Turner Syndrome
A Multi-disciplinary Approach

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Miss Cara Williams
Consultant Gynaecologist
Alder Hey Children's Hospital and Liverpool Women's Hospital

Summary

- What is TS?
- Multi-organ involvement
- MDT approach
- Clinical Guidelines
- Paediatric pathway
- Adult pathway
- Health surveillance
- Support Groups

TSSS Turner Syndrome Support Society

Turner Syndrome

- 25-50/100,000 females
- Phenotypic female with a karyotype containing one X Chromosome and complete or partial absence of the second X Chromosome in association with one or more clinical manifestations
- (Excluding: deletion distal to Xq24 or women over 50 with 5% 45X mosaicism)

Turner Syndrome

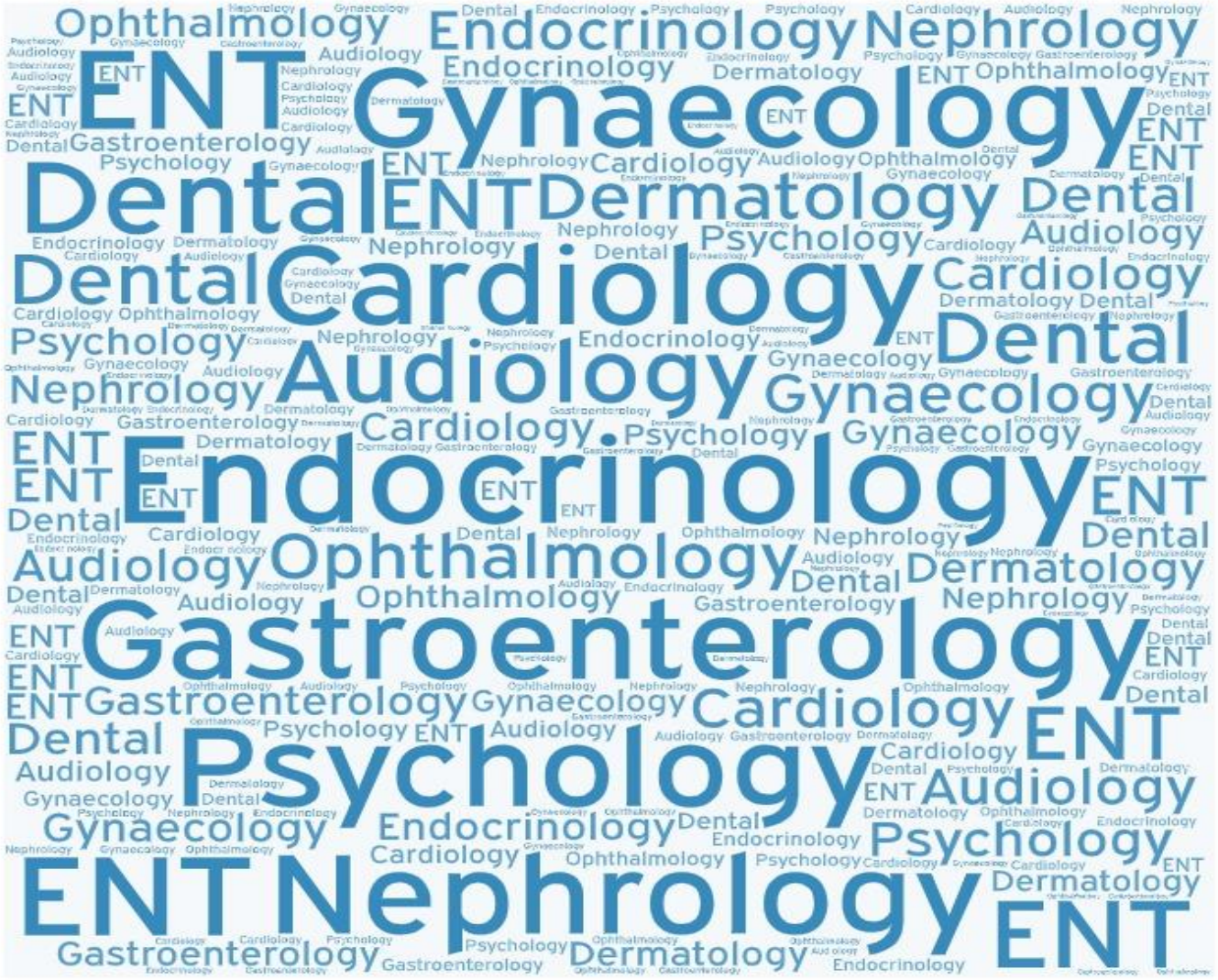
KARYOTYPE	Frequency	DESCRIPTION
45X	40-50%	Monosomy X
45X/46XX	15-25%	
45X/46XY	10%	Mixed Gonadal Dysgenesis
45X/47XXX; 45X/46XX/47XXX	3%	Mosaicism with Triple X
46XX del(p22.3)		Deletion Xp22.3
46X r(X)/46XX	10%	Ring X Chromosome
46X i(Xq)		Isochromosome Xq
46X idic(Xp)		Isodicentric Xp
X-autosome translocation, unbalanced	Rare	Various
46XX del(q24)		Not TS; Premature Ovarian Insufficiency
46X idic(X)(q24)		Not TS; Premature Ovarian Insufficiency

