WilliamsSyndromeClinicalManagementGuidelines

# Management of Williams Syndrome

## A Clinical Guideline

Williams Syndrome Guideline Development Group



# Contents

# Introduction...

## … to Williams Syndrome (WS)

Williams Syndrome is a rare condition, that occurs in at least 1 in 20,000 births. The current definition of WS was agreed by the Williams Syndrome Guideline Development Committee at the Williams Syndrome Management Consensus Meeting held in Manchester in May2009.

It remains pertinent in 2017 when the guidelines were updated.

***"Williams Syndrome is a sporadic genetic disorder due to deletion of a small part of chromosome 7. Features may include a distinctive facial appearance, congenital heart defects and high levels of calcium in infancy. Early feeding problems are common and development is delayed. People with WS have sociable personalities, characteristic behavioural traits and variable degrees of learning disability."***

## … to the Williams Syndrome Guideline Development Project

The guidelines have been developed using a robust methodology based on the one utilised by the Scottish Intercollegiate Guidelines Network (SIGN). The method has been adapted to suit rare conditions where the evidence base is limited and expert consensus plays a greater role.
The papers selected for review and consideration in formulating management recommendations for Williams Syndrome, are listed by clinical sign in the bibliography from page 37. Evidence from these papers was considered, and complemented by consensus on good practice, by the members of the guideline development group, who are listed on page 51. The guidelines were updated and substantially added to in January 2017. In particular sections were added relating to surgical care, behaviour, psychology, mental health and education.

## … to the Williams Syndrome Clinical Management Guidelines

**What are the aims of the guidelines?**

GuidelinesforthemedicalsupervisionofpeoplewithWShavebeenpublishedamongstothersin2001bytheAmericanAcademyofPediatrics Committee on Genetics and in France (CLAD-Ouest) in 2014. Whilst valuable, they are not entirely transferable to the UK. Therefore, in order to optimise the medical and psychological care of people with WS, the aim of the guidelines is to provide clear evidence-based management recommendationsapplicabletoU.K.individuals.

**Who are they aimed at?**

AsWSissorare,itisprobablethattheprimarycareclinicianusuallyresponsibleforcoordinatingthecareofsomeonewiththeconditionwill have had little prior experience of the syndrome. Because WS is a multisystem disorder, people with WS require various tests, screens, assessments,referralsandmultidisciplinaryinterventionsatdifferentstagesoftheirlives.Theseguidelineslayouttheserequirementsina formatthatisaccessibletoanybodywhoisinvolvedinthecareofanindividualwithWS,includingtheirparents.

**How are they constructed?**

The guidelines are divided into recommendations for four age groups: infancy; childhood; adolescence; and adults.

Onpages4-5,recommendedbaselineinvestigationsarelisted.Theseshouldbeconsideredalongsidetheagegroup-specificrecommendations whicharepertinentwhenthediagnosisismade.Foreachagegroup,therecommendedtestsarelisted,andfollow-upoptionsareindicated. Onpages48-49,a SummaryofInvestigationsforChildrenwithWilliamsSyndromesummariseswhen,andhowoften,specifictestsandscreens shouldtakeplaceforchildrenwithWilliamsSyndrome.

# Clinical features and recommended baseline investigations in WS

| Clinical Features of WilliamsSyndrome | Baselineinvestigations<br>(where investigation not initially indicated for a specific clinical feature, please refer to the relevant age group- specific pagefor managementrecommendations) |
|---|---|
| **Confirm diagnosis of Williams Syndrome by testing for microdeletion on chromosome 7 using specialist molecular techniques and refer to a geneticist. (Historically a FISH test was used but this has now been superseded by the Array Comparative Genomic Hybridisation test or more simply the"microarray" test.** | |
| • Distinctive facial features (subtle ininfancy) | |
| • Congenital heart defects (especially supravalvular aortic stenosis (SVAS) and peripheral pulmonary arterystenosis) | • CardiovascularassessmentincludingBP(bloodpressure) measurement in both upper limbs (4 - limb in infants), oxygen saturation pre and post ductally, ECG and Echocardiography. (Chest x-ray may also beindicated.) |
| • Raisedblood/urinecalciumlevelsandnephrocalcinosis | • Blood calcium and urine calcium : creatinineratio |
| • Genitourinary problems (undescended testes,hypospadias) | • Blood creatinine, electrolytes and urinarytract ultrasound |
| • Hypertension | • Plasma renin activity and renal artery dopplerstudies |
| • Inguinalhernias | |
| • Gastrointestinal problems and feeding problems- gastro-oesophageal reflux; rectal prolapse;colonicdiverticular | |
| • Failure to thrive/slow growthrate | • CoeliacscreenandplotweightonappropriateWSgrowth chart |
| • Endocrine abnormalities / shortstature | • Thyroid Function Tests and plot length and occipito frontalheadcircumference(OFC)onWSgrowthchart |
| • Scoliosisandothermusculoskeletalproblems | • Radiology tests asappropriate |

# Clinical features and recommended baseline investigations in WScontinued....

| Clinical Features ofWilliamsSyndrome | Baseline investigations |
|---|---|
| | (where investigation not initially indicated for a specific clinical feature, please refer to the relevant age group- specific page for management recommendations) |
| **Confirm diagnosis of Williams Syndrome by testing for microdeletion on chromosome 7 using specialist molecular techniques and refer to a geneticist. (Historically a FISH test was used but this has now been superseded by the Array Comparative Genomic Hybridisation test or more simply the"microarray" test.** | |
| • Dentalanomalies | |
| • Developmental delay : Across all domains including language (particularlycomprehension),visual,spatialandsocialcognition. | → • Developmental assessment (Ageappropriate) |
| • Distinctive behavioural characteristics (including irritability, hyperactivity, perseverative behaviour, anxiety and overfriendliness). | → • Consideradditionalspecificinvestigationsasappropriate. |
| • Visual problems: Strabismus, poor acuity, visual crowding, poor depth perception and refractive errors (usually hypertonia and astigmatism) | |
| • Auditoryproblems andhypersensitivitytonoise | |
| • Sleepissues | → • First step, parents should keep a sleep diary using http://kidssleepdr.com to discuss with GP. Consider referral to sleep clinic for assessment and sleep management. Further information on sleep issues can be found on the WSF website http://williams-syndrome.org.uk . |

# Recommendations for the management of Williams Syndrome

*~ in infancy(1)~*

AGE 0—1

## Recommended Testing/Screening

- Cardiac screening
- Blood Calcium and Urine Calcium: creatinineratio

## Clinical Management Recommendations

**Ifthediagnosisismadeintheneonatalperiod,acardiacassessmentshouldbecarriedoutand referral made to a paediatric cardiologist for echocardiography. Where the diagnosis is made later in infancy, referral to a paediatric cardiologist should be made within 3 months. At least annual cardiac examination by a paediatric cardiologist should be carried out until 4 years of age. NBThepresenceofSVASorPPASmaybediagnosedininfancywhendevelopmentaldelayorthe typical facial appearance is not recognised. In all such cases the paediatric cardiologist should requesta geneticopinionorarrangeappropriategenetictesting.**

**Measure at diagnosis. Age appropriate normal ranges should be used. 5 - 10% of WS infants may require therapy for hypercalcaemia. If initial tests are normal, further testing need only be performed if symptoms develop. Renal ultrasound to exclude nephrocalcinosis (See below)**

**Management of Hypercalcaemia**

Hypercalcaemia should be treated in a stepwise fashion

- Intravenousfluidstocorrectdehydrationandtomeetincreasedurinarylossescausedbyhypercalcaemia and therapy (Seebelow)
- Loop diuretics such has Frusemide enhance calcium excretion
- Low calcium diet. Achieved by substituting Locasol [SHS International (Nutricia Advanced Medical Nutrition) Liverpool,UK]forallmilkfeeds.Thiscontainscalcium<7mg/100mlandnoaddedvitaminD.Totaldailydietary calciumintakeshouldberestrictedto50%ofrecommendednutrient intake(RNI)
- Calciumrichhardwaterormineral watershouldnotbeused topreparеformula feeds.Boilingtapwater mayhelptoreduce itscalciumcontent.
- Sun-block creams should be used to limit cutaneous vitamin D synthesis
- Vitamin D supplement should be avoided
- In infants with normal renal function, and resistant hypercalcaemia, treatment with intravenous bisphosphonates(usuallyPamidronate)iseffective inreducingserumcalciumlevels.Ininfantswithimpaired renalfunctionlowerdosesofbisphosphonatesshouldbeusedafterdiscussionwitha nephrologist.
- Bloodcalcium,alkalinephosphataseandparathyroidhormone levelsshouldbemeasuredatintervalsuntil valuesbecome normal.
- Thecalciumdietshould be‘relaxed’ifthealkalinephosphataseandparathyroidhormonelevelsstarttorise. ProlongedcalciumandvitaminD restrictionmayresultin rickets.

Refer to nephrologistif nephrocalcinosis is detected with evidence of renal impairment. If renal function is normal, repeat scan at appropriate interval. If structural abnormalities detected investigate as appropriate.

# Recommendations for the management of WilliamsSyndrome

## *~ in neonates &infancy(2)~*

AGE 0—1

| Recommended Testing/Screening | Clinical Management Recommendations |
|---|---|
| • Genitourinaryscreening | Examine male infants for hypospadias and undescended testes (10% and 30% respectively in published series) and refer to a paediatric surgeon according to local guidelines. A urinary tract ultrasound should be performed and structural abnormalities managed accordingly. The incidence of urinary tract infections is increased and should be routinely investigated |
| • Hypertensionscreening | Monitoring blood pressure annually in 4 limbs. Hypertension is defined as the average systolic BP and/or diastolic BP greater than or equal to the 95th centile for gender, age and height on > 3 occasions. If associated with renovasculardisease (RVD), refer to nephrologist. Intervention for the management of hypertension secondary to RVD with either percutaneous transluminal angioplasty and/or surgical vascular reconstruction is not recommended for the initial management of hypertension. Medical management of hypertension under the supervision of a nephrologist is recommended. |
| • Inguinal herniascreening | Examine for inguinal hernias. Their incidence is significantly increased in both sexes, especially in girls. Refer to a paediatric surgeon according to local guidelines. |
| • Gastrointestinal and feeding problems | Take feeding history. Enquire about bowel habit, vomiting and symptoms of gastro oesophageal reflux (GOR). If failing to thrive, measure plasma calcium, thyroid function tests and coeliac screen. Refer for appropriate dietetic support. Manage GOR with standard therapies and investigate for potential hiatus hernias or strictures where symptoms persist or infant fails to thrive. Manage rectal prolapse conservatively, treating constipation. Faltering growth is common in WS. Use the syndrome specific growth charts and consider nasogastric or percutaneous gastrostomy feeding. |
| • Thyroid functiontests(TFTs) | Ensure baseline test are undertaken. Repeat thyroid function test if patient symptomatic. Measure TSH levels and if elevated, consider thyroid scanning and replacement therapy. Plot growth and OFC 3monthly. |
| • Musculoskeletalproblems | Examine for scoliosis and radio-ulnar synostosis. Refer to paediatric orthopaedic surgeon as appropriate. |
| • Dental screening to prevent dentaldisease | Enrol patient in an individualised preventative oral healthcare programme from an early age. Routine follow up and regular dental examinations by a family dentist or local community dental services are essential. Follow guidance in 'Delivering Better Oral Health: an evidenced-base tool kit for prevention'. (www.gov.uk). |

# Recommendations for the management of WilliamsSyndrome

## *~ in neonates & infancy(3)~*

AGE 0—1

| RecommendedTesting/Screening | Clinical ManagementRecommendations |
|---|---|
| • Multidisciplinary developmentassessment | Coordinate an assessment by the local multidisciplinary team within 6 months of diagnosis. Adaptive behaviours especially feeding and sleeping should be reviewed. The assessment should include involvement of a physiotherapist, occupational therapist, speech therapist and if available clinical psychologist. Referral to Early Intervention services and provision of a Key worker should be arranged as soon as possible. |
| • Hearing screening | Newborn hearing screening programme (NHSP) . |
| • Visionscreening | Visual screening should take place once the diagnosis has been made, carried out by the community orthoptist/optometrist where services exist. Referral to the local paediatric ophthalmology services if any abnormality is detected (or community services do not exist). Encourage parents to report any concerns to the orthoptist. |

NB. Anaesthesia

A paediatric anaesthetist should be involved in the perioperative care, for any surgical procedure, in all children with WS. Unless there are existing cardiac problems, cardiac assessment within 12 months prior to a general anaesthetic is sufficient. Pre-op assessment shouldtakeplace1-2weekspriortoplannedsurgery,toassesscardiac,airway,joints,renalandemotionalstatus.Thisshouldinclude anECGtoexcludeprolongedQTinterval.

