Williams Syndrome Clinical Management Guidelines

Management of Williams Syndrome

A Clinical Guideline

Williams Syndrome Guideline Development Group

williams SYNDROME FOUNDATION
www.williams-syndrome.org.uk

A network of centres of expertise
dyscerne
for dysmorphology

nowgen
A Centre for Genetics in Healthcare

Contents

Introduction…

… to Williams Syndrome (WS)

Williams Syndrome is a rare condition, that occurs in 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 May 2009;

"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 where expert consensus plays a greater role. The members of the guideline development group are listed on page 40.

… to the Williams Syndrome Clinical Management Guidelines

What are the aims of the guidelines?

The existing guidelines for the medical supervision of people with WS were published in 2001 by the American Academy of Pediatrics Committee on Genetics (AAPCG). Whilst a valued addition to the available guidance these are not entirely transferable to the UK. Therefore, in order to optimise the medical management of people with WS, the aim of the guidelines is to provide clear evidence-based management recommendations applicable to UK patients.

Who are they aimed at?

As WS is so rare, it is unlikely that the primary care clinicians usually responsible for coordinating the care of people with the condition will have had much prior experience of the syndrome. As it is a multisystem disorder, people with WS require various tests, screenings, assessments, referrals and multidisciplinary interventions at different stages of their lives. These guidelines lay out these requirements in a clear format that are accessible to anybody who is involved in the care of an individual with WS.

How are they used?

The guidelines are divided into recommendations for four age groups:
- Infancy: 0—1 year old
- Childhood: 1—11 years old
- Adolescence: 11—18 years old
- Adulthood: 18 years old +

On page 4, recommended baseline investigations are listed, to be consulted alongside the age group-specific recommendations at the time of diagnosis. For each age group, the recommended tests/screenings are listed, and follow-up options depending on the outcome of the test or screening are indicated.

NB. ABNL= Abnormal

Clinical features and recommended baseline investigations in Williams Syndrome

Clinical Features of Williams Syndrome	Baseline investigations (where investigation not 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 e.g. FISH test*	
• Congenital heart defects (especially supravalvular aortic stenosis (SVAS) and peripheral pulmonary artery stenosis)	• Full cardiovascular assessment including scans and BP (blood pressure) measurement in both upper limbs.
• Raised blood/urine calcium levels	• Serum Ca and Urine Ca: Creatinine Ratio
• Nephrocalcinosis, bladder and renal tract abnormalities	• Renal tract ultrasound to include kidneys and bladder
• Endocrine abnormalities	• Thyroid Function Tests (TFTs)
• Failure to thrive/slow growth rate/feeding problems	• Plot growth on appropriate Williams Syndrome growth chart (see pages 14 and 15)
• Hypertension • Scoliosis and other musculoskeletal problems • Gastrointestinal problems • Distinctive facial features • Dental anomalies • Distinctive behavioural characteristics including irritability, anxiety, overfriendliness • Hypersensitivity to noise	

*Fluorescence in situ hybridisation (FISH) is the most common, but not the only available test for confirming a diagnosis of Williams Syndrome. Some laboratories may use other DNA-based diagnostic techniques.

Recommendations for the management of Williams Syndrome

~ in neonates & infancy (1) ~

AGE 0—1

Recommended Testing/Screening		Clinical Management Recommendations
• **Serum Ca and Urine Ca: creatinine ratio**	→	If normal and under 1 year old, repeat test at 12 months.
	ABNL →	Management of Hypercalcaemia - calcium intake should be equal to or less than half of the recommended nutrient intake (RNI) for the patient's age group. - stop use of supplements containing calcium. - Ensure that infant feeds are prepared using 'soft' water. - Ensure adequate rehydration. - Locasol formula milk (SHS Nutrition) - Steroids (Prenisolone), orally as necessary. - Monitor blood pressure - take sunblock if travelling/in sunny conditions. - 3 monthly follow up. - If serum PTH starts to rise, relax calcium intake but monitor blood and urine calcium levels. - Consider referral to paediatric metabolic bone disorder specialist. - In rare cases, where hypercalcaemia is refractory to hydration and low-calcium diet, intravenous Pamidronate may be necessary.
• **Thyroid Function Tests (TFTs)**	→	Ensure baseline test undertaken. Repeat thyroid function test if patient symptomatic.
	ABNL →	Measure TSH levels and if elevated, consider thyroid scanning.
• **Renal tract screening to include kidneys and bladder**	ABNL →	If nephrocalcinosis refer to nephrologist for 6 monthly screening. If structural abnormalities, management or referral as necessary.
• **Hypertension screening**	→	Annual monitoring of blood pressure in both upper limbs and left leg.
	ABNL →	If associated with renal artery stenosis (RAS), refer to nephrologist. Surgical treatment where necessary. **NB.** If RAS is present, angioplasty is not recommended due to elastinopathy. If essential hypertension, manage with calcium channel blockers where medical management is required (and RAS has been ruled out).
• **Cardiac screening**	→	Full cardiac assessment including scans before one year old if diagnosis made in neonatal period. Annual cardiac examination until 4 years old. Follow up by cardiologist.

Recommendations for the management of Williams Syndrome

~ in neonates & infancy (2) ~

AGE 0—1

Recommended Testing/Screening		Clinical Management Recommendations
• **Feeding & Gastrointestinal issues**	→	Take feeding history. Enquire about bowel habit.
	ABNL →	If problems, refer for appropriate support and treat constipation.
• **Growth**	→	Measure height, weight and occipitofrontal circumference (OFC) at birth and 1-3 monthly.
	ABNL →	Routine paediatric investigations for failure to thrive and reduced growth velocity.
• **Hearing screening**	→	NHS newborn hearing screening programmes throughout UK (NHSP) - screening within the first few weeks.
• **Vision screening**	→	Visual screening should take place between 6 and 12 months. Parents to report any concerns.
	ABNL →	Refer to community optometric/orthoptic service (via GP) if abnormality found.
• **Screening for dental anomalies**	→	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.
	ABNL →	Missing teeth/malocclusion/other dental anomalies: refer to a consultant in paediatric dentistry for multidisciplinary management.
• **Multidisciplinary developmental assessment**	→	Between 0-3 years old. Coordinated by hospital or community paediatrician.

! Anaesthesia

A paediatric anaesthetist should be involved in the pre-op care of children up to 3-4 years old.
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.

Recommendations for the management of Williams Syndrome

~ in childhood (1) ~

AGE 1—11

Recommended Testing/Screening		Clinical Management Recommendations
• **Serum creatinine**	→	In all WS children, test serum creatinine every 2—4 years.
	ABNL →	Investigate/refer as appropriate—check for infection, exclude obstructive lesion(s), undertake detailed renal function tests and/or refer to a nephrologist.
• **Serum Ca and Urine Ca: creatinine ratio**	→	If normal when under 1 year old, repeat test at 12 months.
	ABNL →	Management of Hypercalcaemia - Calcium intake should be equal to or less than half of the recommended nutrient intake (RNI) for the patient's age group. - Stop use of supplements containing calcium. - Ensure that infant feeds are prepared using 'soft' water. - Ensure adequate rehydration. - Locasol formula milk (SHS Nutrition) - Steroids (Prenisolone), orally as necessary. - Monitor blood pressure - Take sunblock if travelling/in sunny conditions. - 3 monthly follow up. - If serum PTH starts to rise, relax calcium intake but monitor blood and urine calcium levels. - Consider referral to paediatric metabolic bone disorder specialist. - In rare cases, where hypercalcaemia is refractory to hydration and low-calcium diet, intravenous Pamidronate may be necessary.
		Monitor for 1—2 years after hypercalcaemia has resolved.
• **Thyroid Function Tests (TFTs)**	→	Test if patient is symptomatic.
	ABNL →	Measure TSH levels and if elevated, consider thyroid scanning, Consider referral to endocrinologist for treatment with L-Thyroxine if patient has overt hypothyroidism, or progressive deterioration of thyroid function.
• **Renal screening**	→	Renal tract ultrasound to include kidneys and bladder if symptomatic.
	ABNL →	If nephrocalcinosis refer to nephrologist for 6 monthly screening.
• **Hypertension screening**	→	Annual monitoring of blood pressure in both upper limbs and left leg.
	ABNL →	If associated with renal artery stenosis (RAS), refer to nephrologist. Surgical treatment where necessary. **NB.** If RAS is present, angioplasty is not recommended due to elastinopathy. If essential hypertension, manage with calcium channel blockers where medical management is required (and RAS has been ruled out).

Recommendations for the management of Williams Syndrome

~ in childhood (2) ~

AGE 1—11

Recommended Testing/Screening		Clinical Management Recommendations
• **Cardiac screening**	→	Annual cardiac examination until 4 years old, and once between 5-13 years old. Full cardiac assessment including scans every 5 years.
• **Feeding & Gastrointestinal issues**	→	Enquire about feeding problems annually. Enquire about bowel habit annually.
	ABNL →	Treat constipation.
• **Screen for coeliac disease**	→	Once, after 3 years of age, with low threshold to repeat if suggestive symptoms.
• **Growth & Puberty**	→	Height, weight and OFC measurements 1-3 monthly until 2 years of age. Annually thereafter (use WS growth charts). Mid parental height centile should be estimated. Check spine clinically for kypho/scoliosis at puberty and x-ray/refer to orthopaedic team as indicated.
	ABNL →	Routine paediatric investigations for abnormal growth velocity and precocious puberty (< 8 years). Where necessary, consider gonadotropin releasing hormone (GnRH) therapy.
• **Hearing screening**	→	18 months: screen for otitis media with effusion (OME) & hyperacusis 3 years: screen for OME & language development 5-10 years: screen for hyperacusis & hearing loss 11-18 years: screen for hyperacusis & high frequency hearing loss
	ABNL →	If hyperacusis, implement a programme of desensitisation (plus maskers if necessary).
• **Vision screening**	→	Visual screening should take place between 6 and 12 months. Parents to report any concerns.
	ABNL →	Refer to community optometric/orthoptic service (via GP) if abnormality found.
• **Screening for dental anomalies**	→	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.
	ABNL →	Missing teeth/malocclusion/other dental anomalies: refer to a consultant in paediatric dentistry for multidisciplinary management.

Recommendations for the management of Williams Syndrome

~ in childhood (3) ~

AGE 1—11

Recommended Testing/Screening	Clinical Management Recommendations
• **Multidisciplinary developmental assessment**	Between 0-3 years old. Should involve local Child Development/ Learning Difficulties (LD) Teams. Involve Child and Adolescent Mental Health Services (CAMHS) if necessary.
	Ongoing review and support of learning and development with further assessment of special educational needs as required.
• **Behavioural & Mental Health issues**	Behavioural management advice and support to family as required. Refer for psychological intervention for anxiety, and when major life events.

! Anaesthesia

A paediatric anaesthetist should be involved in the pre-op care of children up to 3-4 years old.
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.

