual with TS and provider should begin in the teenage years.
- Providers should ensure all screenings are up to date prior to the transition.
- Transition toolkits (as on the Endocrine Society website) are available that address readiness, transfer of records/information, self-care knowledge and skills, and TS-specific areas.
- Barriers to successful transition include wanting to stay with a known provider, ability to receive healthcare from an adult provider with TS knowledge, patient knowledge of medical issues, medications, and costs.
- TS-specific topics to be addressed are the importance of continued estrogen therapy, reproductive issues, TS-associated needs and lifestyle requirements, heart healthcare throughout life, and psychosocial, educational, and vocational issues.

9. Neurocognition and Behavior

9.1 Background

- TS is associated with a neurocognitive (learning) profile that may impact learning and quality of life. Most individuals with TS have average intelligence.
- Individuals with TS may have different learning issues including non-verbal learning difficulties and require evaluation to determine what, if any, are present. This can include problems with attention, memory, organization, emotional and social difficulties, visual-spatial skills (spatial orientation and judging distances), visual memory (remembering faces), language, motor function, social cognition, and academic achievement.

9.2 Early childhood

- Children with TS who have motor delays, feeding difficulties, or social/behavioral problems benefit from early intervention. In addition to fine motor and visual-spatial difficulties, individuals with TS are at increased risk for specific learning difficulties in mathematics (dyscalculia).
- Young children with TS may benefit from behavioral therapy, parent management training, or Applied Behavioral Analysis (ABA) therapy if needed. As children grow up, additional neuropsychological features of TS can emerge; therefore, regular monitoring is important.

9.3 School age

- Verbal reasoning abilities are stronger than nonverbal/visual-spatial reasoning abilities.
- Specific areas of concern are fine motor skill weakness affecting handwriting and drawing, increased risk of attention deficit hyperactivity disorder (ADHD) and struggles specific to mathematics. School-based accommodation or more significant intervention may be needed.
- There can be ongoing difficulties determining distances, with mathematics and reasoning. Difficulties with social skills, anxiety and depression become more noticeable in adolescence.

9.4 Adulthood

- These differences can make independence more challenging.
- Psychiatric disorders including depression and attention disorders in adults with TS are higher than in the general population.
- Individuals with TS report feeling more socially isolated than their peers and have fewer close relationships. Women with TS may benefit from programs to strengthen their social skills.

10. Optimizing care across the lifespan

- Care for women with TS lends itself to telemedicine and online medical records. When feasible, it is recommended that individuals receive care within a multidisciplinary clinic.

10.1 The Role of patient support organizations

- Individuals with TS and their families may benefit from participating in TS support organizations.

10.2 Research Registries for TS

- TS research registries record clinical and psychosocial data from individuals with TS, to improve the understanding of common and rare outcomes.

TS Organizations that Provide Information and Support

Turner Syndrome Association of Australia – https://www.turnersyndrome.org.au/

Turner Syndrome Society of Canada – http://www.turnersyndrome.ca/

Turner Syndrome Foundation (US) – https://www.turnersyndromefoundation.org/

Turner Syndrome Global Alliance - https://tsgalliance.org

Turner Syndrome International Group – https://tsint.org/

Turner Syndrome Society of the United States – http://www.turnersyndrome.org

Turner Syndrome Support Society (UK) – http://tss.org.uk/

Web links for other TS organizations around the world are available at the Turner Syndrome International Group website (https://tsint.org/index.php/web-links).

The original patient-oriented version of the TS Guidelines was developed by Drs. Philippe Backeljauw and Claus H. Gravholt with the input of individuals with TS and advocates. It was updated according to the new guidelines by the Pediatric Endocrine Society Turner Syndrome Special Interest Group including Elizabeth Dabrowski, MD, Giovanna Beauchamp, MD, Melizza Carlucci, MD, Carolina DiBlasi, MD, Victoria Elliott, MD, Doris Fadoju, MD, Karen Klein, MD, Jennifer Law, MD, Roopa Kanakatti Shankar, MD and Nandini Vijayakanthi, MBBS. The authors thank all who dedicated their time to provide important feedback.

Reference: Claus H Gravholt, Niels H Andersen, Sophie Christin-Maitre et al., Clinical practice guidelines for the care of girls and women with Turner syndrome: Proceedings from the 2023 Aarhus International Turner Syndrome Meeting, European Journal of Endocrinology, Volume 190, Issue 6, June 2024, Pages G53–G151, https://doi.org/10.1093/ejendo/lvae050.

Clinical Care in Turner Syndrome

A patient/lay version of the *Clinical Practice Guidelines For Girls and Women with Turner Syndrome, Their Parents, Caregivers and Families*