# Recommendations for the management of Williams Syndrome

## *~ in childhood(1)~*

AGE 2-11

### Recommended Testing/Screening

- Cardiacscreening
- Blood calcium and urine calcium: creatinine ratio
- Genitourinary tractscreening

### Clinical Management Recommendations

**Annual cardiac examination until 4 years of age. Thereafter complete cardiac assessment, including echocardiography, at least every 5 years.**

**Measureatdiagnosis.Ageappropriatenormalrangesshouldbeused.5-10%ofWSchildren may require therapy for hypercalcaemia. If initial tests are normal, further testing should only be performed if symptomsdevelop.**

**Management of Hypercalcaemia**

Hypercalcaemia should be treated in a stepwise fashion

- Intravenous fluids to correct dehydration and to meet increased urinary losses caused by hypercalcaemia and therapy (See below)
- Loop diuretics such has Frusemide enhance calcium excretion
- Low calcium diet. Achieved by substituting Locasol [SHS International (Nutricia Advanced Medical Nutrition) Liverpool, UK] for all milk feeds. This contains calcium <7mg/100ml and no added vitamin D. Total daily dietary calcium intake should be restricted to 50% of recommended nutrient intake (RNI)
- Calcium rich hard water or mineral water should not be used to prepare formula feeds. Boiling tap water may help to reduce it calcium content.
- Sun-block creams should be used to limit cutaneous vitamin D synthesis
- Vitamin D supplement should be avoided
- In infants with normal renal function, and resistant hypercalcaemia, treatment with intravenous bisphosphonates (usually Pamidronate) is effective in reducing serum calcium levels. In infants with impaired renal function lower doses of bisphosphonates should be used after discussion with a nephrologist.

**Assess for urinary tract infections and bladder dyssynergy. Day and night-time urinary incontinence is common and may persist into adulthood. Bladder dyssynergy increases the risk of bladder diverticula and calculi developing. Examine boys for undescended testes and hypospadias. Renal tract ultrasound should be performed to include kidneys and bladder. If recurrent urinary infections occur, consider excluding bladder diverticula, ureteric reflux or stones. If urinary incontinence is prominent consider excluding and treating bladder dysynergy. If nephrocalcinosis exists, with evidence of renal impairment, refer to a paediatric nephrologist. Test serum creatinine every 2—4 years. Undertake detailed renal function tests and/or refer to a nephrologist if evidence of renal impairment.**

# Recommendations for the management of Williams Syndrome

## *~ in childhood (2)~*

AGE 2—11

| Recommended Testing/Screening | Clinical Management Recommendations |
|---|---|
| • **Hypertensionscreening** | Monitor blood pressure annually in both arms. Hypertension is defined as the average systolic BP and/or diastolic BP greater than or equal to the 95th centile for gender, age and height on > 3 occasions. If associated with renovascular disease (RVD), refer to nephrologist. Intervention for the management of hypertension secondary to RVD with either percutaneous transluminal angioplasty and/or surgical vascular reconstruction is not recommended for the initial management of hypertension. Medical management of hypertension under the supervision of a nephrologist is recommended. |
| • **Inguinal herniascreening** | Opportunist examination to exclude development of inguinal hernias. |
| • **Gastrointestinalandfeedingproblems** | Enquire about nutritional problems and bowel habit. Treat constipation. Symptomatic colonic diverticular disease has been reported in children as youngas9years.Considerdiverticulosisinachildwithrecurrentabdominal pain.Screenforcoeliacdiseasearound3yearsofagewithlowthresholdto repeatifsymptomssuggestive.Significantgastro-oesophagealrefluxtends to reduce with age but may remain problematic. Risk of oesophageal strictures ifuntreated. |
| • **Thyroid functiontests(TFTs)** | Test if patient is symptomatic. Measure TSH levels and if elevated, consider thyroid scanning, Consider treatment with L-Thyroxin if patienthasoverthypothyroidism,orprogressivedeteriorationofthyroid function. |
| • **Growth &Puberty** | Chart height, weight and OFC measurements annually (use WS growth charts). Mid parental height centile should be estimated. Routine investigations for abnormal growth velocity and precocious puberty (< 8 years).Wherenecessary,considergonadotropinreleasinghormone(GnRH) therapy. |

# Recommendations for the managementof WilliamsSyndrome

## *~ in childhood(3)~*

AGE 2—11

| Recommended Testing/Screening | Clinical Management Recommendations |
|---|---|
| • **Musculoskeletalproblems** | Enquireaboutskeletalproblems.Checkspineforkyphoscoliosisandrangeofother jointmovements.X-ray/refertopaediatricorthopaedicteamasindicated. |
| • **Screening for dentalanomalies** | Enrol patient in an individualised preventative oral healthcare programme from an early age. Routine follow up and regular dental examinations by a family dentist or local community dental services are essential. Follow guidance in 'Delivering Better Oral Health: an evidenced-base tool kit for prevention' (www.gov.uk). Missing teeth/ malocclusion/prolonged retention of primary teeth and other dental anomalies: refer to a consultant or specialist in paediatric dentistry for multidisciplinary assessment and management. If cardiac anomalies exist, antibiotic prophylaxis may be advised for dental procedures – check withcardiologist. |
| • **Multidisciplinary developmental assessment** | Refer to local Child Development Team. Learning/cognitive disability may include delays of development with difficulties in all domains. Particular difficulties of attention,visual-motoractions,andspatialmemoryareoftennoted.From5yearsto adulthood,speechandlanguagedevelopmentisusuallyrelativelygoodcomparedto visual, motor and spatial abilities. Assessment based on expressive language skills mayoverestimategeneralability.Monitorfeedingandsleeping.Supportlearningand development with assessment of the child's special educational needs and request an Educational Health Care Plan (EHCP) at 2 years of age. (See below) https://www.gov.uk/children-with-special-educational-needs/overview. |
| • **Hearingscreening** | Carryoutat2yearsifspeechisdelayed(Thisislikelytobeduetodevelopmental delay) If hyperacusis is present, consider implementing a programme of desensitisationwithmaskers(ifservicesareavailable). |
| • **Visualscreening** | Visual screening should be carried out at primary school entry and at transition to secondaryeducationbythecommunityorthoptist/optometristunlessanabnormality is detected. Where these services do not exist the child should be seen in the hospitalophthalmicservice.Parentsshouldbeencouragedtoreportanyconcernsto their orthoptist/optometrist. Screening tests suitable for children with learning disabilitiesshouldbeusede.g.crowdedcard/singleoptotypesymbols. |

# Recommendations for the managementof WilliamsSyndrome

*~ in childhood(4)~*

AGE 2—11

| Recommended Testing/Screening | Clinical Management Recommendations |
|---|---|
| • Behavioural & Mental Healthissues | Provide behavioural management advice with support to family as required. Refer for psychological intervention for anxiety or major life events. Consider screening with a behavioural assessment tool. Consider referral to a sleep disorders clinic if problems merit intervention. Involve primary mental health services if available. Be aware of issues related to social vulnerability and put in place appropriate social support structures/environments. Additional advice on this aspect of care can be obtained from the Williams Syndrome Foundation www.williams-syndrome.org.uk. |
| • Educationalissues | Children with WS have difficulties in language and communication; cognition and learning (attention, reading, writing and number development); social, emotional, mental health, sensory and physical needs. Therefore they often need specialist advice from speech and language therapy, occupational therapy, physiotherapy, dietetics, clinical psychology, educational psychology, audiology and other specialists and hence will qualify for an EHCP. WS children and adults have great difficulty in writing with a pen or pencil and should be encourage using a computer for writing and preferably a large keyboard. Development is atypical, which has implications for intervention (e.g. counting is helped by using verbal rather than visual strategies; reading is heavily reliant on phonology in WS; both numeracy and literacy deficits can be related to attention impairments).Further information about the specific requirements of an EHCP and educational advice relating to WS can be obtained through the Williams Syndrome Foundation www.williams-syndrome.org.uk. |

**!NB. Anaesthesia**

*A paediatric anaesthetist should be involved in the perioperative care, for any surgical procedure, in all children with WS. Unless there are existing cardiac problems, cardiac assessment within 12 months prior to a general anaesthetic is sufficient. Pre-opassessmentshouldtakeplace1-2weekspriortoplannedsurgery,toassesscardiac,airway,joints,renalandemotionalstatus.This shouldincludeanECGtoexcludeprolongedQTinterval.*

# Recommendations for the management of WilliamsSyndrome

## *~ in adolescence(1)~*

AGE 11-18

| Recommended Testing/Screening | Clinical Management Recommendations |
|---|---|
| • Cardiacscreening | Cardiac assessment including scans at least every 5 years. Appropriate follow up if symptomatic. |
| • Blood calcium and urine calcium: creatinine ratio | Test if symptoms suggest hypercalcaemia. If present, hypercalcaemia is likely to be due to an alternative diagnosis. Investigate and manage as appropriate. |
| • Genitourinary tractscreening | Take history for urinary tract infections or symptoms of bladder dyssynergia. Check for position of testes. Renal ultrasound at puberty and 5 yearly thereafter or if symptomatic. Test blood creatinine every 2—4 years. Investigate/refer as appropriate for urinary tract infection; exclude obstructive lesion(s); undertake detailed renal function tests and/or refer to a nephrologist if evidence of renal impairment. If nephrocalcinosis persists refer to nephrologist. |
| • Hypertensionscreening | Monitoring blood pressure annually in both arms. Hypertension is defined as the average systolic BP and/or diastolic BP greater than or equal to the 95th centile for gender, age and height on > 3 occasions. If associated with renovascular disease (RVD), refer to nephrologist. Intervention for the management of hypertension secondary to RVD with either percutaneous transluminal angioplasty and/or surgical vascular reconstruction is not recommended for the initial management of hypertension. Medical management of hypertension under the supervision of a nephrologist is recommended. |
| • Inguinalhernias | Examine for inguinal hernias which remain common into adulthood. |
| • Gastrointestinalproblems | Enquire annually about bowel habit. Treat constipation and consider investigating for diverticular disease if relevant and unexplained symptoms. Screen for coeliac disease if symptomatic. The incidence of significant GOR decreases with age but may remain problematic. Treat for response or refer for assessment. Risk of oesophageal strictures causing dysphagia if untreated. |
| • Thyroid functiontests(TFTs) | Test if patient is symptomatic. Measure TSH levels and if elevated, consider thyroid scanning. Consider treatment with L-Thyroxin if patient has overt hypothyroidism, or progressive deterioration of thyroid function. |
| • Growth & sexualhealth | Chart growth annually, and avoid excessive weight gain. Offer contraceptive advice/contact details of organisations who can advise on contraception for people with learning disabilities. |

# Recommendations for the management of WilliamsSyndrome

*~ in adolescence(2)~*

AGE 11-18

| Recommended Testing/Screening | Clinical Management Recommendations |
|---|---|
| • Musculoskeletalproblems | Checkspineclinicallyforkyphoscoliosisatpubertyandx-ray/referto orthopaedicteamasindicated. |
| • Screening for dentalanomalies | Enrol patient in an individualised preventative oral healthcare programme from an early age. Routine follow up and regular dental examinations by a family dentist or local community dental services are essential. Follow guidance in 'Delivering Better Oral Health: an evidenced-base tool kit for prevention'. (www.gov.uk) Missing teeth/malocclusion/prolonged retention of primary teeth and other dental anomalies: refer to a consultant or specialist in paediatric dentistry for multidisciplinary assessment and management. If cardiac anomalies exist, antibiotic prophylaxis may be advised for dental procedures - check with cardiologist |
| • Multidisciplinary developmental assessment | InvolvelocalChildDevelopmentorLearningDifficulties(LD)Teams.Advice and support may be required in areas of disability including visual-motor skills (e.g. stair descent, crossing road), spatial memory, navigation skills (e.g. using public transport, learning a walked route, strategies when lost), planning ahead / problem solving and attention deficits. Additional assessments for the EHCP will need to be required in most cases https:// www.gov.uk/children-with-special-educational-needs/overviewRefer for psychological intervention for anxiety, and when major life events occur. Be aware of issues related to social vulnerability and put in place appropriate social support structures/environments. Additional advice on thisaspectofcarecanbeobtainedfromtheWilliamsSyndromeFoundation www.williams-syndrome.org.uk. |
| • Hearingscreening | Arrangeroutineaudiologycheckat11and18yearsforhyperacusis&high frequency hearing loss. If hyperacusis is present consider implementing a programme of desensitisation withmaskers. |
| • Visualscreening | Screensforstrabismusandrefractiveerrorcanbecarriedoutifindicatedby thelocaloptometristwhomayrefertolocalophthalmologyservices. |

# Recommendations for the managementof WilliamsSyndrome

## *~ in adolescence(3)~*

AGE 11-18

### Recommended Testing/Screening

- **Mental health issues**

- **Educationalissues**

### Clinical Management Recommendations

Phobias, anxiety and sleep problems are significantly more common among young people with WS. Social and behavioural problems may also be indications of poor mental health. Underlying causes include impairments in attention, social understanding, emotion recognition, sensory processing (in particular hyperacusis), adaptive behaviours and disrupted sleeping patterns. Assessment and intervention must also take account of potential situational factors (e.g. major life events, inadequate support systems, inappropriate environment).