Multi-organ involvement

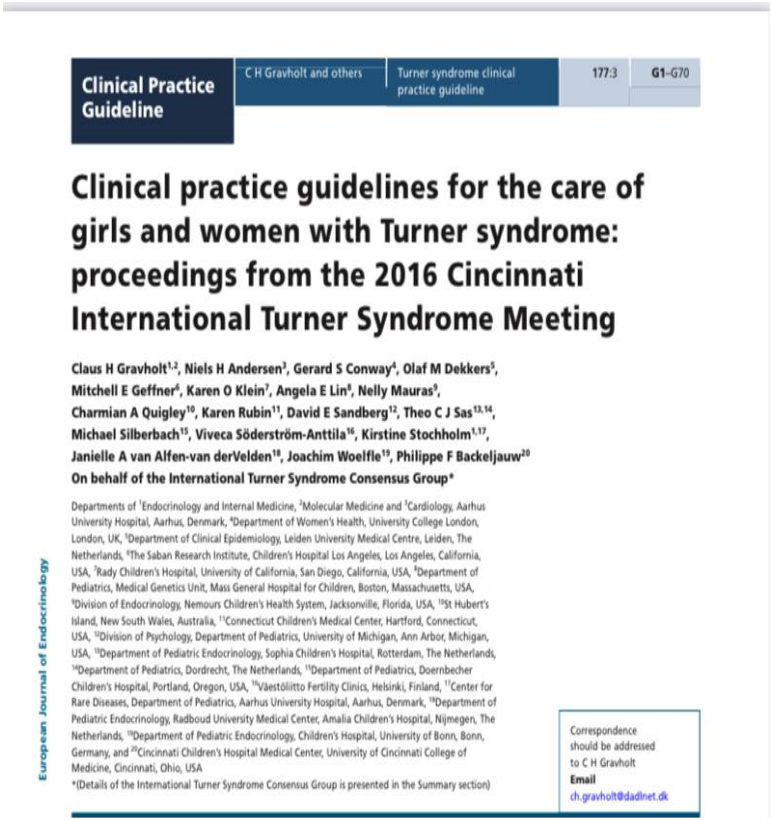
- Growth and Puberty
  - Short stature
  - Delayed puberty
  - Infertility
- Cardiovascular Health
  - Bicuspid aortic valve
  - Coarctation of the aorta
  - Aortic dilatation/aneurysm
  - Aortic stenosis
  - Ischaemic heart disease
  - Hypertension
  - Stroke

- SN Hearing loss
- Lymphoedema
- Hypothyroidism
- Diabetes
- Dyslipidaemia
- Deranged liver function
- IBD
- Coeliac disease
- Renal anomalies (horseshoe kidney, renal agenesis
- Osteopaenia/porosis
- Skin/nails/eyes/mouth
- Cognitive and psychosocial problems

MDT


Ophthalmology
Endocrinology
Nephrology
ENT
Gynaecology
Dermatology
Dental
Psychology
Cardiology
Audiology
Gastroenterology

Clinical Guidelines



Clinical Practice Guideline | C H Gravholt and others | Turner syndrome clinical practice guideline | 177:3 | G1–G70

Clinical practice guidelines for the care of girls and women with Turner syndrome: proceedings from the 2016 Cincinnati International Turner Syndrome Meeting