Recommendations for the management of Williams Syndrome

~ in adolescence (1) ~

AGE 11-18

Recommended Testing/Screening		Clinical Management Recommendations
• **Serum creatinine**		In all WS adolescents, test serum creatinine every 2—4 years.
	ABNL	Investigate/refer as appropriate—check for infection, exclude obstructive lesion(s), undertake detailed renal function tests and/or refer to a nephrologist.
• **Serum Ca and Urine Ca: creatinine ratio**		Test if symptomatic of hypercalcaemia.
	ABNL	If abnormal, investigate and manage as appropriate.
• **Thyroid Function Tests (TFTs)**		Test if patient is symptomatic.
	ABNL	Measure TSH levels and if elevated, consider thyroid scanning, Consider referral to endocrinologist for treatment with L-Thyroxine if patient has overt hypothyroidism, or progressive deterioration of thyroid function.
• **Renal screening**		Renal tract ultrasound at puberty, before leaving paediatric care, and 5 yearly thereafter, or if symptomatic.
	ABNL	If nephrocalcinosis refer to nephrologist for 6 monthly screening.
• **Hypertension screening**		Annual monitoring of blood pressure.
	ABNL	If associated with renal artery stenosis (RAS), refer to nephrologist. Surgical treatment where necessary. **NB.** If RAS is present, angioplasty is not recommended due to elastinopathy.
		If essential hypertension, manage with calcium channel blockers where medical management is required (and RAS has been ruled out).
• **Cardiac screening**		Cardiac examination once between 5-13 years old and 13-21 years old (follow up if symptomatic). Full cardiac assessment including scans every 5 years.
• **Gastrointestinal issues**		Enquire about bowel habit annually.
	ABNL	Treat constipation and consider investigating for diverticular disease.

Recommendations for the management of Williams Syndrome

~ in adolescence (2) ~

AGE 11-18

Recommended Testing/Screening		Clinical Management Recommendations
• **Screen for coeliac disease**	→	If patient symptomatic.
• **Growth & Sexual Health**	→	Check spine clinically for kypho/scoliosis at puberty and x-ray/refer to orthopaedic team as indicated. Weigh annually, and avoid excessive weight gain. Offer contraceptive advice/contact details of organisations who can advise on contraception for people with learning disabilities.
	ABNL →	Consider GnRH therapy for precocious puberty.
• **Hearing screening**	→	11-18 years: screen for hyperacusis & high frequency hearing loss
	ABNL →	If hyperacusis, implement a programme of desensitisation (plus maskers if necessary).
• **Screening for dental anomalies**	→	Ensure patient enrolled in an individualised preventative oral healthcare programme. Routine follow up and regular dental examinations by a family dentist or local community dental services are essential.
	ABNL →	Missing teeth/malocclusion/other dental anomalies: refer to a consultant in paediatric dentistry for multidisciplinary management.
• **Multidisciplinary developmental assessment**	→	Should involve local Child Development/ Learning Difficulties (LD) Teams. Involve Child and Adolescent Mental Health Services (CAMHS) if necessary. Ongoing review and support of learning and development with further assessment of special educational needs as required. Referral to local Connexions service may be appropriate/helpful.
• **Behavioural & Mental Health issues**	→	Behavioural management advice/support for family as required. Access to social skills training, and programmes to teach basic self help and daily living skills. Refer for psychological intervention for anxiety, and when major life events. **NB.** Apparent friendliness and sociability can mask depression and anxiety.

! Anaesthesia

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.

Recommendations for the management of Williams Syndrome

~ in adulthood (1) ~

AGE 18+

Recommended Testing/Screening		Clinical Management Recommendations
• **Serum creatinine**		In all WS adults, test serum creatinine every 2—4 years.
	ABNL	Investigate/refer as appropriate—check for infection, exclude obstructive lesion(s), undertake detailed renal function tests and/or refer to a nephrologist.
• **Serum Ca and Urine Ca: creatinine ratio**		Test if symptomatic of hypercalcaemia.
	ABNL	If abnormal, investigate and manage as appropriate.
• **Thyroid Function Tests (TFTs)**		Test if/when patient is symptomatic, and check for anti-thyroid antibodies.
	ABNL	Measure TSH levels and if elevated, consider thyroid scanning, If compensated hypothyroidism present, refer to endocrinologist and monitor TFT and TSH annually. If TSH level significantly low, consider thyroid replacement therapy.
• **Renal screening**		Bladder & kidney ultrasonography every 5 years and if/when symptomatic.
	ABNL	If nephrocalcinosis refer to nephrologist for 6 monthly screening.
• **Hypertension screening**		Annual monitoring of blood pressure.
	ABNL	If associated with renal artery stenosis (RAS), refer to nephrologist. Surgical treatment where necessary. **NB.** If RAS is present, angioplasty is not recommended due to elastinopathy.
		If essential hypertension, manage with calcium channel blockers where medical management is required (and RAS has been ruled out). Consider referral to renal specialist for care of adults with hypertension.
• **Cardiac screening**		Full assessment including scans, every 5 years throughout life.

Recommendations for the management of Williams Syndrome

~ in adulthood (2) ~

AGE 18+

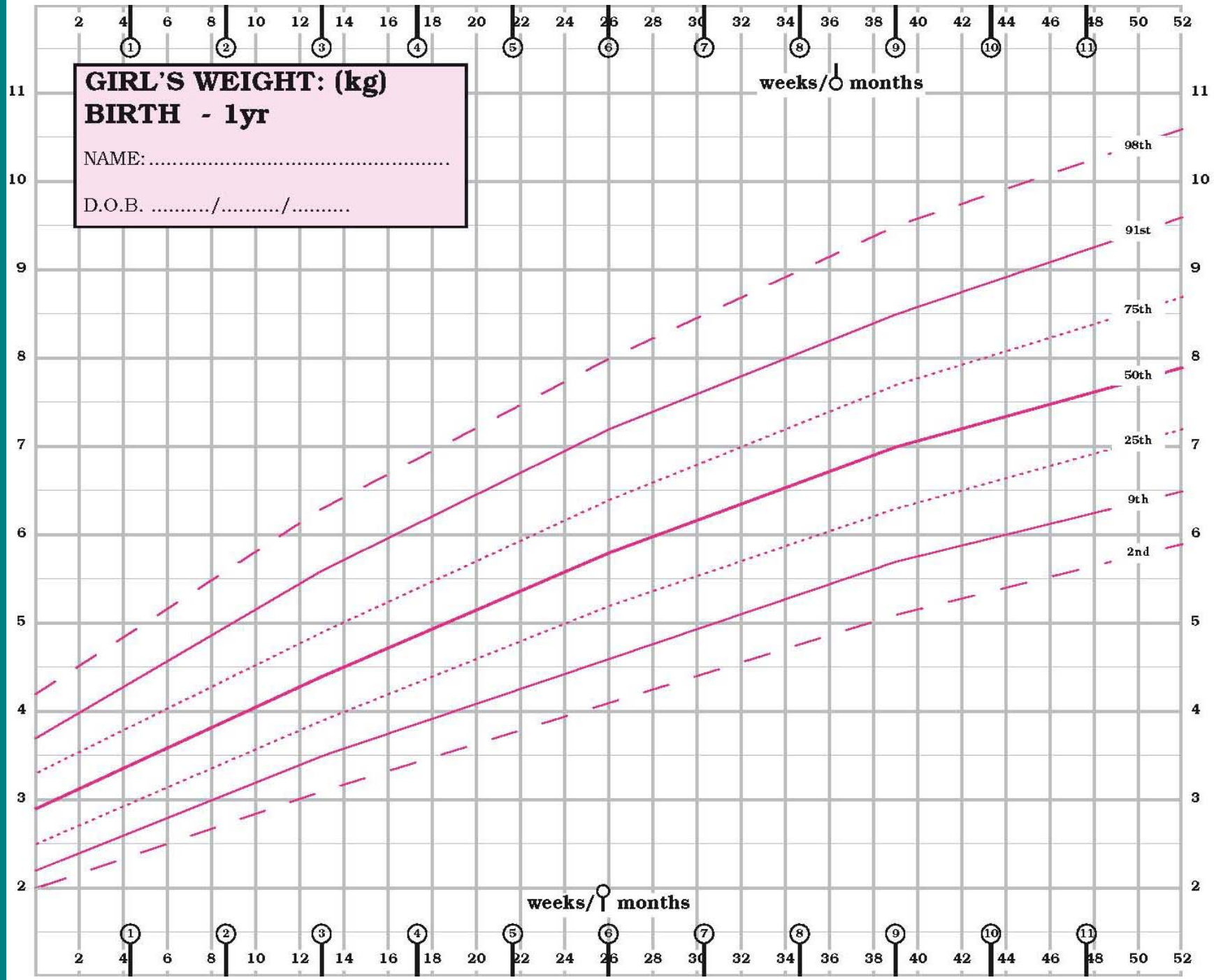
Recommended Testing/Screening		Clinical Management Recommendations
• **Gastrointestinal issues**		Enquire about bowel habit annually.
	ABNL	Treat constipation and consider investigating for diverticular disease.
• **Screen for coeliac disease**		If patient symptomatic.
• **Screening for diabetes**		At 30 years old: Oral Glucose Tolerance Test (OGTT), (or fasting insulin if considered more appropriate). Repeat OGTT if rapid weight gain. NB/ Do **not** use haemoglobin A1C as a screening tool.
	ABNL	Control impaired glucose tolerance with exercise & diet. Avoid large glucose loads over a short time period. Avoid diabetogenic drugs. Manage clinical diabetes in WS in the same way as in general population.
• **Growth & Sexual Health**		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.
• **Hearing screening**		Every 10 years (for hearing loss and wax build-up).
• **Screening for dental anomalies**		Routine follow up and regular dental examinations by a family dentist or local community dental services are essential.
	ABNL	Missing teeth/malocclusion/other dental anomalies: refer to a consultant in Adult Restorative Dentistry or Special Care for multidisciplinary management.
• **Behavioural & Mental Health issues**		Access to support for employment, self help and independent living. Social skills intervention as needed. Refer for psychological intervention/support for anxiety, and when major life events. **NB.** Apparent friendliness and sociability can mask depression and anxiety.