NB. Apparent friendliness and sociability can mask depression and anxiety.

TheevidencebasefortreatmentsformentalhealthproblemsinWSislimited. Potentially useful interventions include: programmes to enhance adaptive and self-help skills and social functioning and understanding; cognitive-behavioural therapies including mindfulness; education and occupational interventions. The provision of a suitable supportive and structured environment is important and advice to improve sleeping patterns may also be required.

The evidence base for pharmacological treatments is weak. There are some positive reports for SSRI's and non-SSRIs in the treatment of depression and anxiety and for methylphenidate to improve attention and hyperactivity. However unwanted side effectsarealsoverycommon.Nationalguidancerecommendsannualreviewofmental healthissuesinyoungpersonswithlearningdisability

https://www.nice.org.uk/guidance/qs142.

Additional assessments for the EHCP will be needed on transition from primary to secondary and secondary to 16+ education https://www.gov.uk/children-with-special- educational-needs/overview. Access to social skills training, and programmes to teach basic self-help and daily living skills will be useful.

FurtherinformationaboutthespecificrequirementsofanEHCPrelatingtoWScanbe obtained through the Williams Syndrome Foundation.www.williams-syndrome.org.uk.

Be aware of issues related to social vulnerability and put in place appropriate social support structures/environments. Additional advice on this aspect of care can be obtained from the Williams Syndrome Foundation www.williams-syndrome.org.uk.

# Recommendations for the management of WilliamsSyndrome

## *~ in adolescence(4)~*

AGE 11—18

**NB. Anaesthesia**

- *A paediatric anaesthetist should be involved in the perioperative care, for any surgical procedure, in all children with WS.*
- *Unless there are existing cardiac problems, cardiac assessment within 12 months prior to a general anaesthetic is sufficient.*
- *Pre-op assessment should take place 1-2 weeks prior to planned surgery, to assess cardiac, airway, joints, renal and emotional status.*
- *This should include an ECG to exclude prolonged QT interval.*

# Recommendations for the management of WilliamsSyndrome

## *~ inadulthood(1)~*

AGE 18+

| Recommended Testing/Screening | Clinical Management Recommendations |
|---|---|
| • Cardiacscreening | Assessment including scans, every 5 years throughout life. Adults with Williams Syndrome should be referred to their regional Adult Congenital Cardiology Service for routine follow up. |
| • Blood calcium and urine calcium: creatinineratio | Testifsymptomssuggesthypercalcaemia.Ifpresent,hypercalcaemiaislikelytobedueto an alternativediagnosis.Investigateandmanageasappropriate. |
| • Genitourinarytractscreening | Check for urinary tract infection and symptoms of bladder dyssynergy: day or night time incontinence. Bladder & kidney ultrasonography every 5 year. Investigate evidence of renal scarring, bladder diverticulae or calculi. If nephrocalcinosis persists refer to nephrologist. Test serum creatinine every 2—4 years. |
| • Hypertensionscreening | Monitor blood pressure annually in both arms. In adults with WS, hypertension is defined as the average systolic BP and/or diastolic BP greater than or equal to 140/90mmHg. If associated with renovascular disease (RVD), refer to nephrologist. Intervention for the management of hypertension secondary to RVD with either percutaneous transluminal angioplasty and/or surgical vascular reconstruction is not recommended for the initial management of hypertension. Medical management of hypertension under the supervision of a physician is recommended. |
| • Inguinalhernias | Examine for inguinal hernias which remain common into adulthood. |
| • Gastrointestinalissues | Enquire about bowel habit. Treat constipation and consider investigating for diverticular disease. Screen for coeliac disease if symptomatic. Treat symptoms of gastro oesophageal reflux for response or refer for treatment. |
| • Thyroidfunctiontests(TFTs) | Repeat if patient is symptomatic (check for anti-thyroid antibodies). Consider thyroid scanning and thyroid hormone replacement therapy. |
| • Growth & sexualHealth | Weigh annually, and avoid excessive weight gain—encourage an ‘active’ lifestyle. Offer contraceptive advice/contact details of organisations who can advise on contraception for people with learning disabilities. |
| • Screeningfordiabetes | At 30 years old: Oral Glucose Tolerance Test (OGTT), or fasting insulin if considered more appropriate. Control impaired glucose tolerance with exercise & diet. Avoid large glucose loads. Avoid diabetogenic drugs. Manage clinical diabetes in WS by current national guidelines. |

# Recommendations for the management of WilliamsSyndrome

## *~ in adulthood(2)~*

AGE 18+

| Recommended Testing/Screening | Clinical Management Recommendations |
|---|---|
| • Musculoskeletalproblems | Investigate or refer if symptomatic |
| • Screening fordentalanomalies | Enrol patient in an individualised preventative oral healthcare programme from an early age. Routine follow up and regular dental examinations by a family dentist or local community dental services are essential. Follow guidance in 'Delivering Better Oral Health: an evidenced-base tool kit for prevention'. (www.gov.uk) Missing teeth/ malocclusion/prolonged retention of primary teeth and other dental anomalies: refer to a consultant or specialist in paediatric dentistry for multidisciplinary assessment and management. If cardiac anomalies exist, antibiotic prophylaxis may be advised for dental procedures - check with cardiologist. |
| • Hearing screening | Screen every 5 -10 years (for hearing loss). |
| • Visionscreening | As required by the local optician. |
| • Mental healthissues | Phobias and anxieties are significantly more common among young people with WS than in the general population. Social and behavioural problems may also be indications of poor mental health. Underlying causes include impairments in executive functioning; social understanding; emotion recognition; sensory processing (in particular hyperacusis); adaptive behaviours and disrupted sleeping patterns.<br>Assessment and intervention must take account of these potential situational factors (e.g. major life events, inadequate support systems, inappropriate environment).<br>NB. Apparent friendliness and sociability can mask depression and anxiety. The evidence base for treatments for mental health problems in WS is limited.<br>Particularly useful interventions include: programmes to enhance adaptive and self- help skills and social functioning and understanding; cognitive-behaviour therapies including mindfulness; education and occupational interventions. The provision of a suitable supportive and structured environment is also important.<br>The evidence base for pharmacological treatments is weak. There are some positive reports forSSRI'sandnon-SSRIsinthetreatmentofdepressionandanxiety.Alsoformethylphenidate to improve attention and hyperactivity. However unwanted side effects are also very common.<br>Access to support for employment, self-help and independent living is important and social skills intervention may be required. |

# Recommendations for the managementof WilliamsSyndrome

## *~ in adulthood(3)~*

AGE 18+

### Recommended Testing/Screening

- **Educationalissues**

### Clinical Management Recommendations

An EHCP will normally have been requested at an earlier age. This can be extended to age 25 and can be requested by the young person themselves from 16 years of age. https://www.gov.uk/children-with-special-educational-needs/overview

FartherinformationaboutthespecificrequirementsofanEHCPrelatingtoWScan be obtained through the Williams Syndrome Foundation www.williams-syndrome.org.uk.

Support for employment, self-help, independent living and sexual health/education is vital. Support should include areas of intellectual disability which can negatively impact independence, such as navigation; using public transport; learning a walked route to get to place of employment; strategies when lost and how to ask for help; safe road crossing; planning ahead; problem solving (e.g. packing a bag for the day, keeping effects in order).

Beawareofissuesrelatedtosocialvulnerabilityandputinplaceappropriatesocial support structures/environments. Additional advice on this aspect of care can be obtained from the Williams Syndrome Foundationwww.williams-syndrome.org.uk.

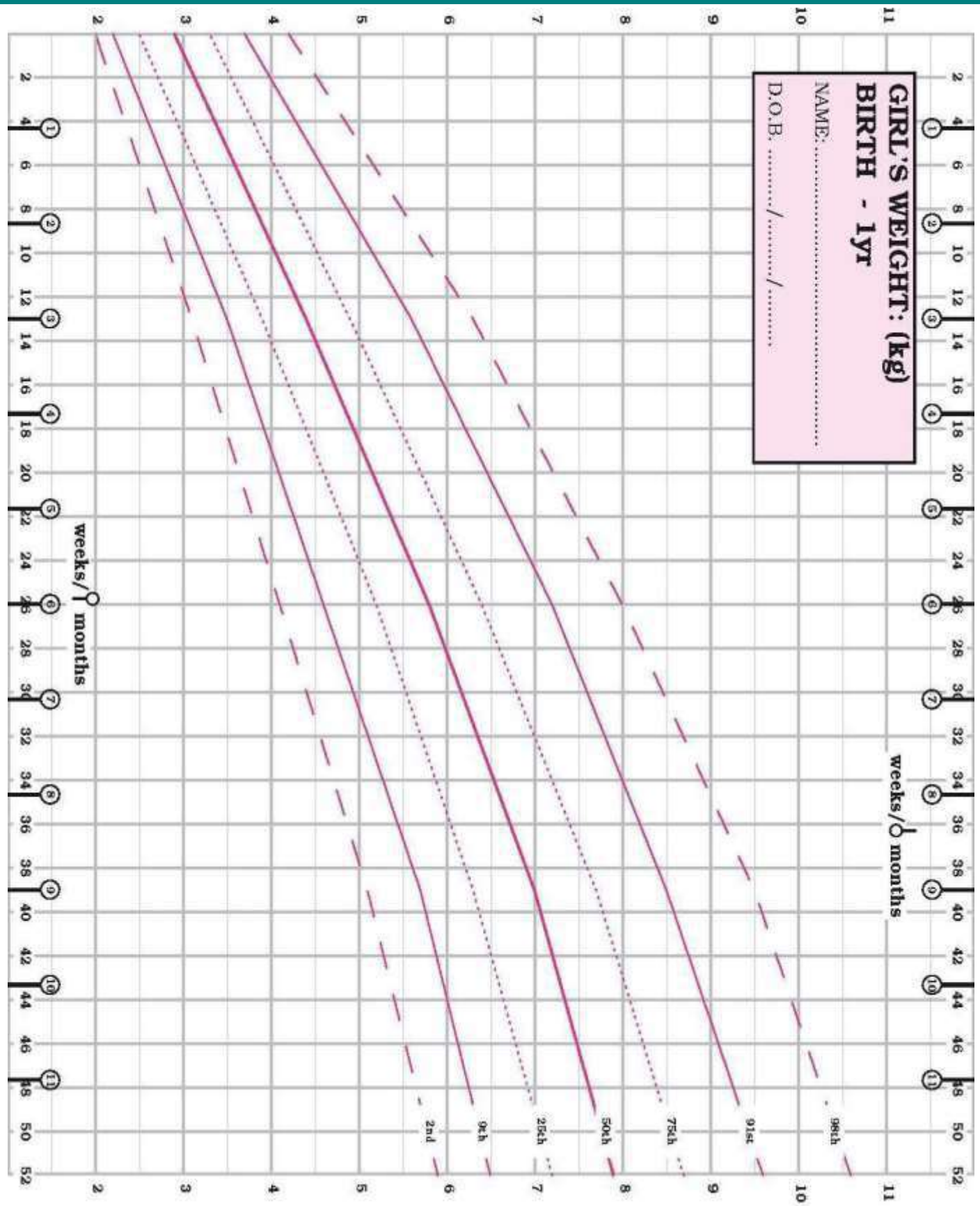
!General anaesthesia for any surgical procedure remains a significant risk and the anaesthetist should be fully aware of the particular issues relating to WS. Unless there are existing cardiac problems, cardiac assessment within 12 months prior to a general anaesthetic is sufficient. Pre-operative assessment should take place 1-2 weeks prior to planned surgery, to assess cardiac, airway, joints, renal and emotional status. This should include an ECG to exclude prolonged QT interval.