Claus H Gravholt[1,2], Niels H Andersen[3], Gerard S Conway[4], Olaf M Dekkers[5], Mitchell E Geffner[6], Karen O Klein[7], Angela E Lin[8], Nelly Mauras[9], Charmian A Quigley[10], Karen Rubin[11], David E Sandberg[12], Theo C J Sas[13,14], Michael Silberbach[15], Viveca Söderström-Anttila[16], Kirstine Stochholm[1,17], Janielle A van Alfen-van derVelden[18], Joachim Woelfle[19], Philippe F Backeljauw[20]

On behalf of the International Turner Syndrome Consensus Group*

Departments of [1]Endocrinology and Internal Medicine, [2]Molecular Medicine and [3]Cardiology, Aarhus University Hospital, Aarhus, Denmark, [4]Department of Women's Health, University College London, London, UK, [5]Department of Clinical Epidemiology, Leiden University Medical Centre, Leiden, The Netherlands, [6]The Saban Research Institute, Children's Hospital Los Angeles, Los Angeles, California, USA, [7]Rady Children's Hospital, University of California, San Diego, California, USA, [8]Department of Pediatrics, Medical Genetics Unit, Mass General Hospital for Children, Boston, Massachusetts, USA, [9]Division of Endocrinology, Nemours Children's Health System, Jacksonville, Florida, USA, [10]St Hubert's Island, New South Wales, Australia, [11]Connecticut Children's Medical Center, Hartford, Connecticut, USA, [12]Division of Psychology, Department of Pediatrics, University of Michigan, Ann Arbor, Michigan, USA, [13]Department of Pediatric Endocrinology, Sophia Children's Hospital, Rotterdam, The Netherlands, [14]Department of Pediatrics, Dordrecht, The Netherlands, [15]Department of Pediatrics, Doernbecher Children's Hospital, Portland, Oregon, USA, [16]Väestöliitto Fertility Clinics, Helsinki, Finland, [17]Center for Rare Diseases, Department of Pediatrics, Aarhus University Hospital, Aarhus, Denmark, [18]Department of Pediatric Endocrinology, Radboud University Medical Center, Amalia Children's Hospital, Nijmegen, The Netherlands, [19]Department of Pediatric Endocrinology, Children's Hospital, University of Bonn, Bonn, Germany, and [20]Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, Ohio, USA

*(Details of the International Turner Syndrome Consensus Group is presented in the Summary section)

Correspondence should be addressed to C H Gravholt
Email
ch.gravholt@dadlnet.dk

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Cardiovascular Health in Turner Syndrome: A Scientific Statement From the American Heart Association

Michael Silberbach MD, Chair Jolien W. Roos-Hesselink, MD, PhD, Vice Chair Niels H. Andersen, PhD, DMSc
Alan C. Braverman, MD Nicole Brown, MD R. Thomas Collins , MD Julie De Backer, MD, PhD Kim A. Eagle, MD, FAHA
Loren F. Hiratzka, MD, FAHA Walter H. JohnsonJr, MD, FAHA
Daniella Kadian-Dodov, MD Leo Lopez, MD
Kristian H. Mortensen, MD, PhD Siddharth K. Prakash, MD, PhD, FAHA Elizabeth V. Ratchford, MD Arwa Saidi, MB.BCH, MEd Iris van Hagen, MD, PhD Luciana T. Young, and MD, FAHA
and On behalf of the American Heart Association Council on Cardiovascular Disease in the Young; Council on Genomic and Precision Medicine; and Council on Peripheral Vascular Disease