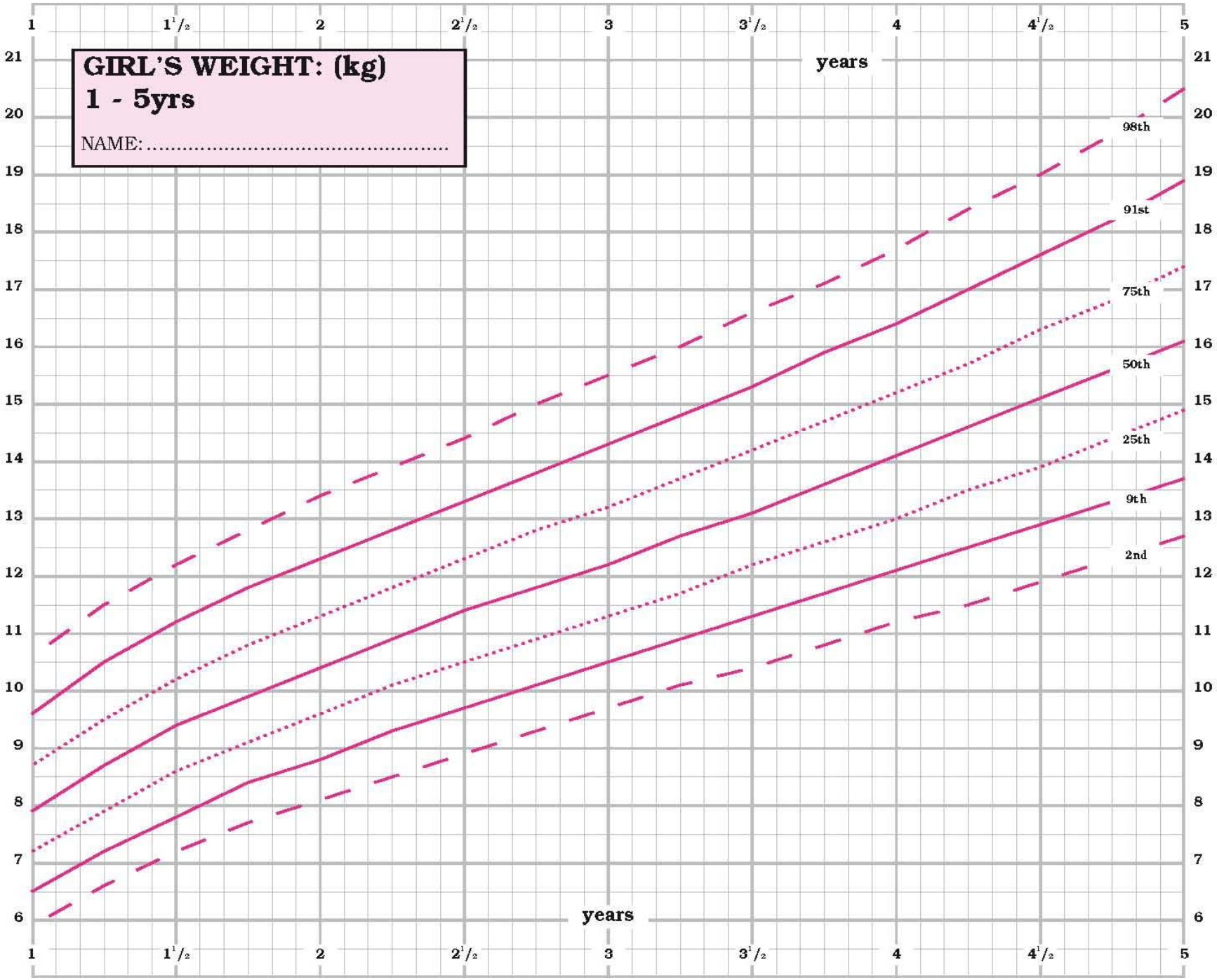
! Anaesthesia

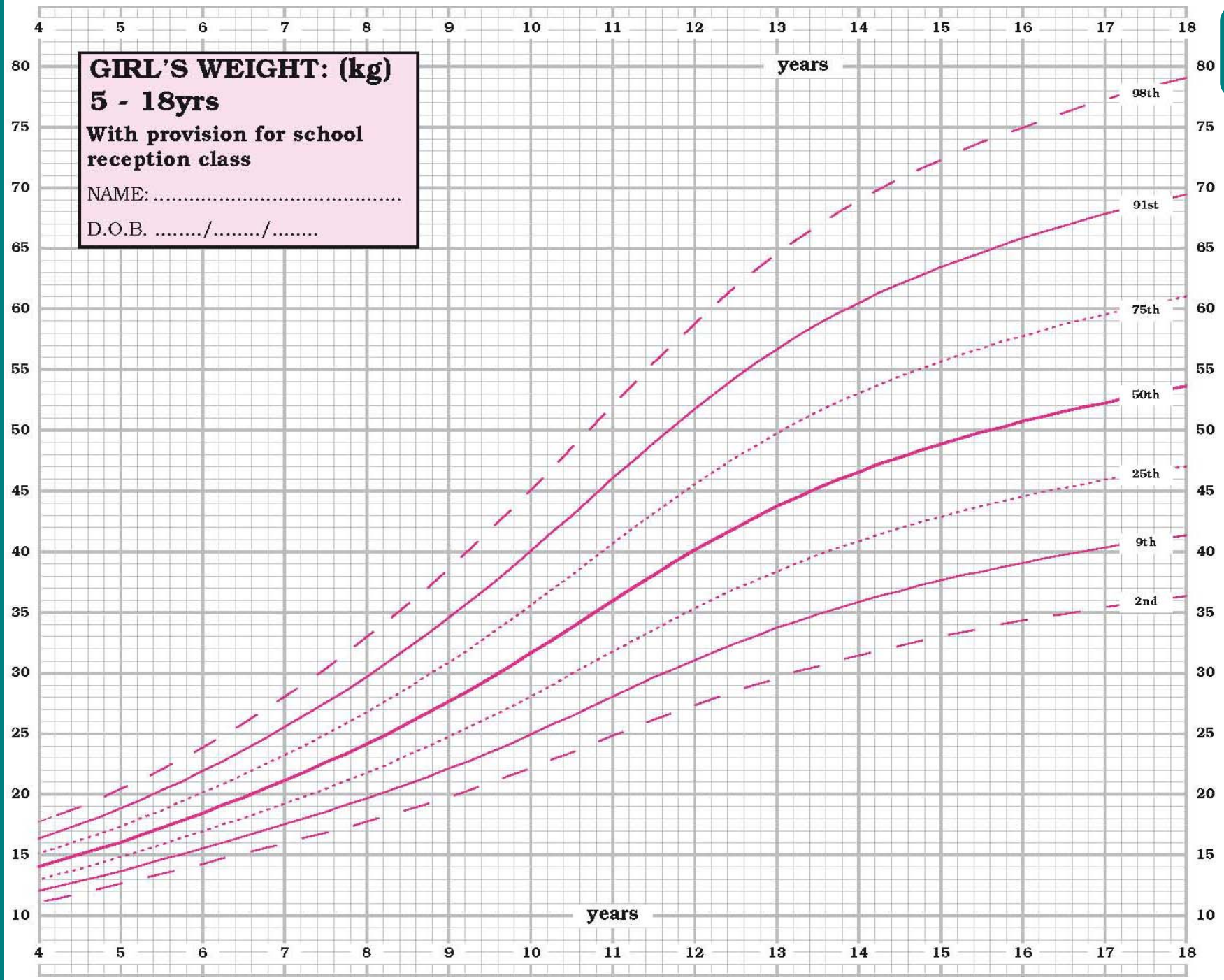
Unless there are existing cardiac problems, cardiac assessment within 12 months prior to a general anaesthetic is sufficient.
Pre-op assessment should take place 1-2 weeks prior to planned surgery, to assess cardiac, airway, joints, renal and emotional status.