## Williams SyndromeGrowth Charts

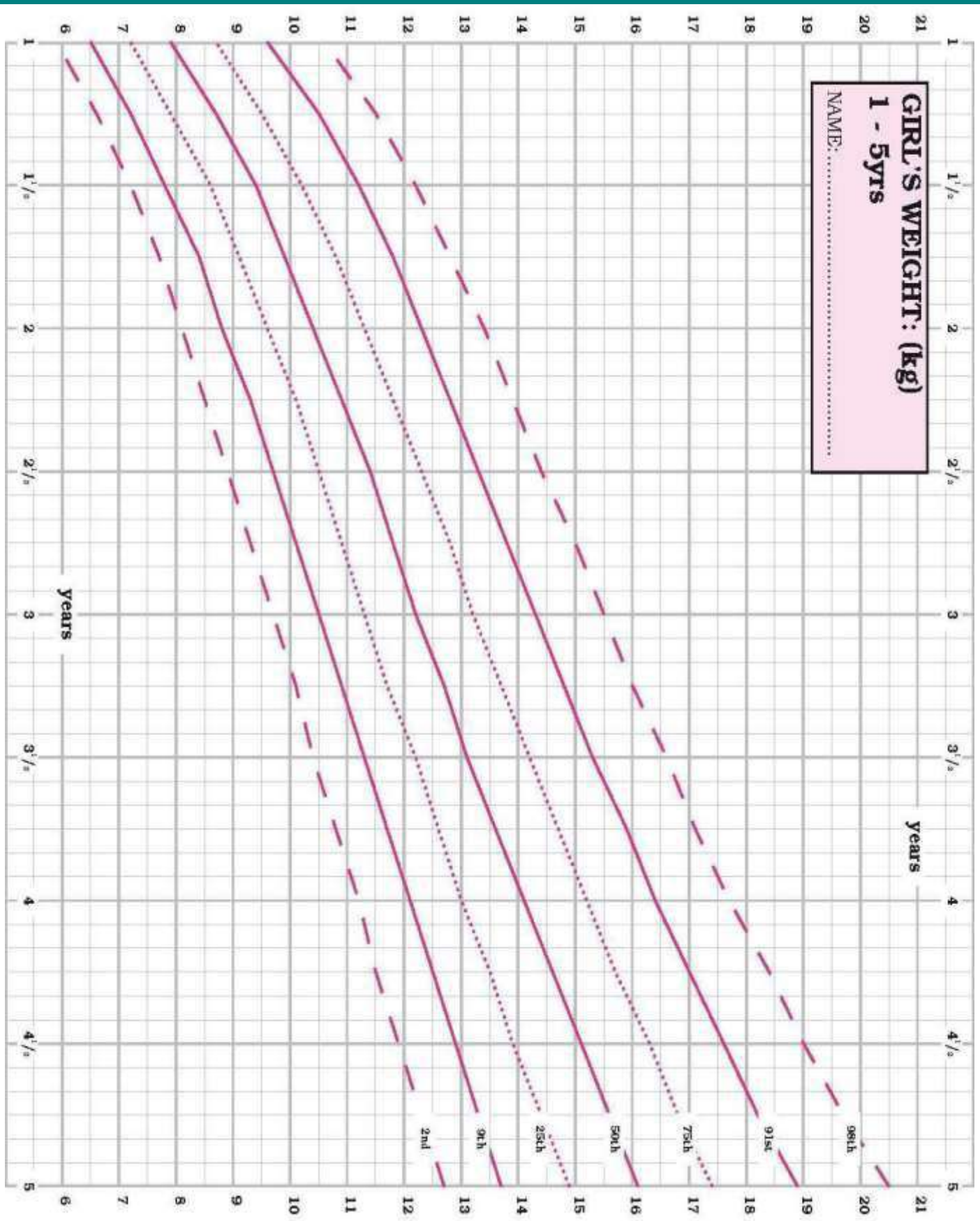


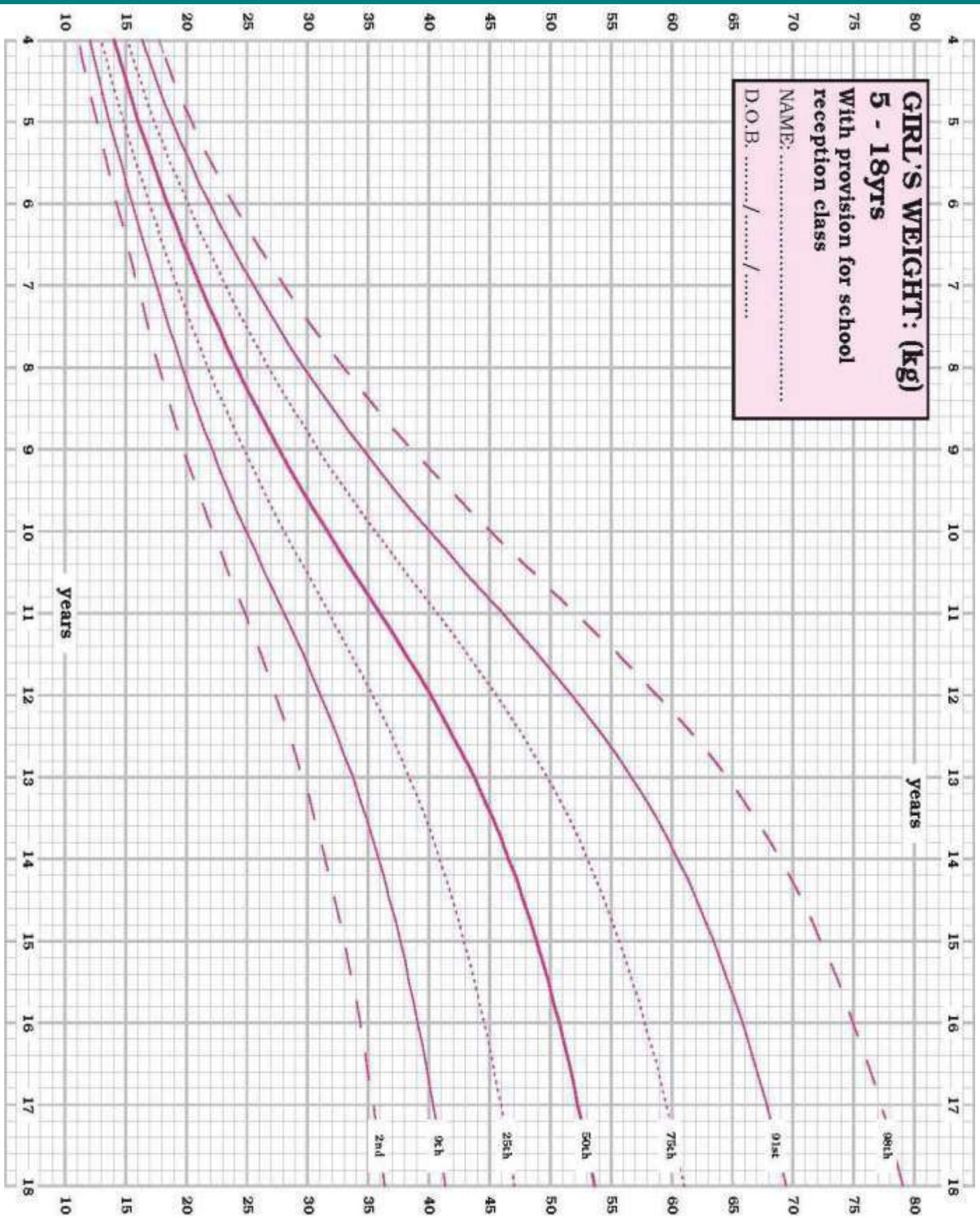
All growth charts are reproduced with the kind permissions of HarlowPrinting Limited and Dr Neil Martin.

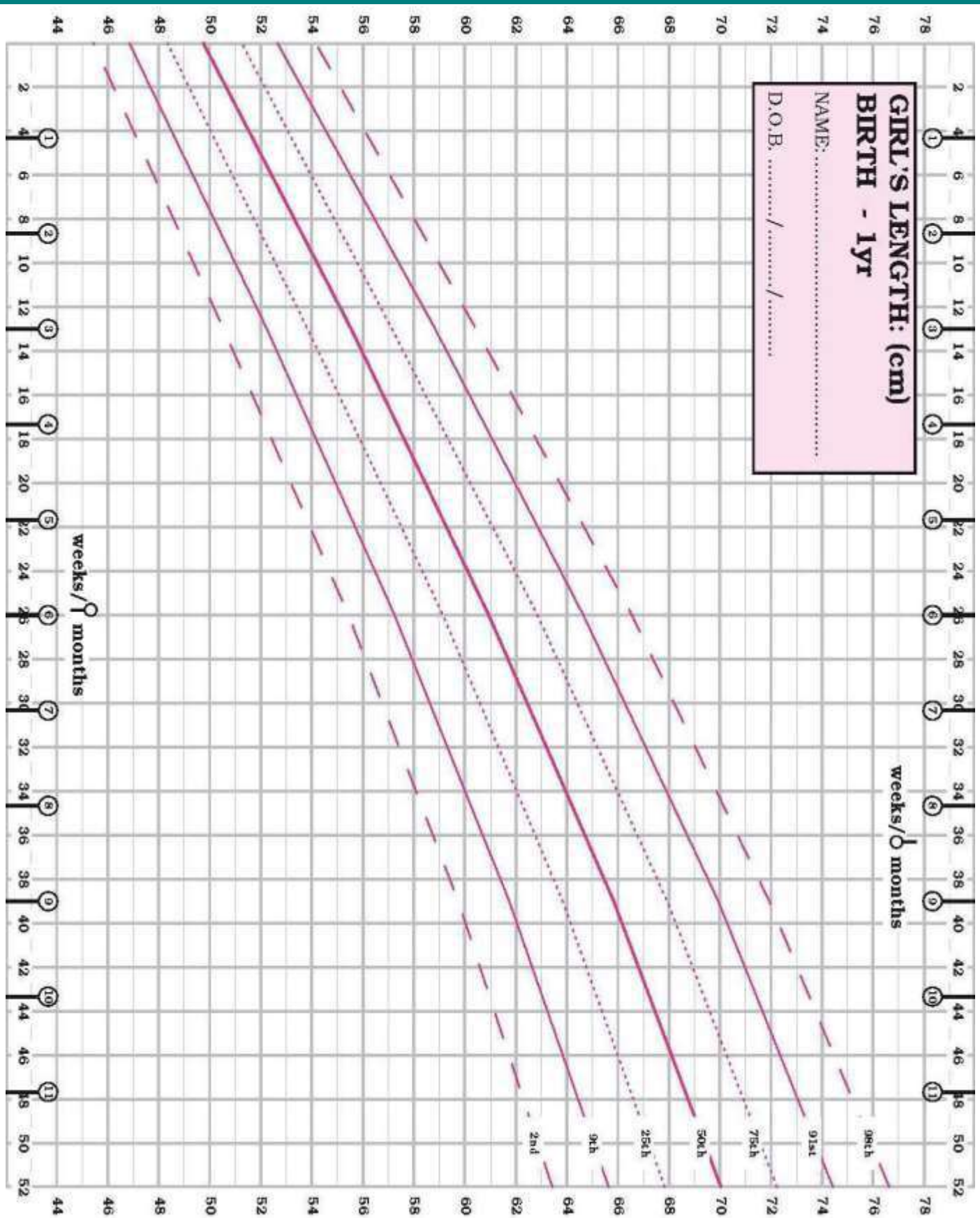
From: Martin, N. D. T.,W.R. Smith,et al. (2007).*"New height, weight and head circumferencechartsforBritishchildrenwith Williamssyndrome."*
**Arch Dis Child 92(7):598-601.**

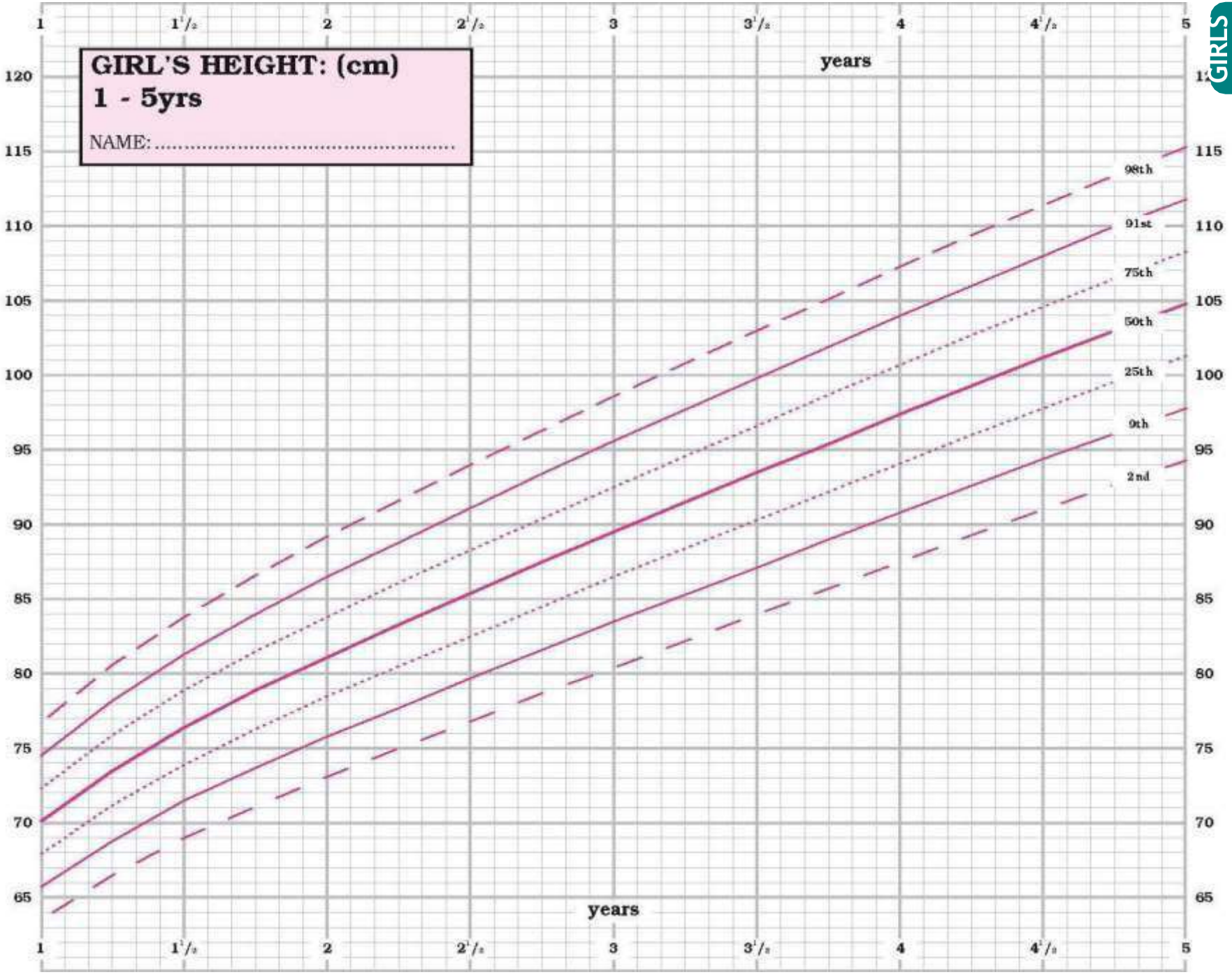



GIRLS 0—1 WEIGHT


GIRL'S WEIGHT: (kg)
1 - 5yrs
NAME:
years
98th
91st
75th
50th
25th
9th
2nd
GIRLS
WEIGHT
1—5