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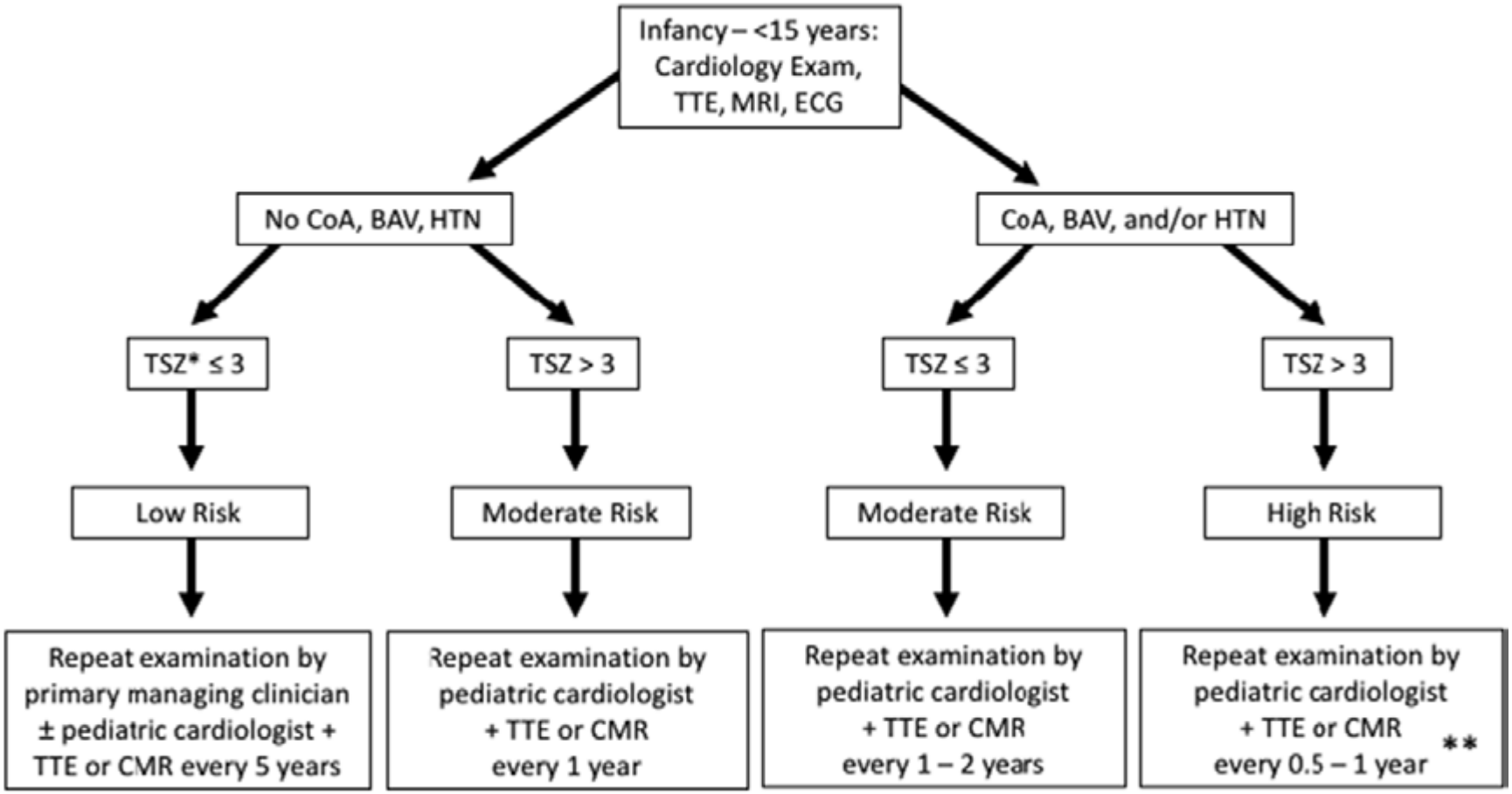
Cardiac monitoring