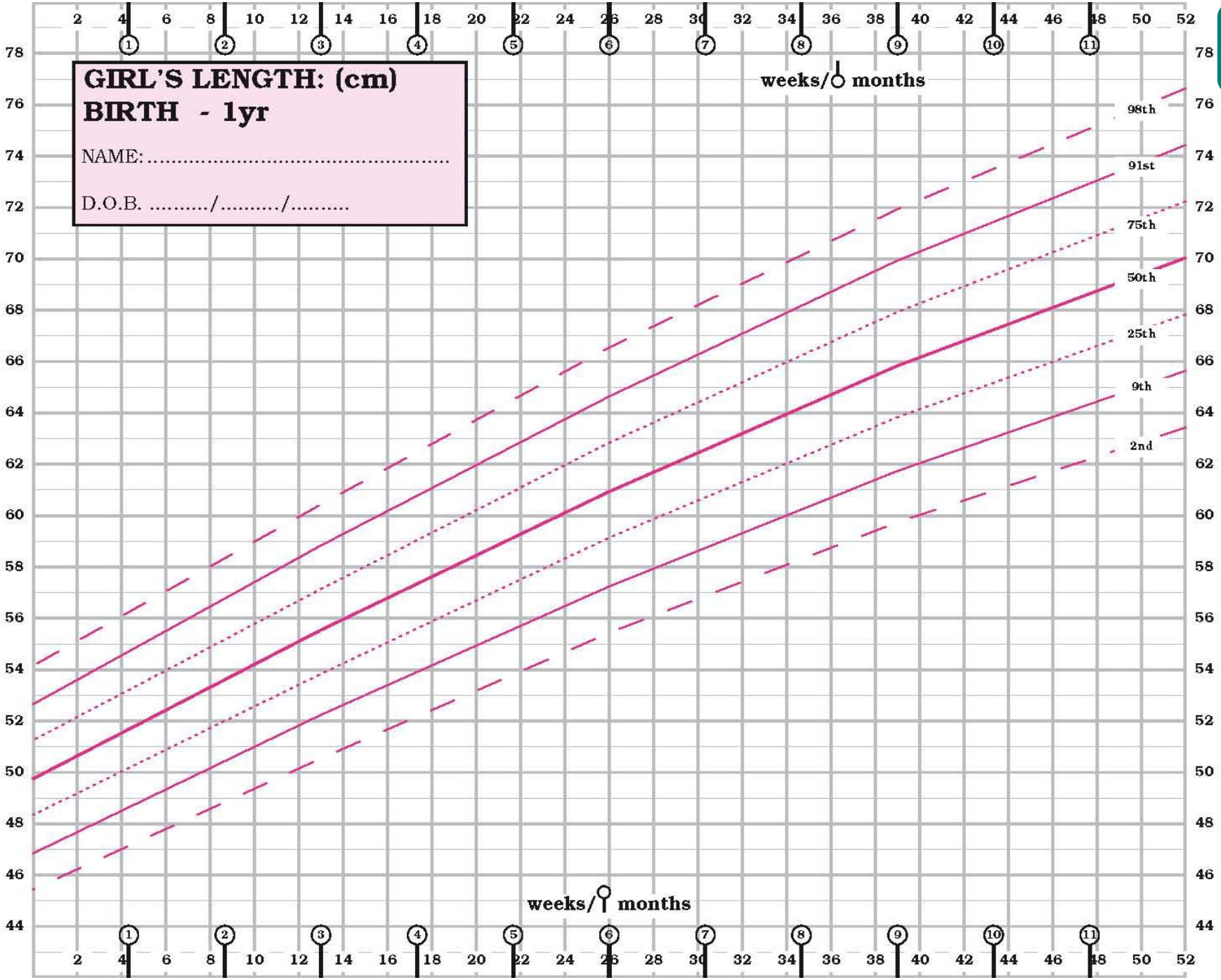
Williams Syndrome Growth Charts

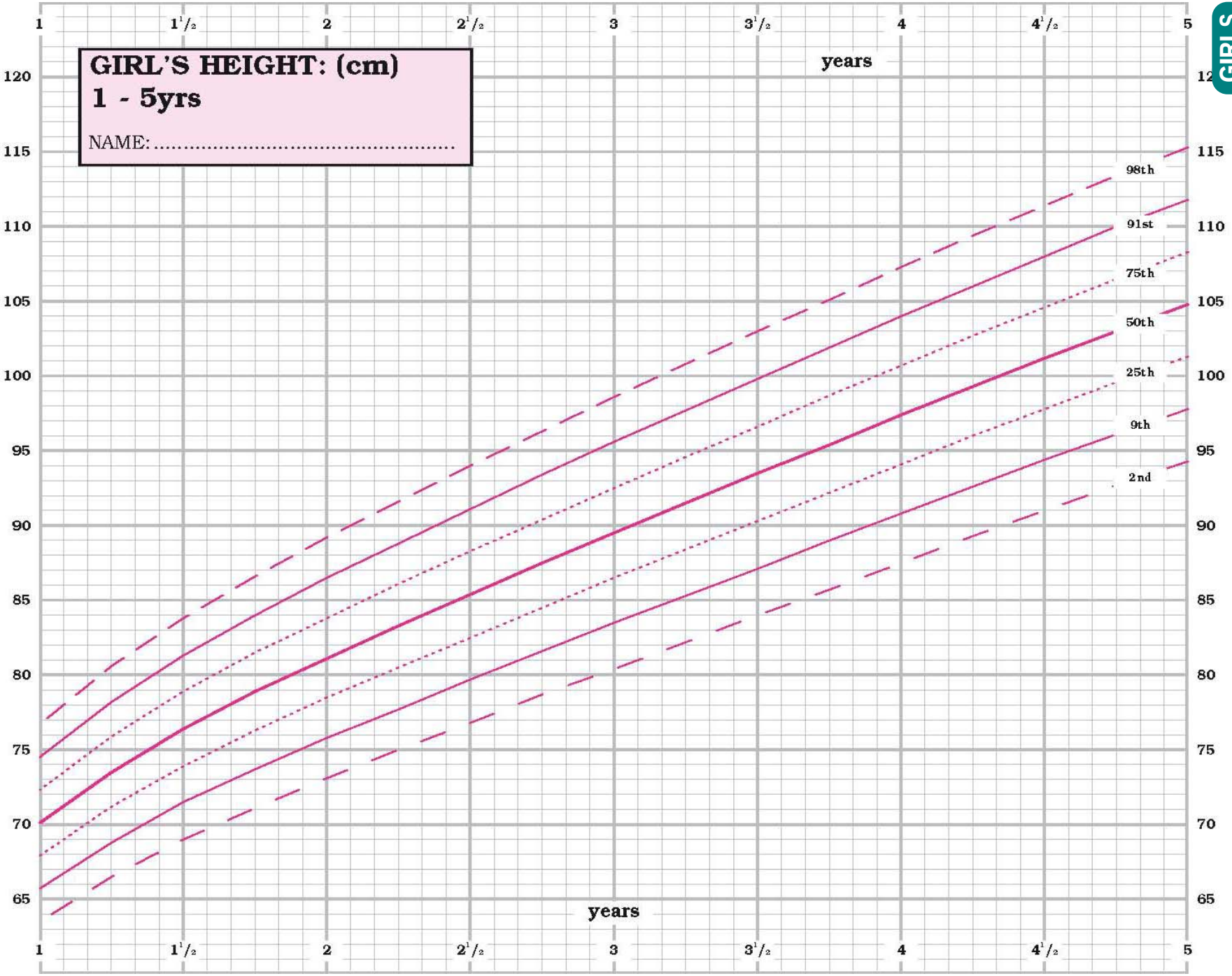
From: Martin, N. D. T., W. R. Smith, et al. (2007). *"New height, weight and head circumference charts for British children with Williams syndrome."* **Arch Dis Child 92(7): 598-601.**

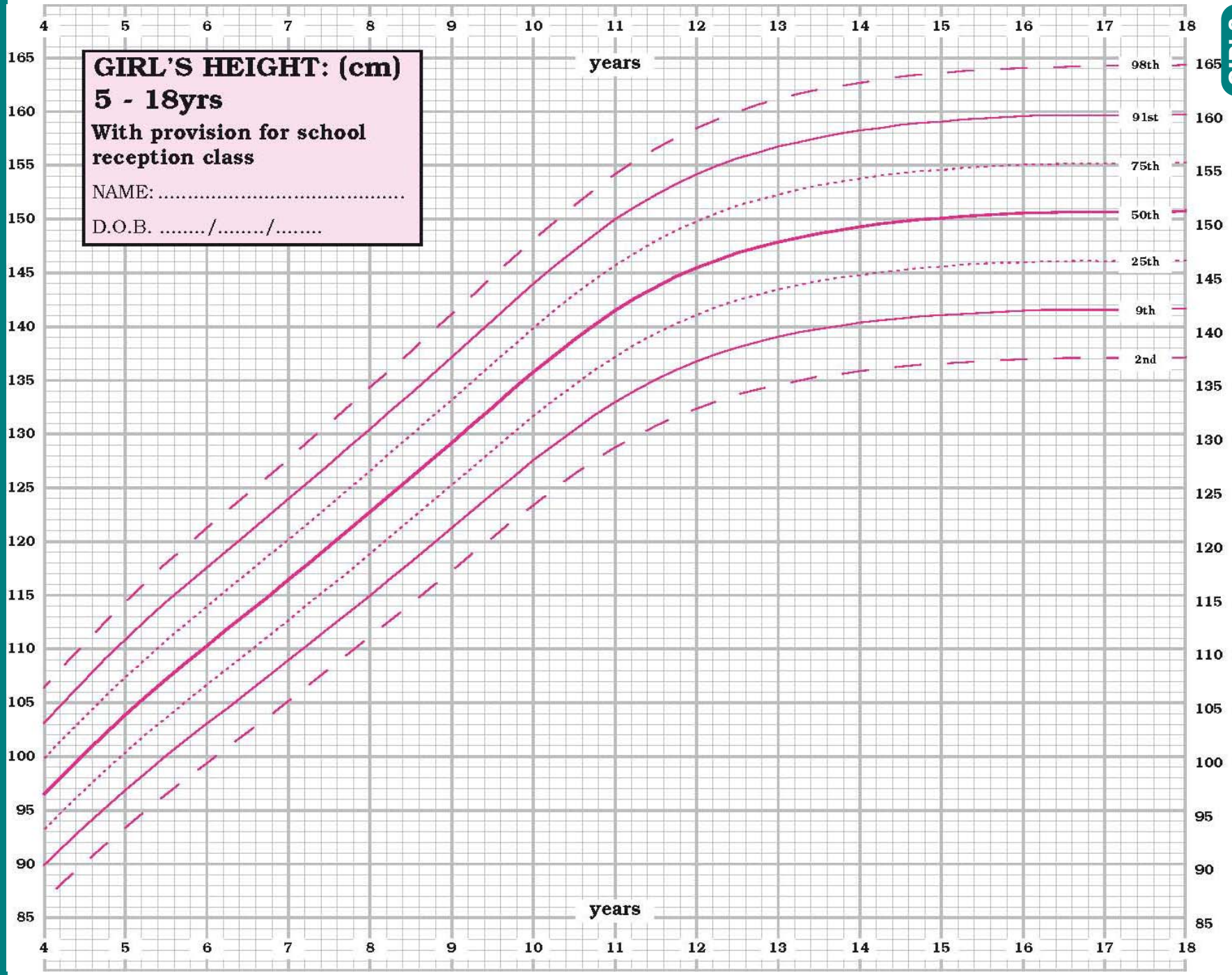

GIRL'S WEIGHT: (kg)
BIRTH - 1yr
NAME: .....
D.O.B. ...../...../.....
weeks/ months
98th
91st
75th
50th
25th
9th
2nd
weeks/ months

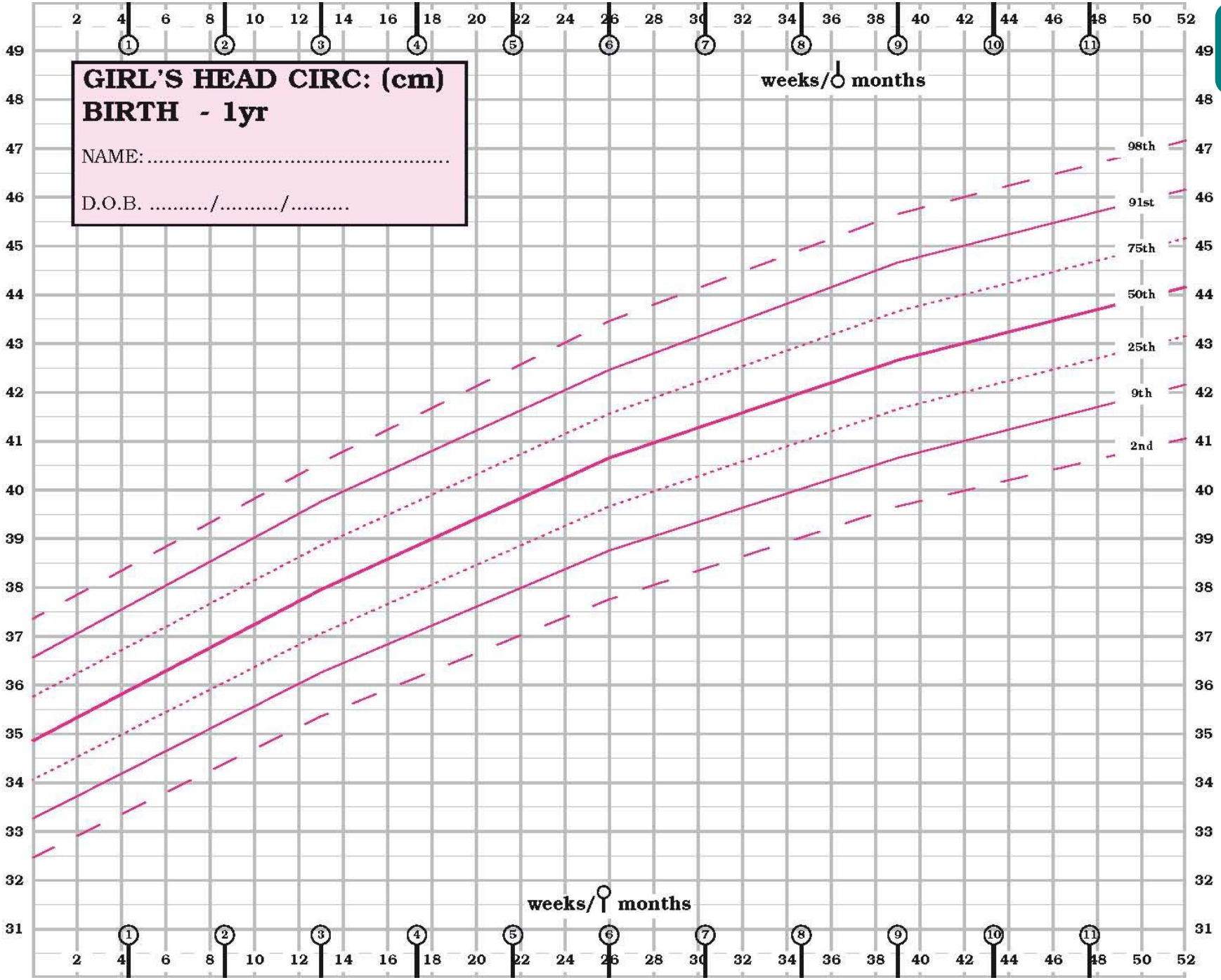

GIRL'S WEIGHT: (kg)
1 - 5yrs
NAME: .....
years
98th
91st
75th
50th
25th
9th
2nd
1
1 1/2
2
2 1/2
3
3 1/2
4
4 1/2
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21