GIRL'S WEIGHT: (kg)
5 - 18yrs
With provision for school reception class
NAME: .....
D.O.B. ...../...../.....
years
98th
91st
75th
50th
25th
9th
2nd
GIRLS
5-18
WEIGHT


GIRL'S LENGTH: (cm)
BIRTH - 1yr
NAME: .....
D.O.B. ...../...../.....
weeks/♀ months
weeks/♂ months
98th
91st
75th
50th
25th
9th
2nd
GIRLS
0—1
LENGTH


GIRL'S HEIGHT: (cm)
1 - 5yrs
NAME: .....
years
98th
91st
75th
50th
25th
9th
2nd
120
115
110
105
100
95
90
85
80
75
70
65
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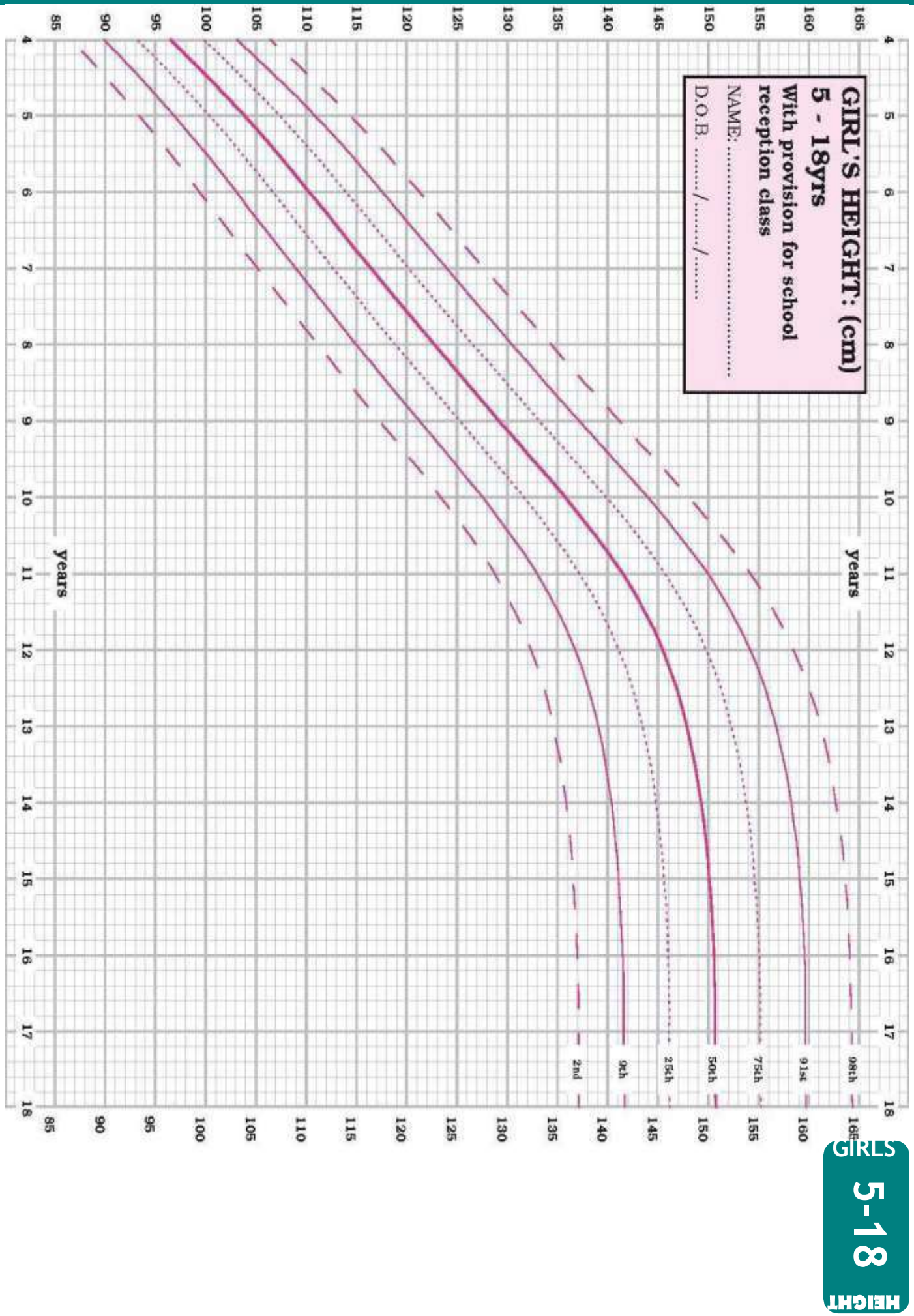
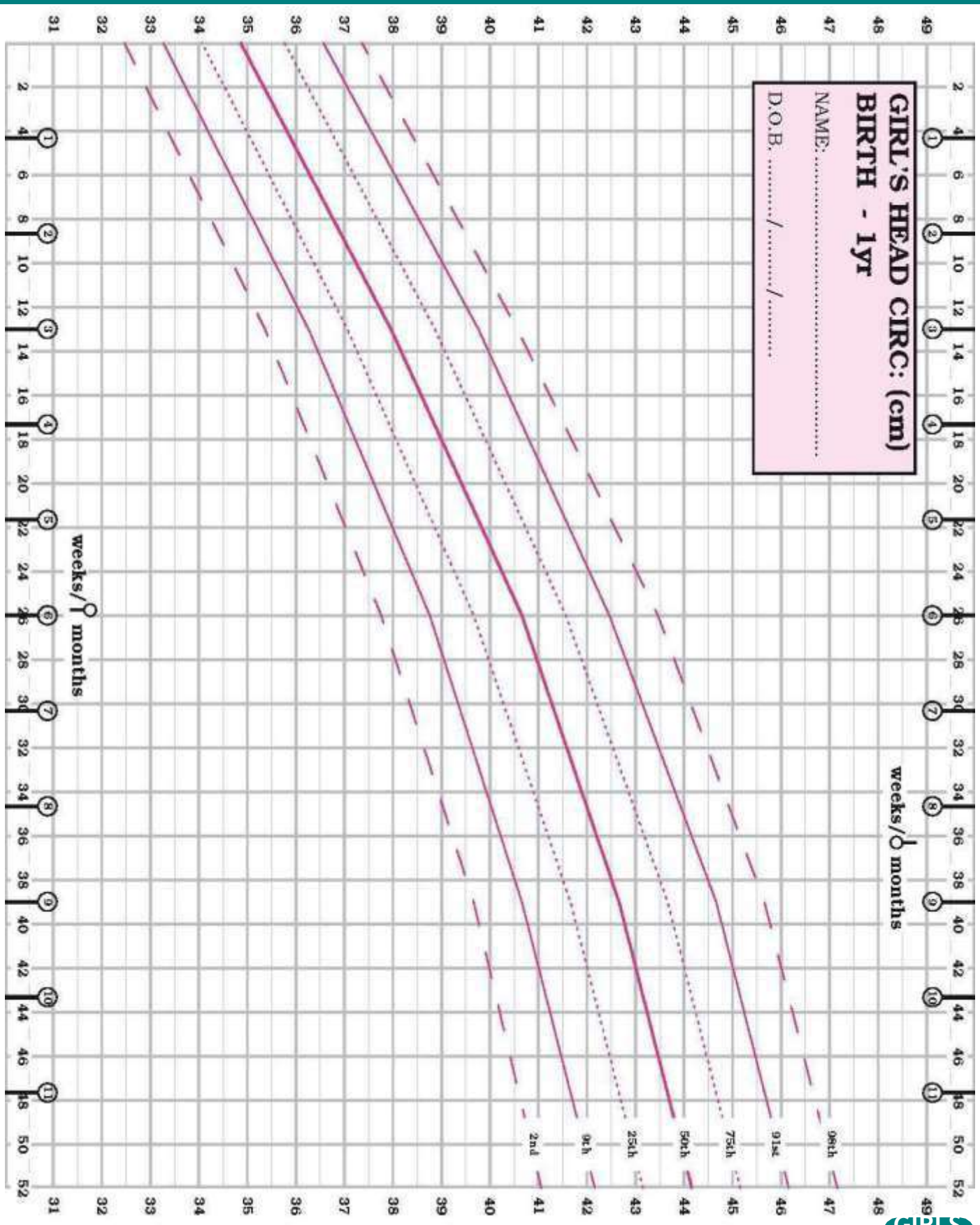
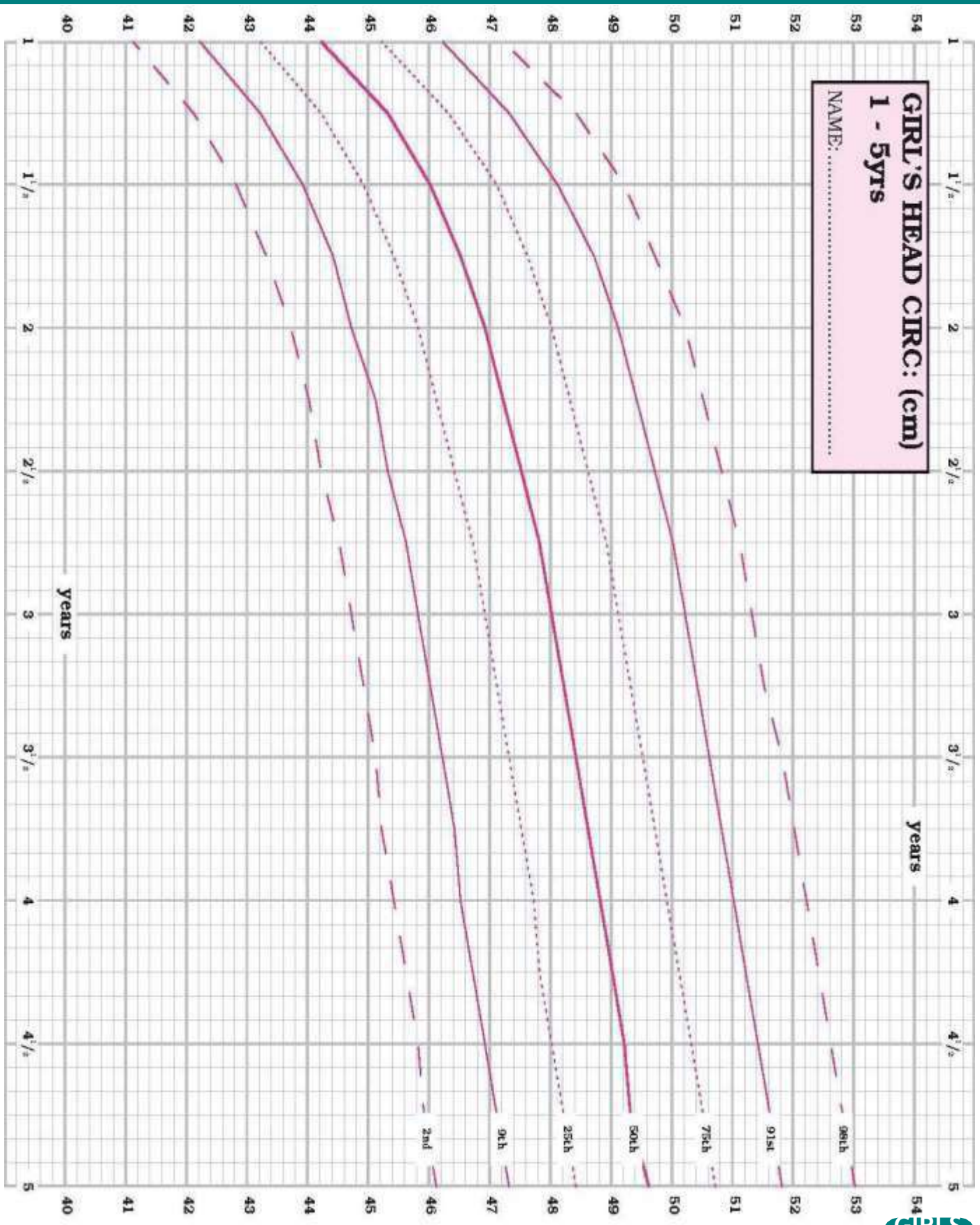
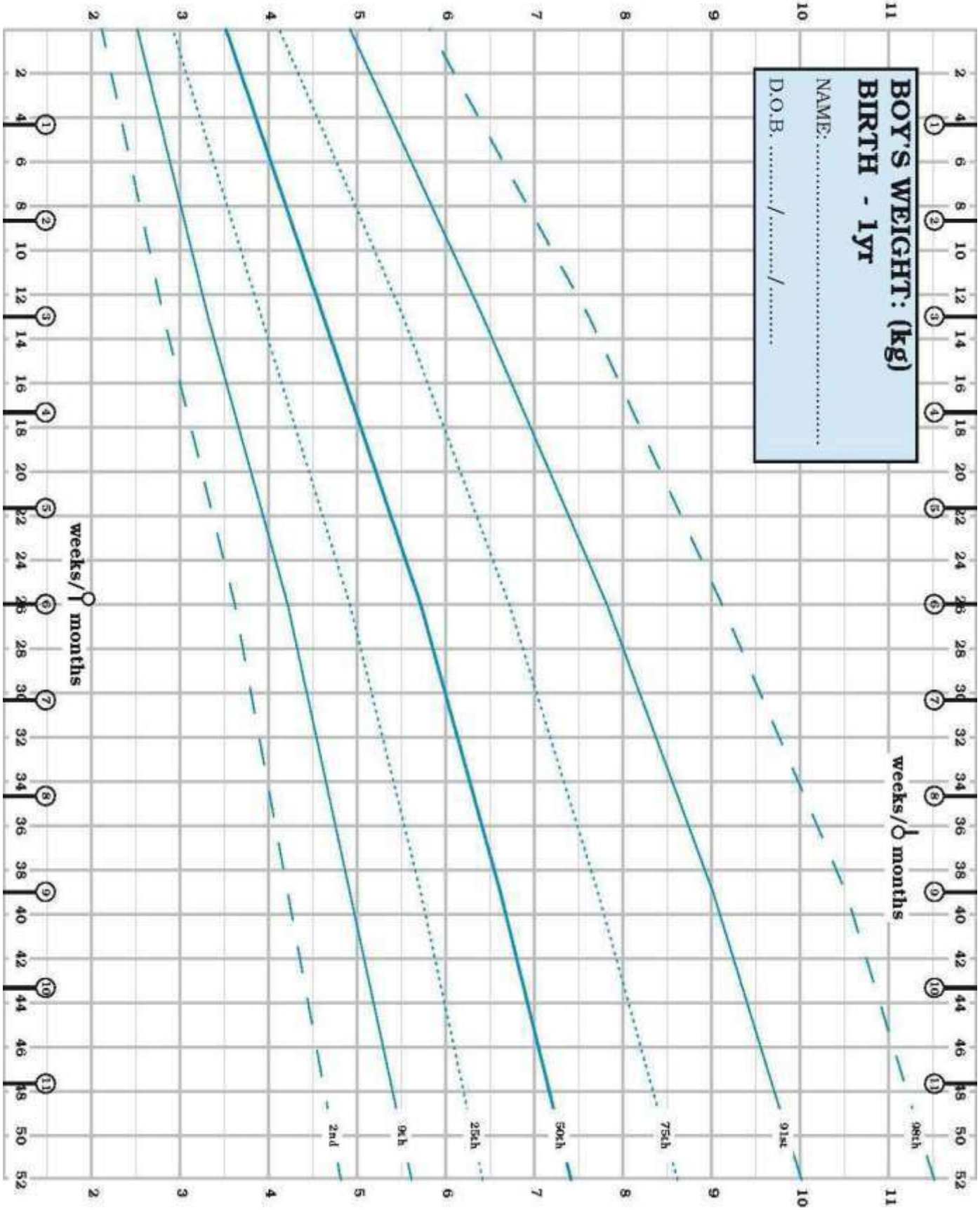
1 1/2
2
2 1/2
3
3 1/2
4
4 1/2
5