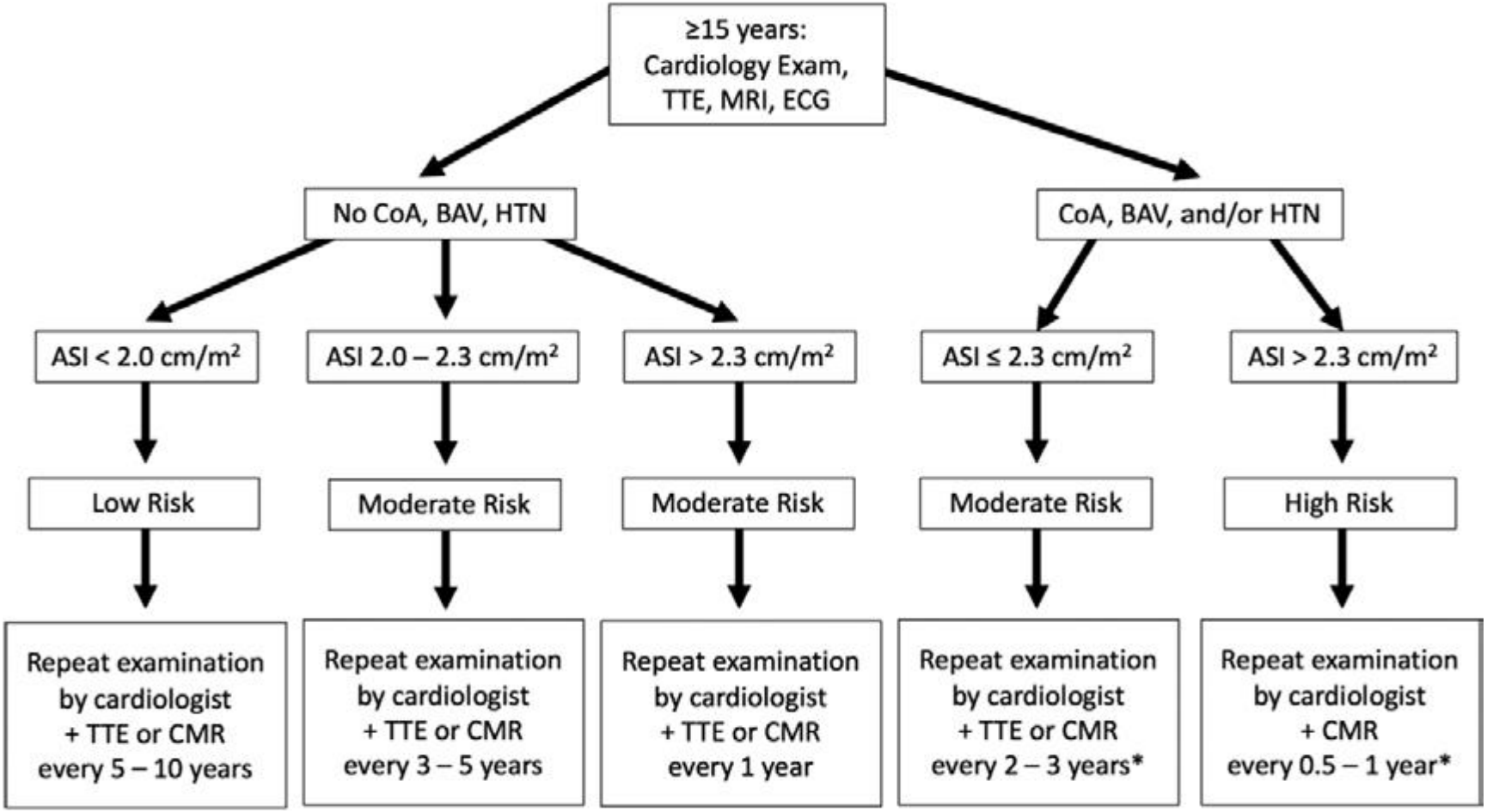
- Infant/child diagnosed with TS – TTE at diagnosis and MRA as soon as feasible without GA
- Adults diagnosed with TS – TTE + MRA at time of diagnosis
- Absence of BAV/significant disease at diagnosis
  - Children – TTE/MRA every 5 years
  - Adults – TTE/MRA every 10 years
  - MRA before any anticipated pregnancy
- Risk factors for aortic dissection – frequency of imaging guided by MDT led by Cardiologist with special interest in TS aortopathy

Cardiac monitoring



Modified from Gravholt et al

Cardiac monitoring



Modified from Gravholt et al

Aortic dissection

- Aortic dissection occurs at smaller aortic dimensions than in non-TS aortopathies
- Pregnancy confers an additional risk especially in those undergoing ART
- Risk of Dissection even if normal cardiac imaging prior to pregnancy

- Low threshold for antihypertensives
- Heart-healthy lifestyle
- MDT care with input from Cardiologist with special interest in aortopathies

Growth and Puberty

- Growth
  - Growth Hormone +/- Oxandralone
  - Initiated early (4-6 years)
  - Oxandralone >aged 10 years
  - Stopped when HV reduces/after start of induction of puberty
  - Risks: Intracranial hypertension, slipped femoral epiphyses
  - Not thought to adversely affect BP/Aortic size

Growth and Puberty

- Puberty
  - Spontaneous puberty possible in TS mosaic
  - Regular menstrual cycles – 6%
  - Induction of puberty aged 11-12 years
    - In keeping with their peers
    - Development of secondary sexual characteristics
    - Uterine growth
    - Attainment of peak bone mass
  - Transdermal Estradiol patches in incremental doses over 2-3 years
  - Progestogen added when breakthrough bleeding starts
  - Combined HRT until 50 years
  - BMD every 3-5 years