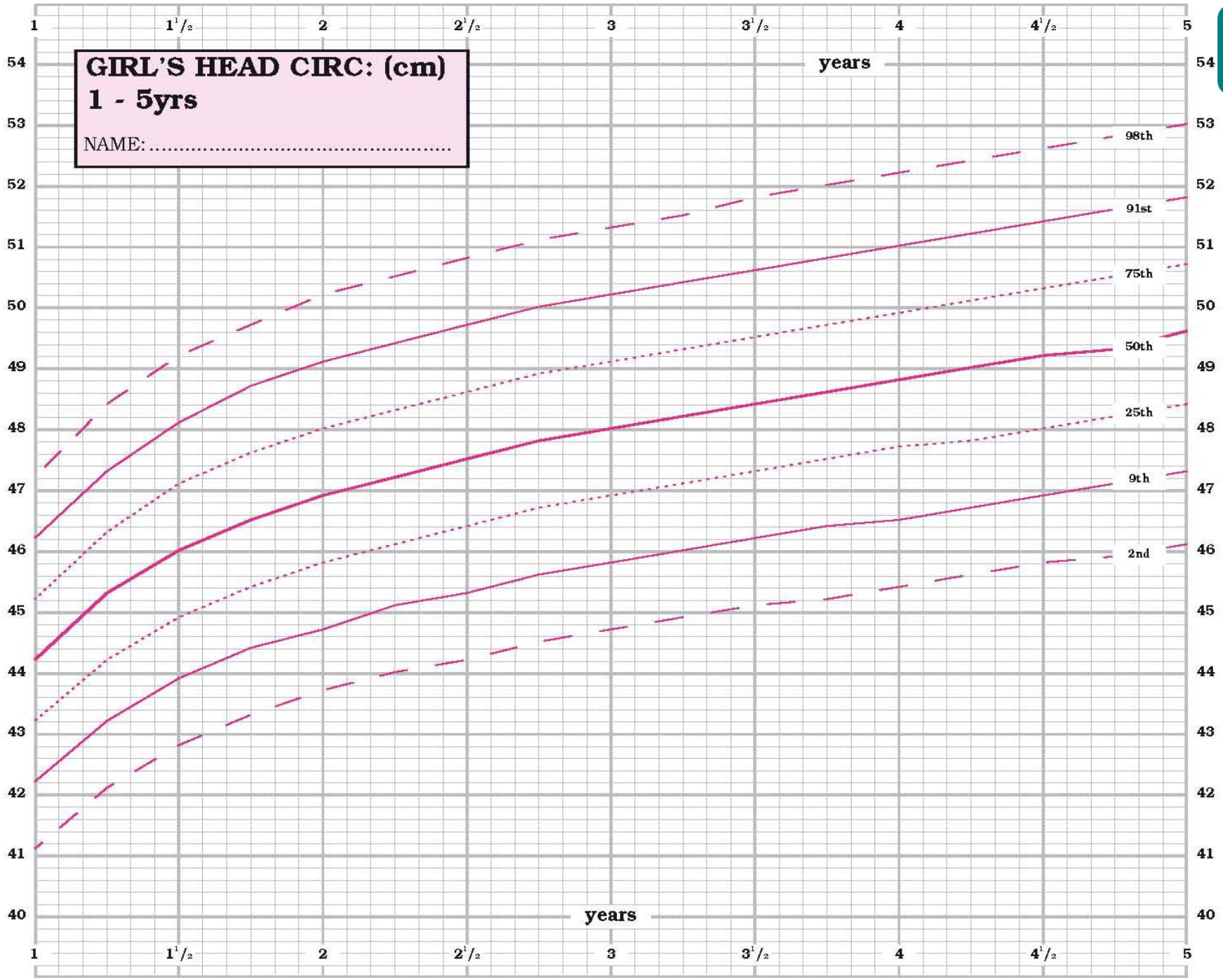

GIRL'S WEIGHT: (kg)
5 - 18yrs
With provision for school reception class
NAME: .....
D.O.B. ...../...../.....
years
years
98th
91st
75th
50th
25th
9th
2nd
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
80 75 70 65 60 55 50 45 40 35 30 25 20 15 10

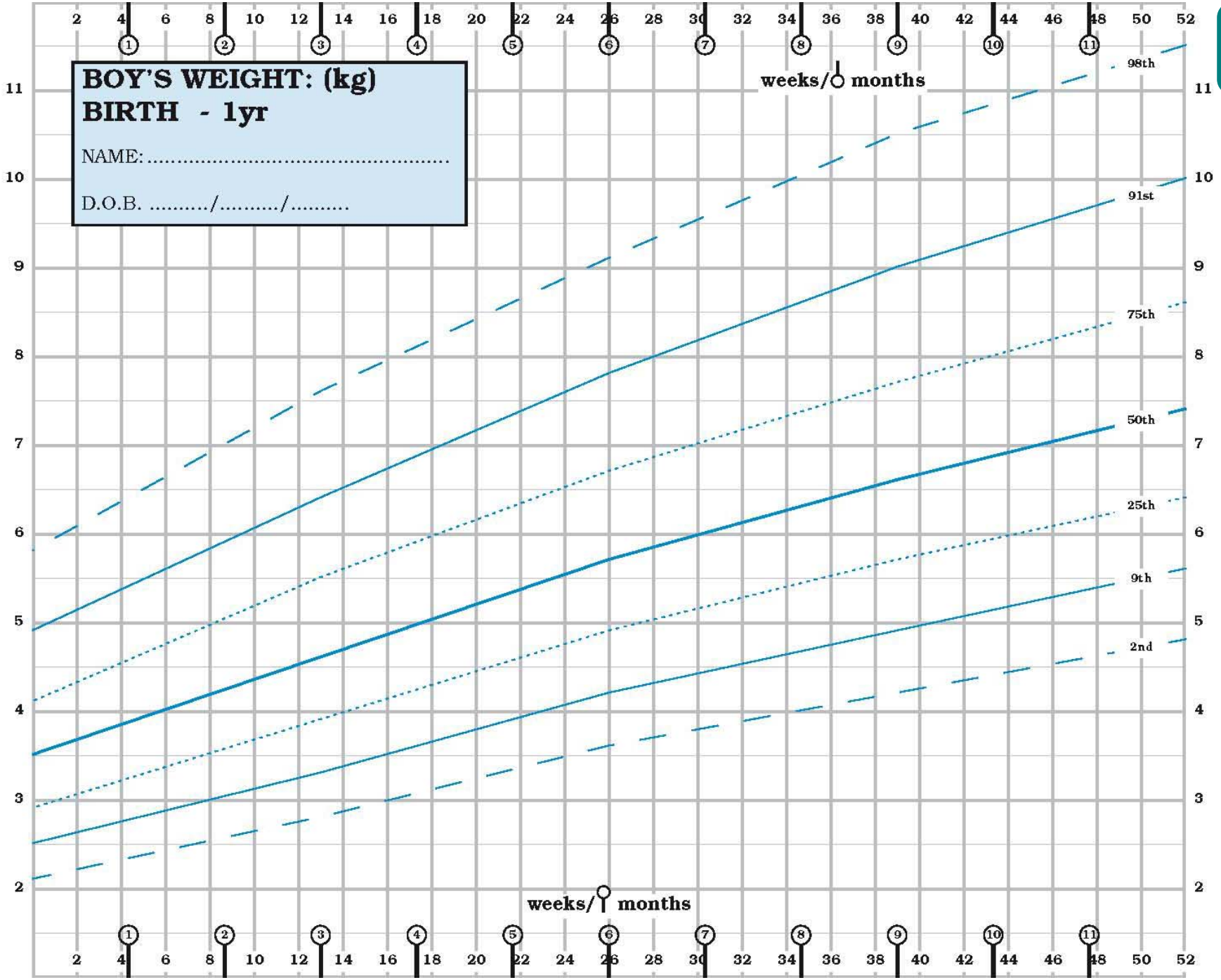

GIRL'S LENGTH: (cm)
BIRTH - 1yr
NAME: .....
D.O.B. ...../...../.....
weeks/ months
98th
91st
75th
50th
25th
9th
2nd
weeks/ months

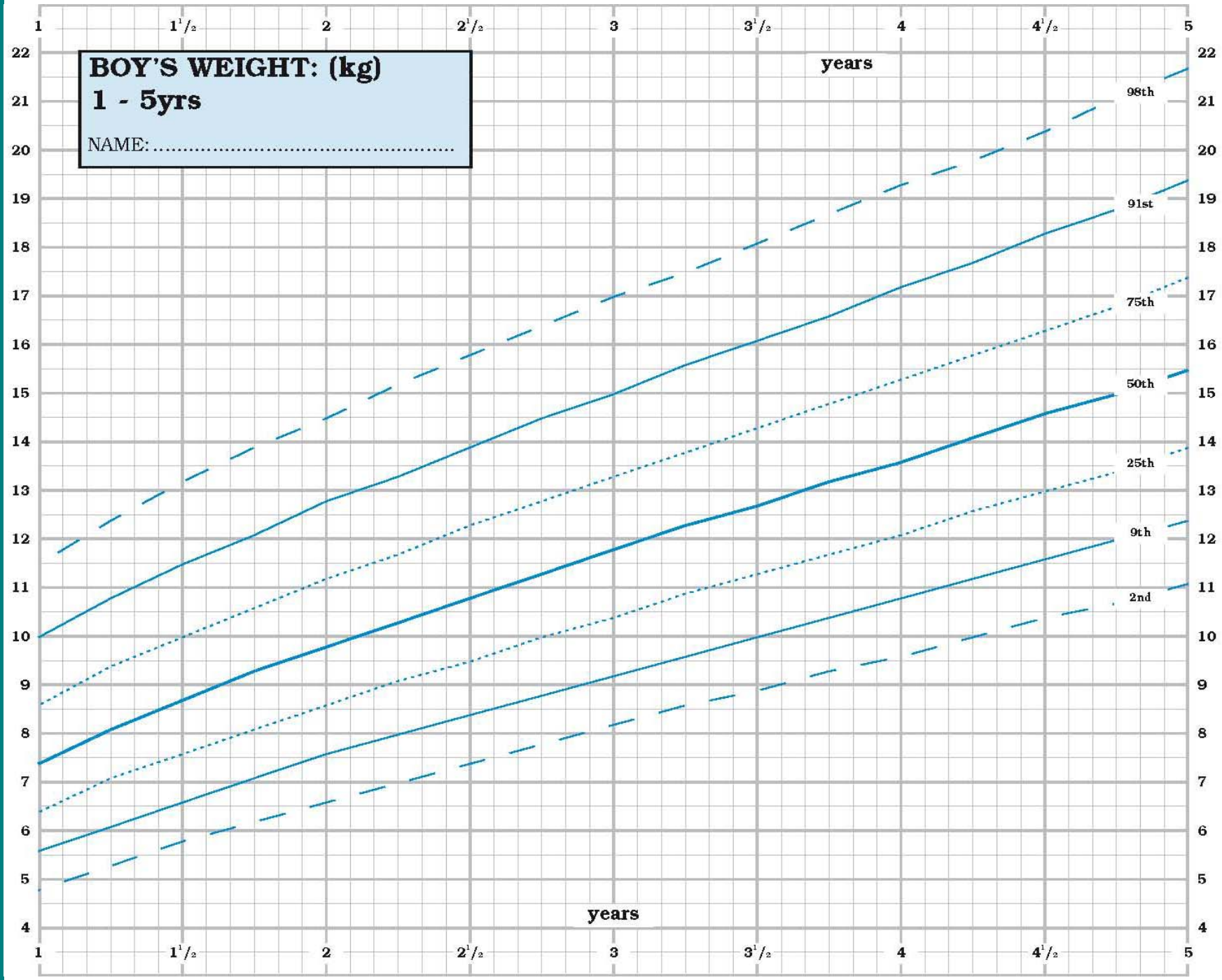

GIRL'S HEIGHT: (cm)
1 - 5yrs
NAME: .....
years
98th
91st
75th
50th
25th
9th
2nd
1
1 1/2
2
2 1/2
3
3 1/2
4
4 1/2
5
120
115
110
105
100
95
90
85
80
75
70
65