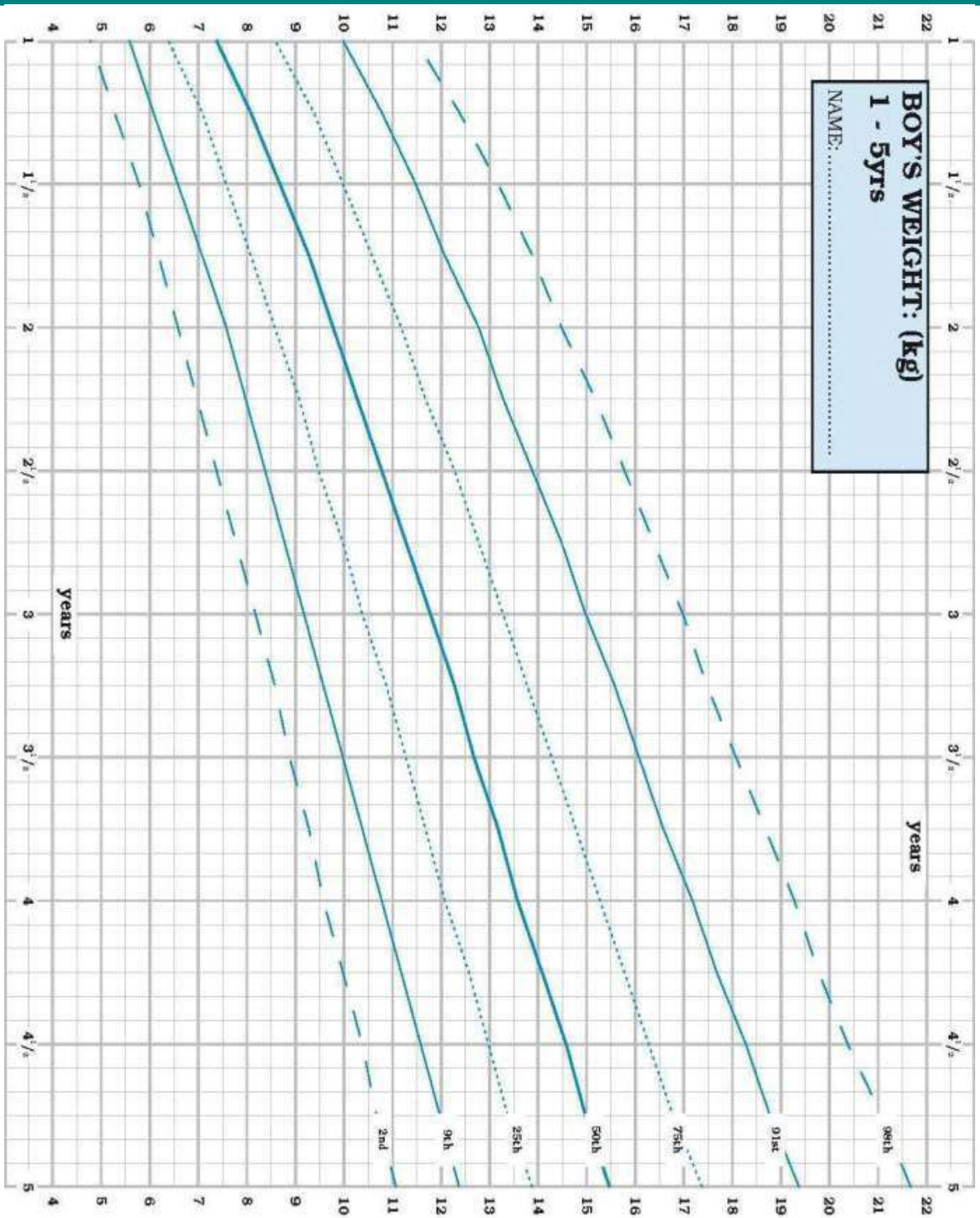

GIRL'S HEIGHT: (cm)
5 - 18yrs
With provision for school reception class
NAME: .....
D.O.B. ...../...../.....
years
98th
91st
75th
50th
25th
9th
2nd
GIRLS
5-18
HEIGHT


GIRL'S HEAD CIRC: (cm)
BIRTH - 1yr
NAME: .....
D.O.B: ...../...../.....
weeks/ months
weeks/ months
98th
91st
75th
50th
25th
9th
2nd
GIRLS
0—1
OFC

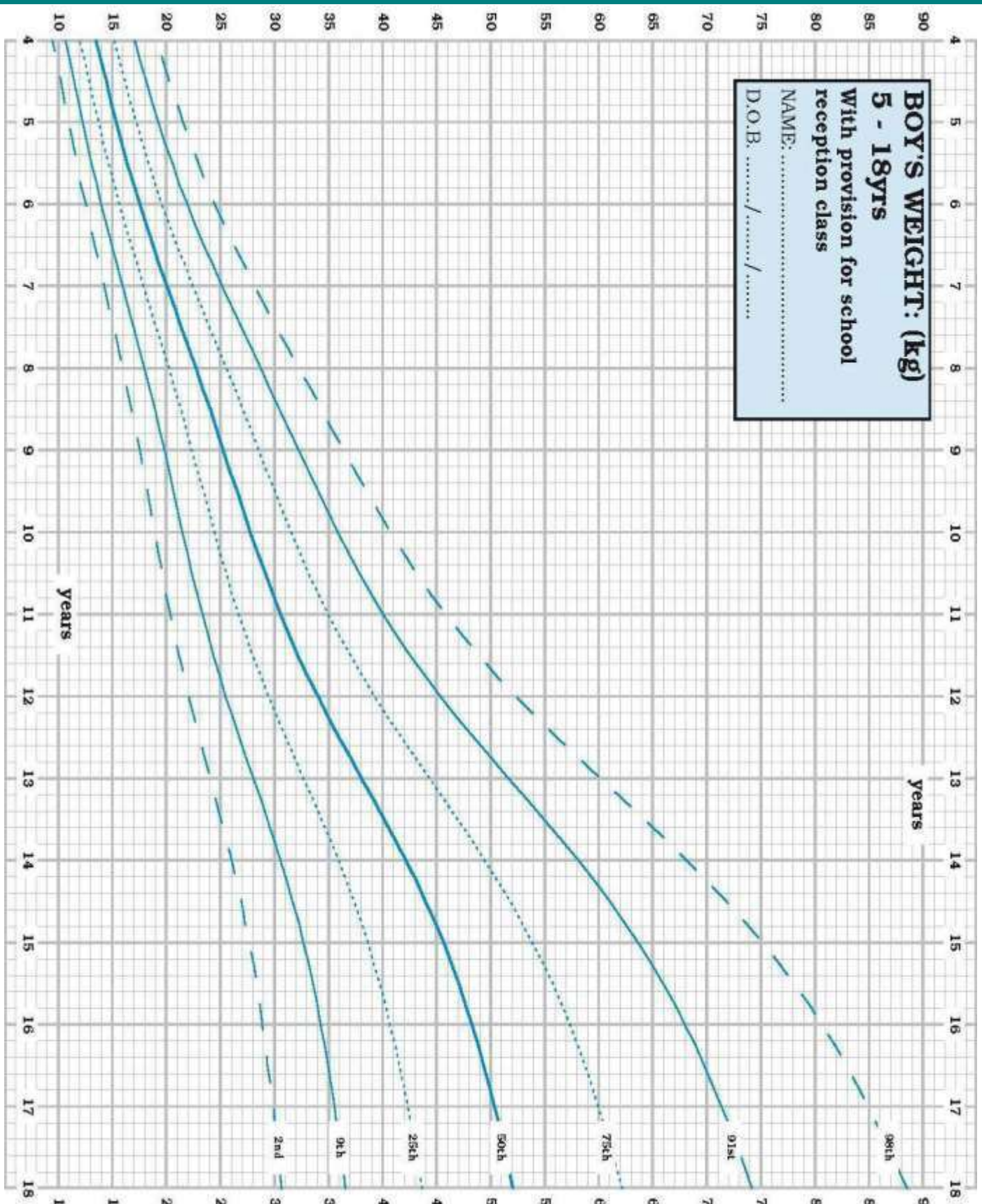

GIRL'S HEAD CIRC: (cm)
1 - 5yrs
NAME:.....
years
98th
91st
75th
50th
25th
9th
2nd
GIRLS
1—5
OFC