Fertility

- Spontaneous pregnancy 4.8-7.6%
- Miscarriage after spontaneous pregnancy 30.8-45.1% (general population 20%)
- Infertility one of the greatest issues affecting QoL

- Fertility preservation for those with persistent ovarian function
  - Oocyte cryopreservation following controlled ovarian hyperstimulation (>12 years)

- Pregnancy through ovum donation IVF
- Surrogacy and adoption

Pregnancy

- Increased risk of hypertension, pre-eclampsia, diabetes and Caesarean section (↑in multiple pregnancy)
- Normal cardiac screening prior to pregnancy does not preclude possibility of aortic dissection/rupture
- Pre-pregnancy counselling for ALL women with TS
- MRA within 2 years of pregnancy

Pregnancy

- No aortic dilatation or RF – TTE at 20/40
- ASI>2cm/m^2 – TTE every 4-6 weeks until 6 months postpartum
- MRA (without gadolinium) in pregnancy if suspect aortic disease

- Strict BP control (135/85mmHg)
- Careful monitoring of renal function
- Consider LDA from 12 weeks until delivery to reduce risk of PET

- ASI <2cm/m^2 – vaginal delivery
- ASI >2cm/m^2 – epidural analgesia and expedited vaginal delivery or CS

Psychosocial issues

- High levels of shyness and social anxiety
- Reduced self-esteem
- Increased risk of social isolation, and obsessive behaviour

- 10% intellectual disability
- 50-75% dyscalculia

Alder Hey

- Paediatric Endocrinology
  - Main Clinicians over seeing care
  - Diagnosis
  - Screening and referral for associated medical conditions
    - TTE at diagnosis
  - Initiation of GH therapy
  - Induction of puberty
  - DSD referral - bilateral gonadectomy if Y fragment (risk of Gonadoblastoma)

- Joint Endogynae clinics
  - Adolescents
  - Induction of puberty
  - Initiation of HRT
  - Transition planning

Transition

- Paediatric to Adult services
- Parental oversight to patient autonomy
- Vulnerable age
  - Competing issues with health care – education/employment/relationships/peers/finances

- Health promotion
- Encourage and support independent self-care

- Transition pathways
- Continuity of care

LWH TS Clinic

- MDT TS Clinic – 6 x per year
  - Cardiology
  - Gynaecology
  - Endocrinology
  - Psychology
  - Genetics
  - Referral to other specialties as required
- Patients seen annually for general health surveillance and health promotion
  - Height/weight/BMI
  - BP
  - Echocardiogram (MRA as required)
  - Screening bloods: LFT/Bone/TTG/TFT/HBA1C/Lipids
  - BMD every 3-5 years

Health Surveillance

Table 6 Recommendations for screening in Turner syndrome at diagnosis and throughout life (excluding those covered elsewhere, i.e. cardiac and neuropsychological).

	At diagnosis	**After diagnosis** (childhood)	**After diagnosis** (adults)
Weight/BMI	Yes	Every visit	Every visit
Blood pressure	Yes	Every visit	Every visit
Thyroid function (TSH and (free) T4)	Yes	Annually	Annually
Lipids			Annually if at least one cardiovascular risk factor[¤] or regional recommendation
Aminotransferase, GGT and alkaline phosphatase		Annually after 10 years of age	Annually
HbA1c with or without fasting plasma glucose		Annually after 10 years of age	Annually
25-Hydroxyvitamin D		Every 2–3 years after 9–11 years of age	Every 3–5 years
Celiac screen		Starting at 2 years; thereafter every two years	With suggestive symptoms
Renal ultrasound	Yes		
Audiometric evaluation	Yes*	Every 3 years	Every 5 years
Ophthalmological examination	Yes[#]		
Dental evaluation	Yes, if no previous care has been established		
Clinical investigation for congenital hip dysplasia	Yes, in newborns		
Skin examination	At diagnosis	Annually	Annually
Bone mineral density			Every 5 years and when discontinuing estrogen
Skeletal assessment		5–6 years and 12–14 years (see 6.1.10.)	

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Support Group

- www.tss.org.uk
- www.missinganx.com
- Social media campaign aimed at raising awareness of TS