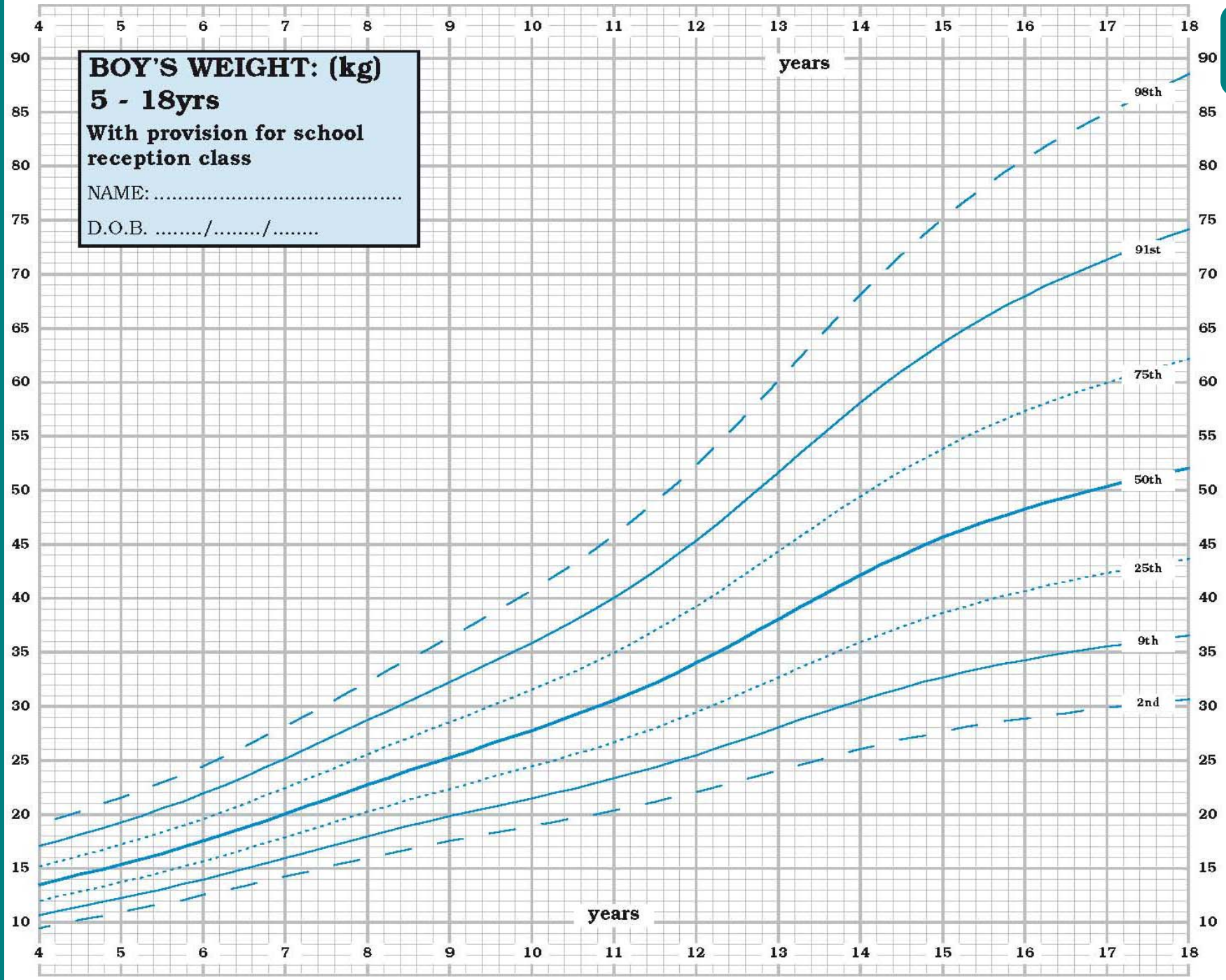

GIRL'S HEIGHT: (cm)
5 - 18yrs
With provision for school reception class
NAME: .....
D.O.B. ...../...../.....
years
98th
91st
75th
50th
25th
9th
2nd
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85

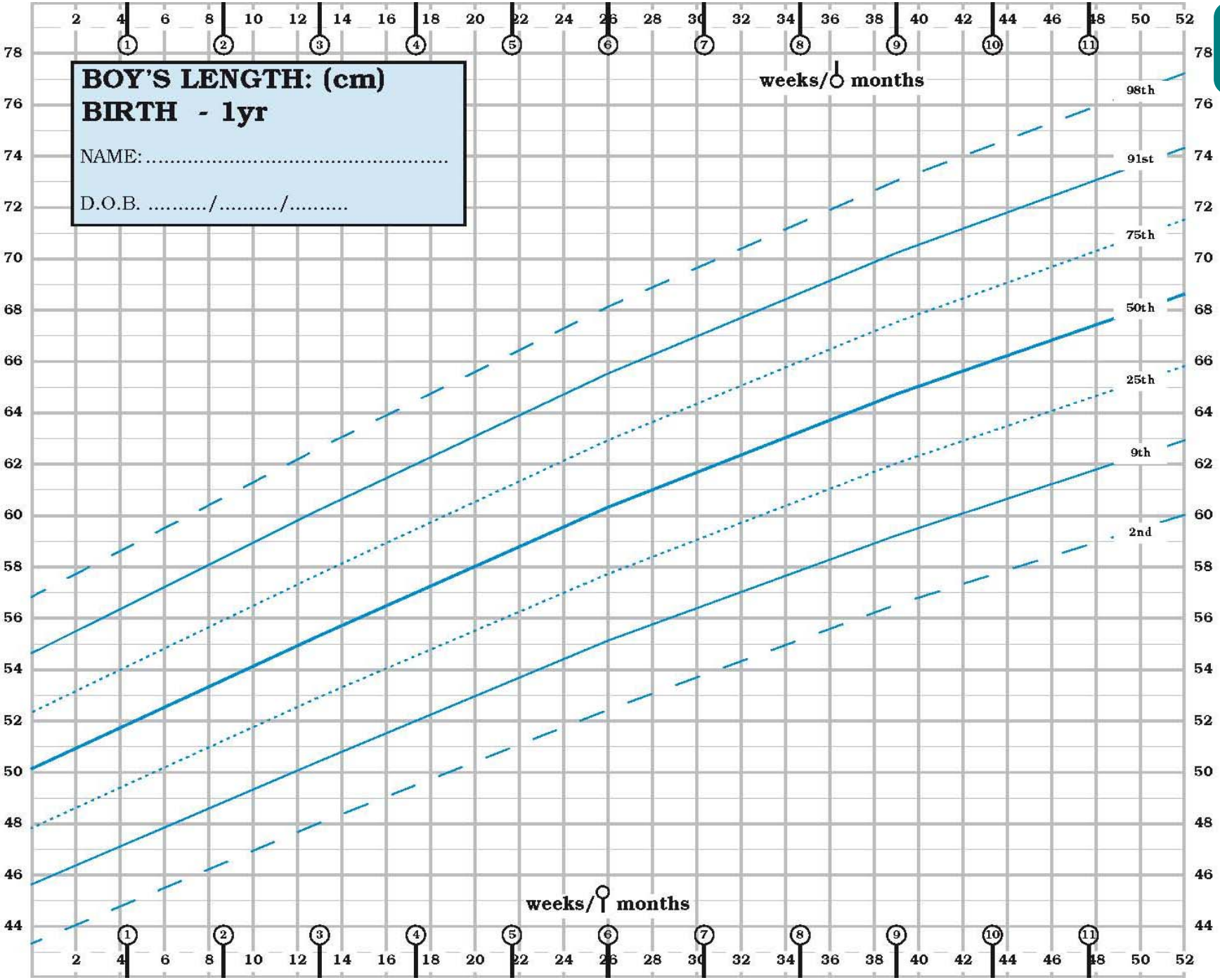

GIRL'S HEAD CIRC: (cm)
BIRTH - 1yr
NAME: .....
D.O.B. ...../...../.....
weeks/ months
98th
91st
75th
50th
25th
9th
2nd
weeks/ months