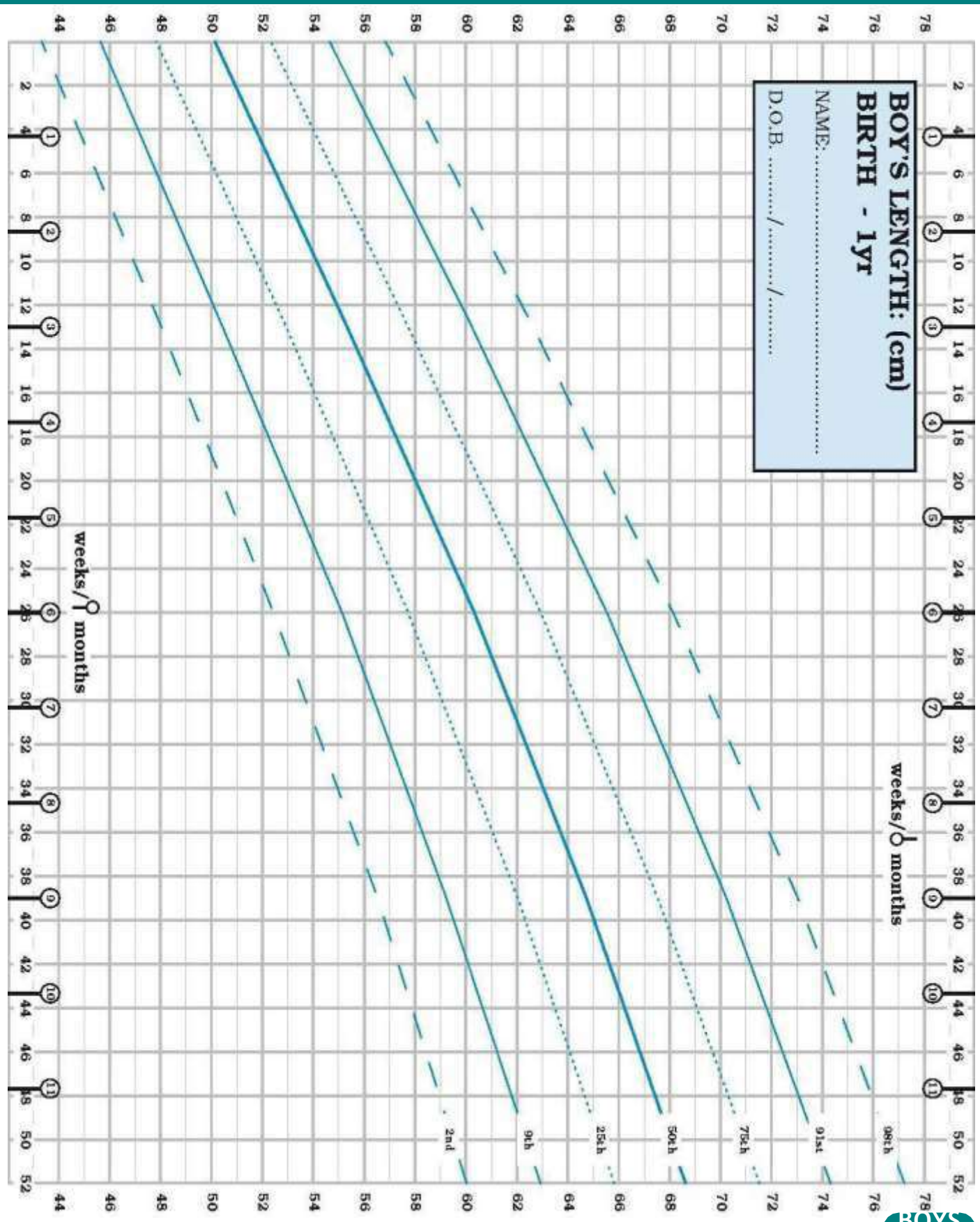



BOYS
0—1
WEIGHT

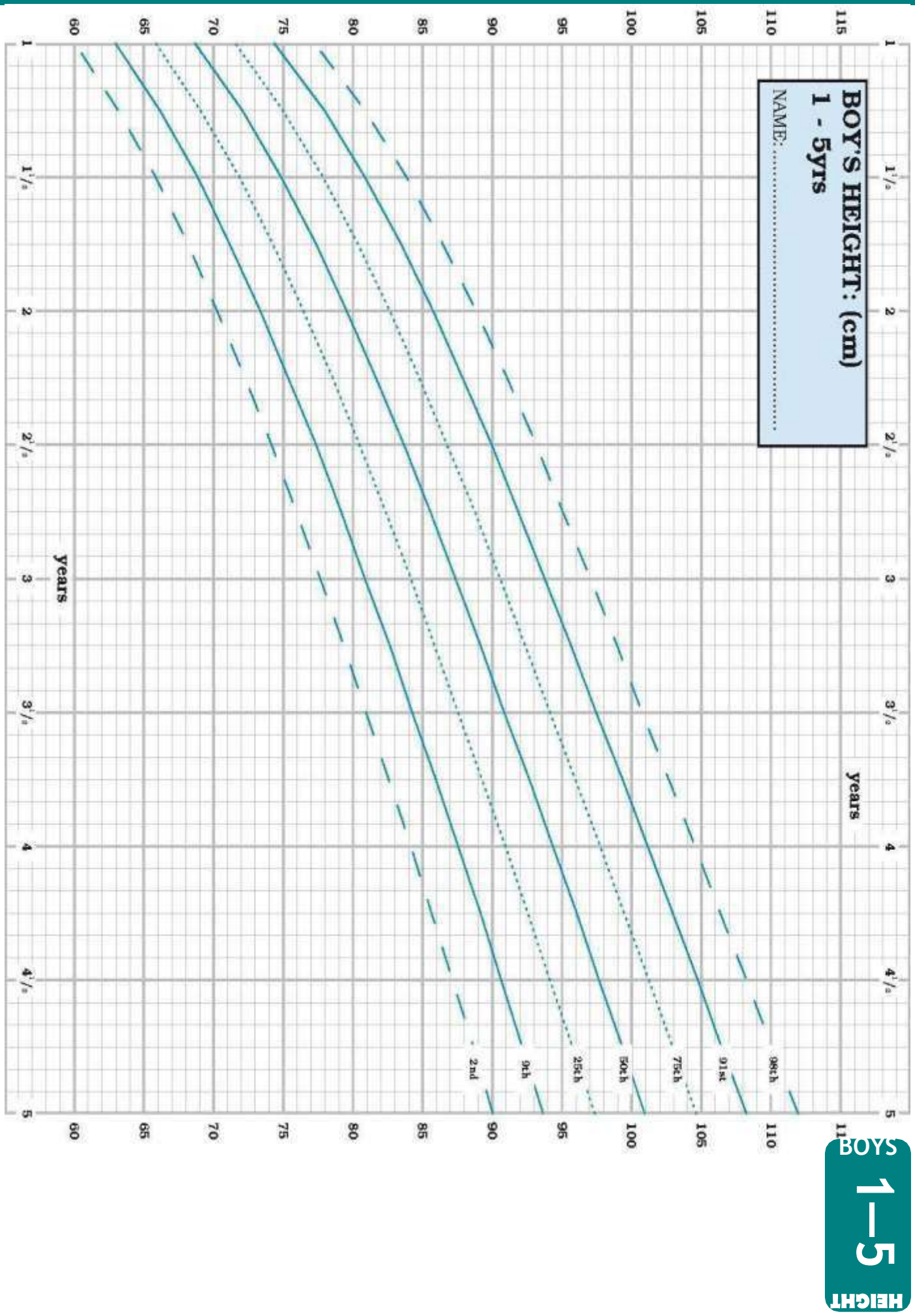


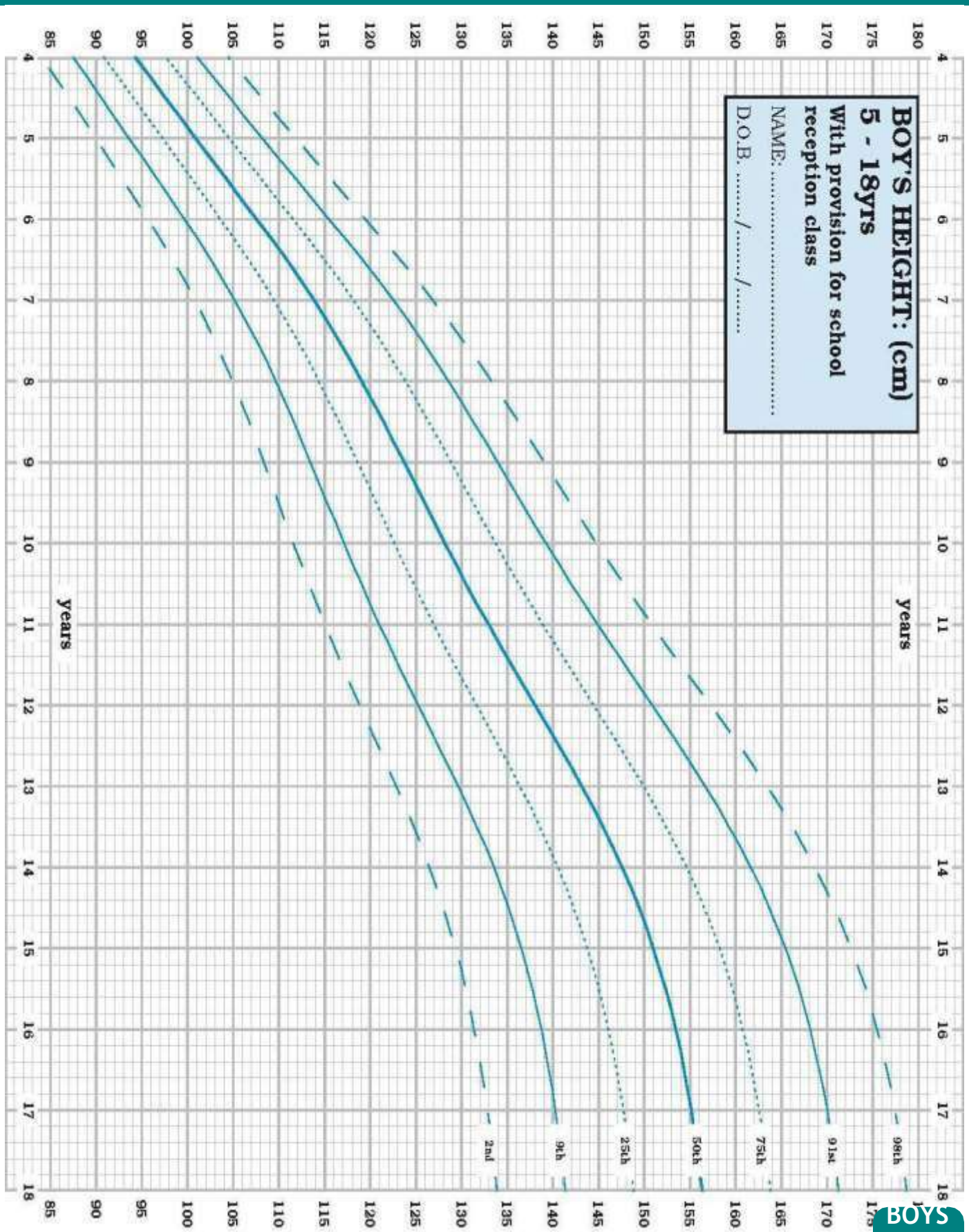

BOYS
1—5
WEIGHT

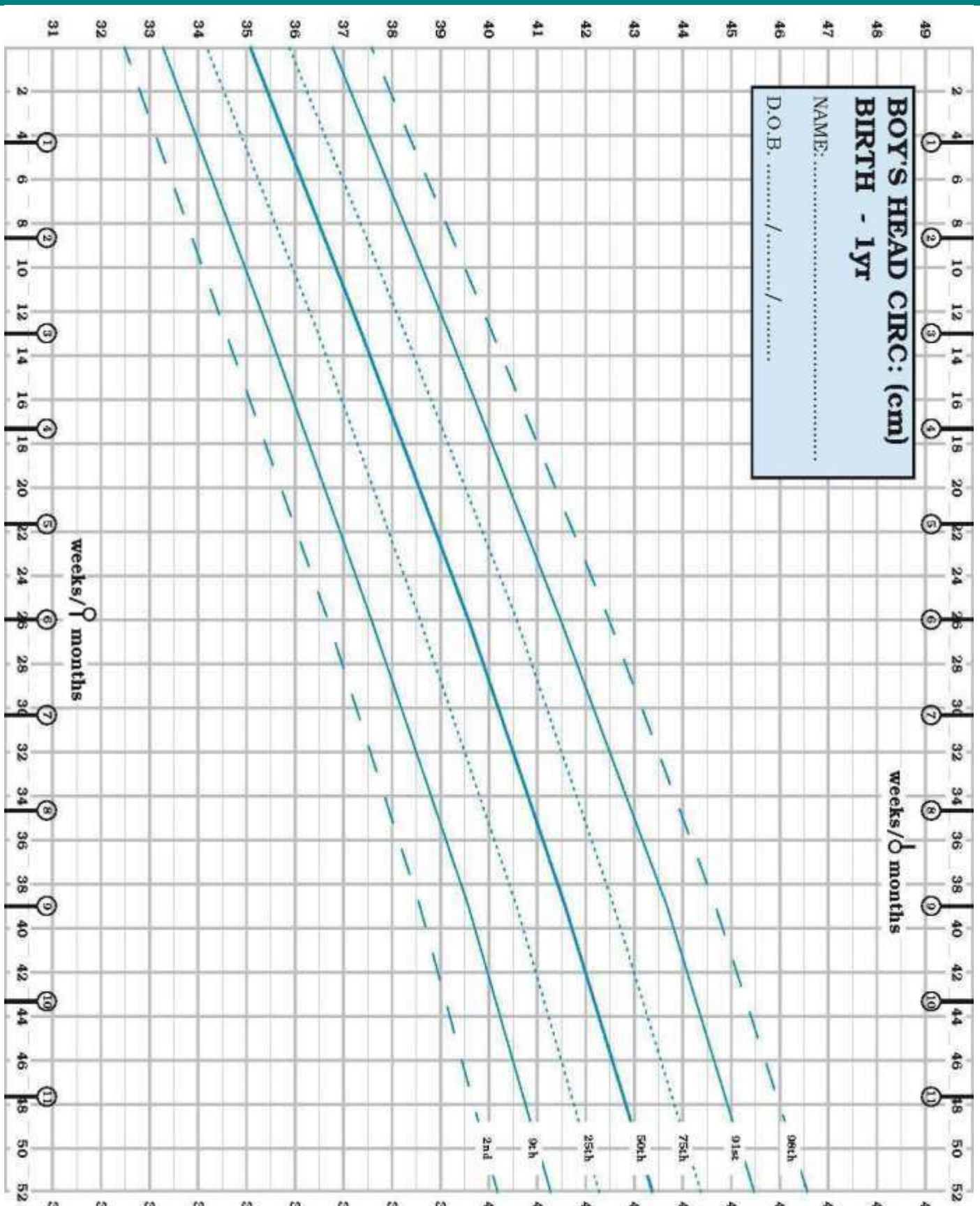

BOY'S WEIGHT: (kg)
5 - 18yrs
With provision for school reception class
NAME: .....
D.O.B. ...../...../.....
years
98th
91st
75th
50th
25th
9th
2nd
years
BOYS
5-18
WEIGHT

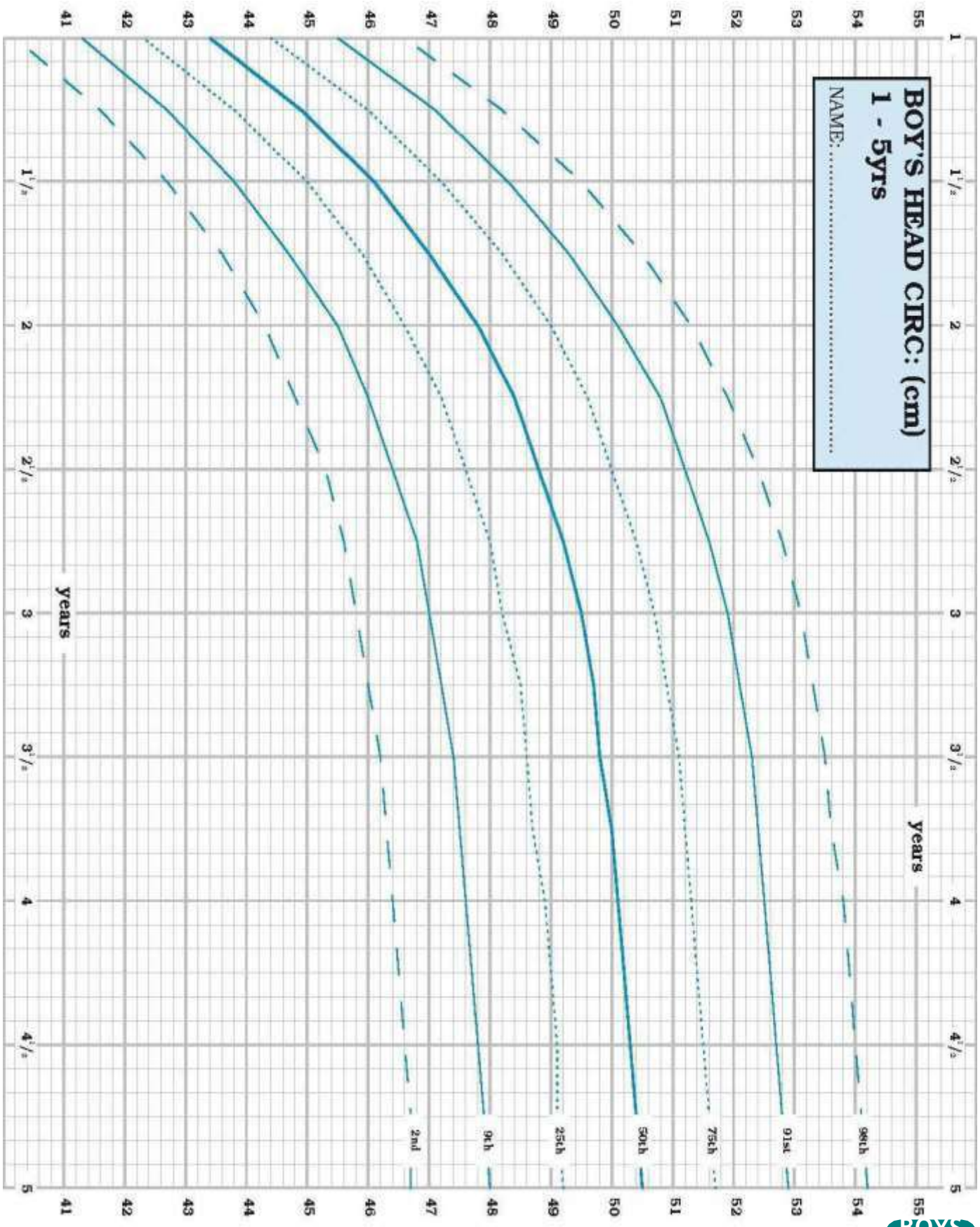



BOYS
0—1
LENGTH


BOY'S HEIGHT: (cm)
1 - 5yrs
NAME:
years
years
98th
91st
75th
50th
25th
9th
2nd
BOYS
1—5
HEIGHT


BOY'S HEIGHT: (cm)
5 - 18yrs
With provision for school reception class
NAME: .....
D.O.B. ...../...../.....
years
years
98th
91st
75th
50th
25th
9th
2nd
BOYS
5-18
HEIGHT


BOY'S HEAD CIRC: (cm)
BIRTH - 1yr
NAME: .....
D.O.B. ...../...../.....
weeks/ months
weeks/ months
2nd
9th
25th
50th
75th
91st
98th
BOYS
0—1
OFC


BOY'S HEAD CIRC: (cm)
1 - 5yrs
NAME:
years
98th
91st
75th
50th
25th
9th
2nd
BOYS
1—5
OFC

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# Summary of Investigations for Children with WilliamsSyndrome

Thetablebelowliststhetestsandscreeningwhichshouldbecarriedoutinchildrenwith WilliamsSyndrome,andspecifiesatwhatage and how often they should be undertaken. For clinical management and follow up recommendations, please see the full set of UK Clinical Management Guidelines for Williams Syndrome, available from the Williams Syndrome Foundation website : www.williams-syndrome.org.uk.

| Test/Screening | Age/Frequency | | | |
|---|---|---|---|---|
| | At diagnosis | Neonates & Infants (0—1) | Children (2—11) | Adolescents (11—18) |
| Cardiac screening | Cardiac assessment, 4 limb BP, oxygen saturation, ECG and Echocardiography | Cardiac assessment, 4 limb BP, oxygen saturation, ECG and Echocardiography | Cardiac assessment until 4 years and 5 yearly in childhood | Cardiac assessment 5 yearly |
| Hyperclacaemia / hypercalcuria screening | Blood calcium and urine calcium : creatinine ratio | Blood calcium and urine calcium : creatinine ratio | Blood calcium if symptomatic | Blood calcium if symptomatic |
| Genitourinary tract examination | Examination, blood creatinine, electrolytes and urinary tract ultrasound | Examination, blood creatinine, electrolytes and urinary tract ultrasound | Creatinine and electrolytes every 2 – 4 years and investigate if symptomatic. | Investigate if symptomatic. |
| Hypertension screening | Plasma renin activity and renal artery Doppler | Plasma renin activity and renal artery Doppler | Annual BP in both arms | Annual BP in both arms |
| Inguinal hernia examination | Examination | Examination | Annual general examination. | Annual general examination. |
| Gastrointestinal examination | Coeliac screen and growth assessment | Coeliac screen and growth assessment | Coeliac screen at 3 years and annual general examination. | Coeliac screen at 3 years and annual general examination. |
| Endocrine & growth screening | Thyroid Function Tests (TFTs) | Thyroid Function Tests (TFTs) | Annual growth assessment and measure TFTs if symptomatic. | Annual growth assessment and sexual health assessment |

# Summary of Investigations for Children with Williams Syndrome
## continued...

Thetablebelowliststhetestsandscreeningwhichshouldbecarriedoutinchildrenwith Williams Syndrome,andspecifiesatwhatageand how often they should be undertaken. For clinical management and follow up recommendations, please see the full set of UK Clinical Management Guidelines for Williams Syndrome, available from the Williams Syndrome Foundation website:www.williams-syndrome.org.uk.

| Test/Screening | Age/Frequency | | | |
|---|---|---|---|---|
| | At diagnosis | Neonates & Infants (0—1) | Children (2—11) | Adolescents (11—18) |
| Musculo skeletal screening | Examination and radiology as indicated. | Examination and radiology as indicated. | Annual general examination. | Annual general examination. |
| Dental screening | Referral to oral healthcare programme | Referral to oral healthcare programme | Annual dental examination | Annual dental examination |
| Developmental screening | Referral for multidisciplinary assessment | Referral for multidisciplinary assessment | Annual developmental assessment | |
| Auditory screening | Audiology review. | Referral to newborn hearing screening programme. | Audiology review if speech is delayed. | Assessment at 11 and 18 years for high frequency hearing loss |
| Visual screening | Referral to community orthoptist/optometrist | Referral to community orthoptist/optometrist | Visual screening at school entry by community orthoptist/optometrist. | Assessment by local optometrist as indicated. |
| Mental Health screening | | | Behavioural coaching and clinical psychology assessment as indicated | Assessment by local services as indicated. |
| Educational screening | | | Input by appropriate professionals to EHCP | Review of EHCP at 11 and 16 years. |

# Other Resources

- **PersonalHealthRecordforWilliamsSyndrome(BlueBook)**
  AllbabiesintheUK areissuedwitharedbooktorecordtheirhealth,growthanddevelopment.SimilarBlueBookshavebeen developedforseveralrareconditionsrequiringmulti-disciplinarymanagement.AspartofthisprojectaBlue BookhasbeendesignedforpeoplewithWS.TheprimaryaimoftheBlueBookistoempowerpatientsand theirfamilies,givingthemmoreinformationaboutandultimatelymorecontrolovertheirhealth.Itwillalso benefit the healthcare professionals involved in managing these patients, by facilitating inter-speciality communication, educating non-specialists and allied healthcare professionals, providing areadily accessible summary 'snapshot' of a patient's condition, and they can also be used as a tool for clinical audit and research. They are available from the Williams Syndrome Foundation patient (see below).


- **The Williams Syndrome Foundation UK(www.williams-syndrome.org.uk)**
  The Williams Syndrome Foundation is run for parents by parents. They aim to be the first point of contact for individuals with Williams Syndrome, their families, and professionals needing support and information regarding the Syndrome. The Foundation actively supports research into the educational, behavioural, social, scientific and medical aspects of the Syndrome, and seeks to organise their financial and personnel resources so as to achieve their mission on a sustainable basis.

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- **DYSCERNE: A Network of Centres of Expertise in Dysmorphology, funded by the European Commission Public Health Executive Agency (DG Sanco) Project:2006122 (www.dyscerne.org)**

- **Nowgen—A Centre for Genetics inHealthcare(www.nowgen.org.uk)**

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