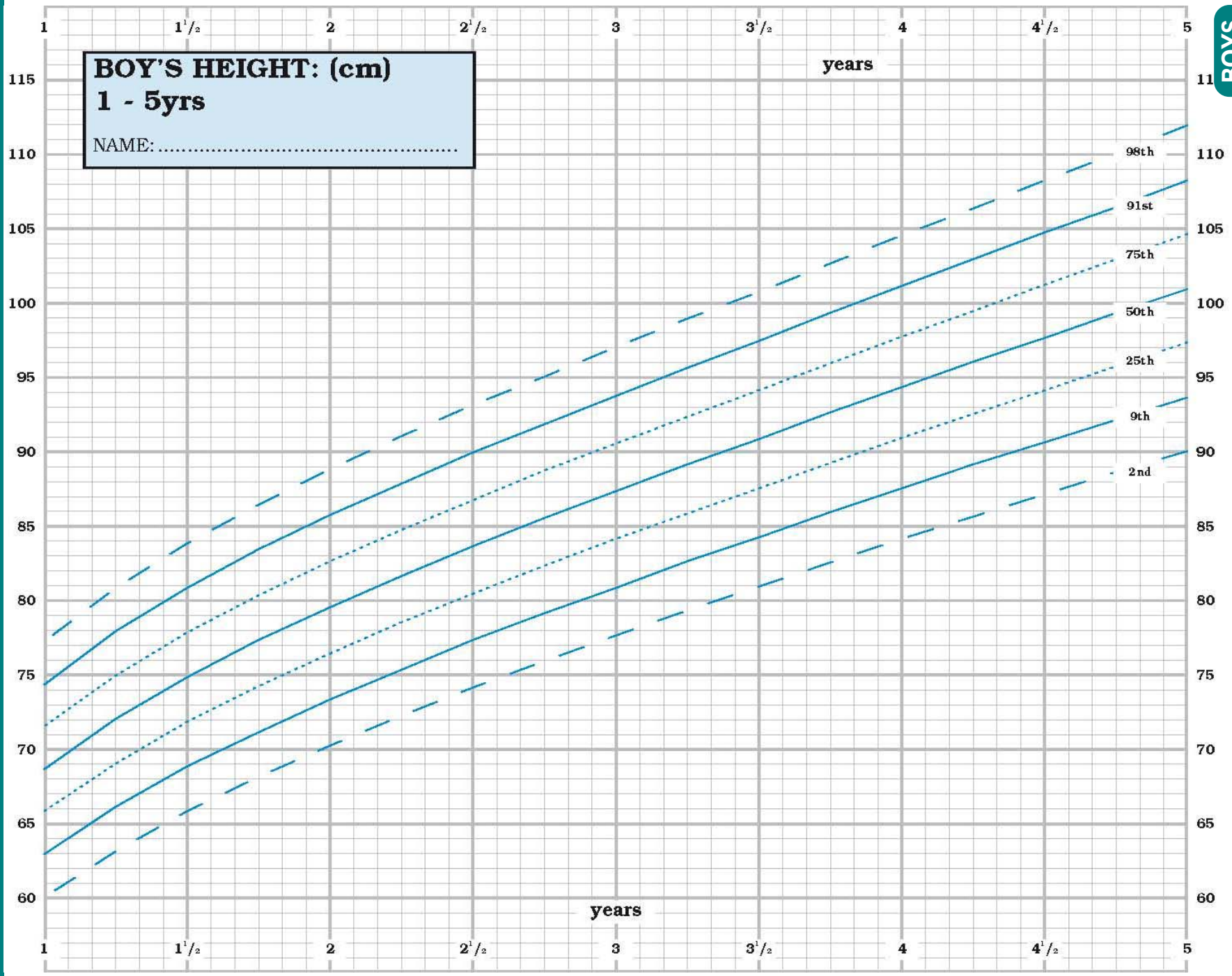

GIRL'S HEAD CIRC: (cm)
1 - 5yrs
NAME:.....
years
98th
91st
75th
50th
25th
9th
2nd
1
1 1/2
2
2 1/2
3
3 1/2
4
4 1/2
5
54
53
52
51
50
49
48
47
46
45
44
43
42
41
40

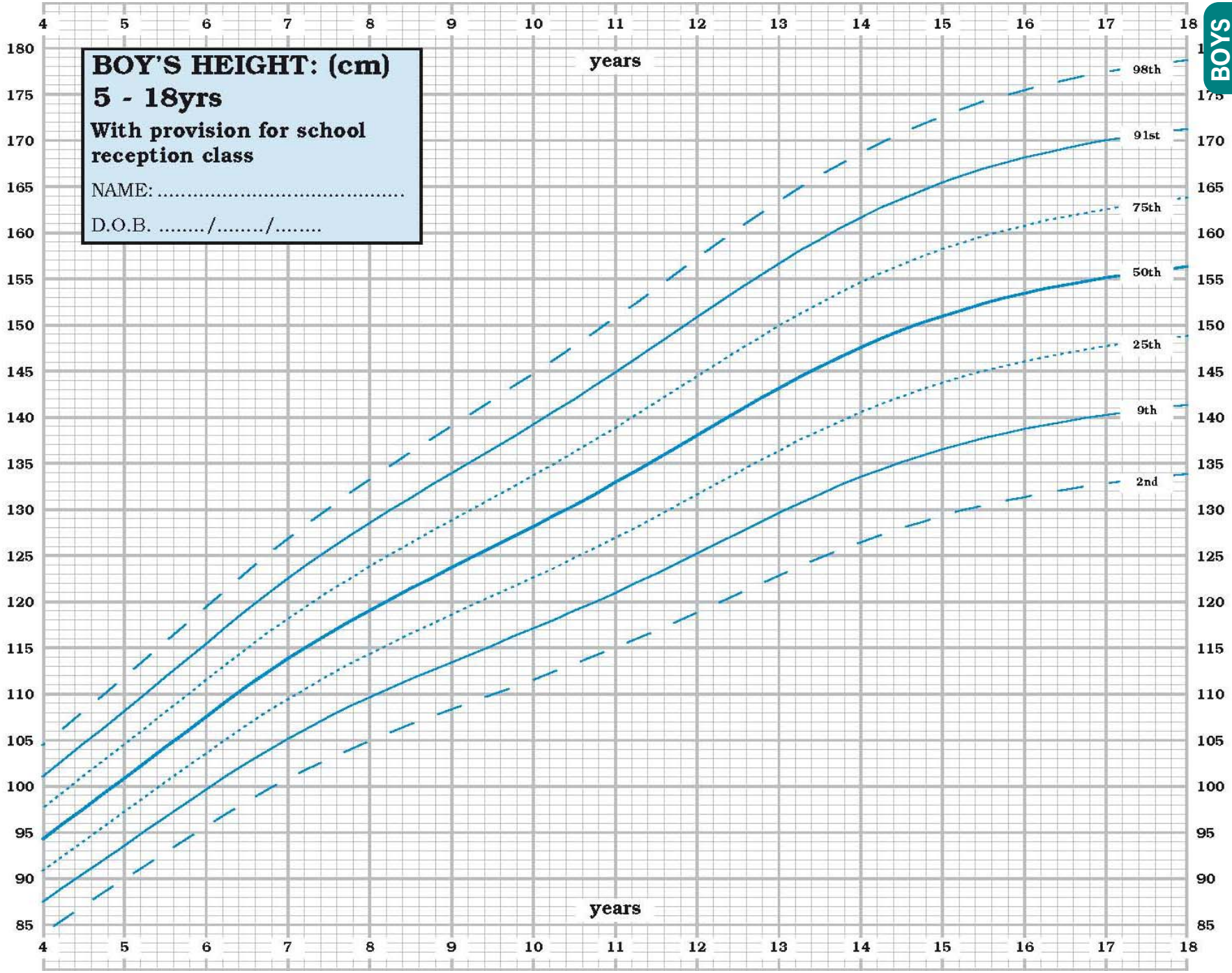

BOY'S WEIGHT: (kg)
BIRTH - 1yr
NAME: .....
D.O.B. ...../...../.....
weeks/ months
98th
91st
75th
50th
25th
9th
2nd
weeks/ months

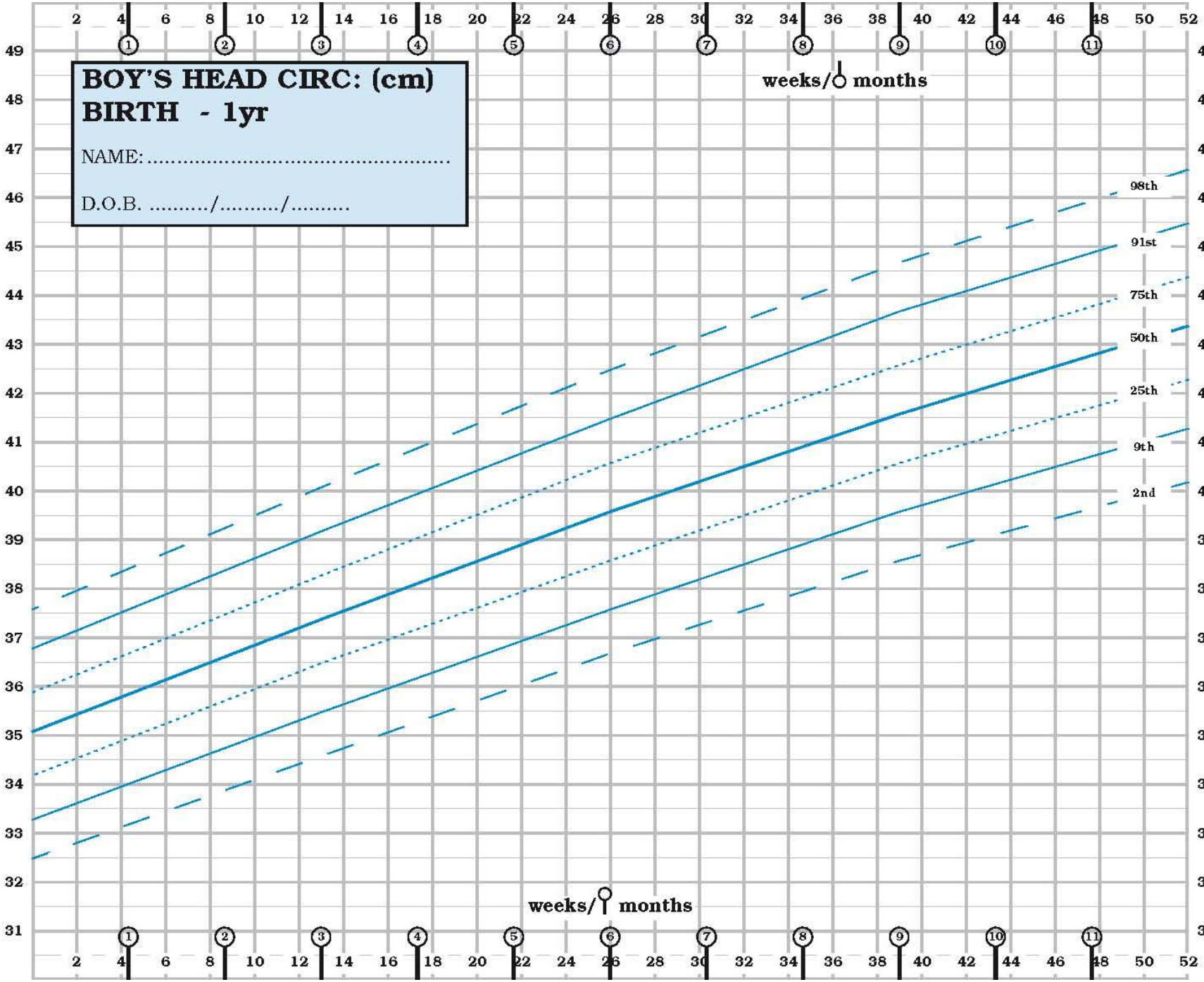

BOY'S WEIGHT: (kg)
1 - 5yrs
NAME: .....
years
98th
91st
75th
50th
25th
9th
2nd
years

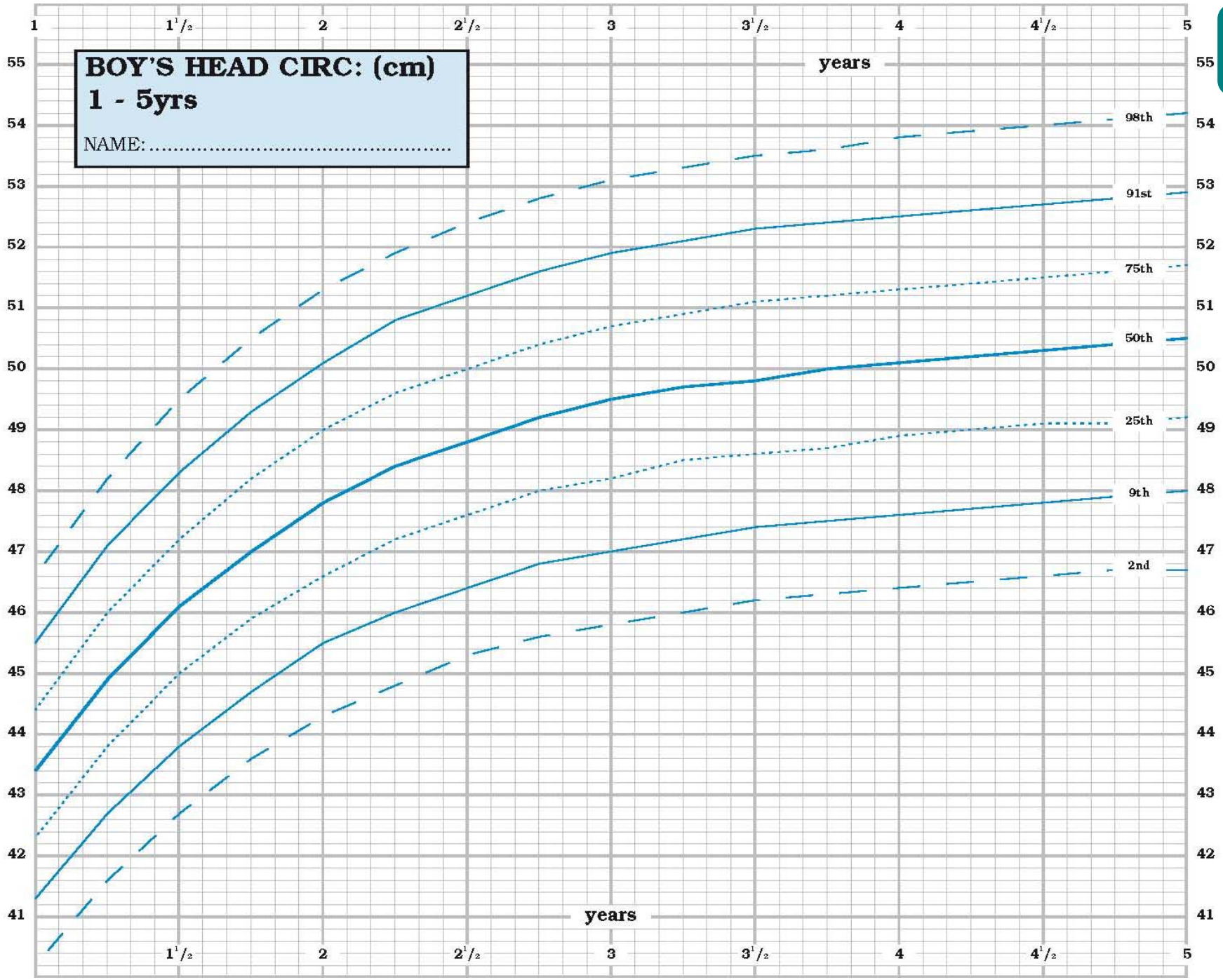

BOY'S WEIGHT: (kg)
5 - 18yrs
With provision for school reception class
NAME: .....
D.O.B. ...../...../.....
years
years
98th
91st
75th
50th
25th
9th
2nd
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10


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


BOY'S HEIGHT: (cm)
1 - 5yrs
NAME: .....
years
years
98th
91st
75th
50th
25th
9th
2nd
1
1 1/2
2
2 1/2
3
3 1/2
4
4 1/2
5
115
110
105
100
95
90
85
80
75
70
65
60


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


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


BOY'S HEAD CIRC: (cm)
1 - 5yrs
NAME:.....
years
98th
91st
75th
50th
25th
9th
2nd
1
1 1/2
2
2 1/2
3
3 1/2
4
4 1/2
5
55
54
53
52
51
50
49
48
47
46
45
44
43
42
41

Bibliography

General papers & Guidelines

- American Academy of Pediatrics, Committee on Genetics (2001). "Health Care Supervision for Children With Williams Syndrome." Pediatrics **107** (5): 1192-1204.
- Cherniske, E. M., T. O. Carpenter, et al. (2004). "Multisystem study of 20 older adults with Williams syndrome." Am J Med Genet A 131(3): 255-64.
- Dallapiccola, B. M., R. Gianotti, A (2000). "Linee guida perla sindrome di Williams." Rivista Italiana di Pediatria: 244 - 253.
- Ferrero, G. B., E. Biamino, et al. (2007). "Presenting phenotype and clinical evaluation in a cohort of 22 Williams-Beuren syndrome patients." Eur J Med Genet 50(5): 327-37.
- Greenberg, F. (1990). "Williams syndrome professional symposium." American Journal of Medical Genetics 37(S1): 85-88.
- Pober, B. R. and C. A. Morris (2007). "Diagnosis and management of medical problems in adults with Williams-Beuren syndrome." Am J Med Genet C Semin Med Genet 145C(3): 280-90.
- Scottish Intercollegiate Guidelines Network (2008). "SIGN 50: A Guideline Developer's Handbook." http://www.sign.ac.uk/pdf/sign50.pdf
- Udwin, O., Yule, W. & Howlin, P. (2007). "Williams Syndrome - Guidelines for Parents." UNPUBLISHED - from Williams Syndrome Foundation web-site: www.williams-syndrome.org.uk
- Udwin, O., Yule, W. & Howlin, P. (2007). "Williams Syndrome - Guidelines for Teachers." UNPUBLISHED - from Williams Syndrome Foundation web-site: www.williams-syndrome.org.uk
- Udwin, O., Davies, M., Howlin, P. & Stinton, C. (2007). "Adults with Williams Syndrome Guidelines for Families and Professionals." UNPUBLISHED - from Williams Syndrome Foundation website: www.williams-syndrome.org.uk
- Udwin, O., Davies, M., Stinton, C. & Howlin, P. (2007). "Adults with Williams Syndrome Guidelines for Employers and Supervisors." UNPUBLISHED - from Williams Syndrome Foundation website: www.williams-syndrome.org.uk

Anaesthesia

- Astuto, M., D. Sapienza, et al. (2007). "Spinal anesthesia for inguinal hernia repair in an infant with Williams syndrome: case report." Paediatr Anaesth 17(2): 193-5.
- Bragg, K., G. M. Fedel, et al. (2005). "Cardiac arrest under anesthesia in a pediatric patient with Williams syndrome: a case report." AANA J 73(4): 287-93.
- Burch, T. M., F. X. McGowan, Jr., et al. (2008). "Congenital Supravalvular Aortic Stenosis and Sudden Death Associated with Anesthesia: What's the Mystery?" Anesth Analg 107(6): 1848-1854.
- Horowitz, P. E., S. Akhtar, et al. (2002). "Coronary artery disease and anesthesia-related death in children with Williams syndrome." J Cardiothorac Vasc Anesth 16(6): 739-41.
- Kawahito, S., H. Kitahata, et al. (1998). "Anaesthetic management of a patient with Williams syndrome undergoing aortoplasty for supravalvular aortic stenosis." Can J Anaesth 45(12): 1203-6.
- Kohase, H., R. Wakita, et al. (2007). "General anesthesia for dental treatment in a Williams syndrome patient with severe aortic and pulmonary valve stenosis: suspected episode of postoperatively malignant hyperthermia." Oral Surg Oral Med Oral Pathol Oral Radiol Endod 104(4): e17-20.
- Matthews, A. J. and J. M. Vernon (1991). "Masseter spasm in Williams syndrome." Anaesthesia 46(8): 706.
- Medley, J., P. Russo, et al. (2005). "Perioperative care of the patient with Williams syndrome." Paediatr Anaesth 15(3): 243-7.
- Patel, J. and M. J. Harrison (1991). "Williams syndrome: masseter spasm during anaesthesia." Anaesthesia 46(2): 115-6.

Calcium metabolism

- Brooke, B. S., A. Bayes-Genis, et al. (2003). "New insights into elastin and vascular disease." Trends Cardiovasc Med 13(5): 176-81.
- Bzdúch, V. (1993). "Hypercalcemic phase of williams syndrome." The Journal of Pediatrics 123(3): 496-496.
- Cagle, A. P., S. G. Waguespack, et al. (2004). "Severe Infantile Hypercalcemia Associated With Williams Syndrome Successfully Treated With Intravenously Administered Pamidronate." Pediatrics 114(4): 1091-1095.

Bibliography continued…

Calcium metabolism continued…

- Mathias, R. S. (2000). "Rickets in an infant with Williams syndrome." Pediatr Nephrol 14(6): 489-92.
- McTaggart, S. J., J. Craig, et al. (1999). "Familial occurrence of idiopathic infantile hypercalcemia." Pediatr Nephrol 13(8): 668-71.
- Nicholson, W. R. and K. A. Hockey (1993). "Williams syndrome: a clinical study of children and adults." J Paediatr Child Health 29(6): 468-72.
- Oliveri, B., S. R. Mastaglia, et al. (2004). "Long-term control of hypercalcaemia in an infant with williams-Beuren syndrome after a single infusion of biphosphonate (Pamidronate)." Acta Paediatr 93(7): 1002-3.
- Pober, B. R., R. V. Lacro, et al. (1993). "Renal findings in 40 individuals with Williams syndrome." Am J Med Genet 46(3): 271-4.
- Rodd, C. and Goodyer, P. (1999). "Hypercalcemia of the newborn: etiology, evaluation, and management." Pediatr Nephrol 13(6): 542-7.
- Sforzini, C., D. Milani, et al. (2002). "Renal tract ultrasonography and calcium homeostasis in Williams-Beuren syndrome." Pediatr Nephrol 17(11): 899-902.
- Weber, K. T., R. U. Simpson, et al. (2008). "Vitamin D and calcium dyshomeostasis-associated heart failure." Heart 94(5): 540-541.

Cardiovascular

- Bird, L. M., G. F. Billman, et al. (1996). "Sudden death in Williams syndrome: report of ten cases." J Pediatr 129(6): 926-31.
- Brown, J. W, M. Ruzmetov et al. (2002). "Surgical repair of congenital supravalvular aortic stenosis in children." Eur J Cardiothor Surg 21(1): 50-6.
- Bruno, E., N. Rossi, et al. (2003). "Cardiovascular findings, and clinical course, in patients with Williams syndrome." Cardiol Young 13(6): 532-6.
- Burch, T. M., F. X. McGowan, Jr., et al. (2008). "Congenital Supravalvular Aortic Stenosis and Sudden Death Associated with Anesthesia: What's the Mystery?" Anesth Analg 107(6): 1848-1854.
- Casanelles M del, C., J. J. Gil-Fernandez, et al. (2003). "Portal hypertension in Williams syndrome: report of two patients." Am J Med Genet A 118A(4): 372-6.
- Cherniske, E. M., T. O. Carpenter, et al. (2004). "Multisystem study of 20 older adults with Williams syndrome." Am J Med Genet A 131(3): 255-64.
- Collins, R. T., II, P. Kaplan, et al. (2008). "Abstract 5717: Cardiovascular Abnormalities and Outcomes in a Large Williams Syndrome Cohort." Circulation 118 (18_MeetingAbstracts): S_990-c-991.
- Coskun, T. S., O. K. Coskun, et al. (2007). "Surgical repair of congenital supravalvular aortic stenosis in adult." ASAIO J 53(6): e5-6.
- De Rubens Figuero, J., L. M. Rodriguez, et al. (2008). "Cardiovascular spectrum in williams-beuren syndrome: the mexican experience in 40 patients." Tex Heart Inst J 35(3): 279-85.
- Eronen, M., M. Peippo, et al. (2002). "Cardiovascular manifestations in 75 patients with Williams syndrome." J Med Genet 39(8): 554-8.
- Giddins, N. G., J. P. Finley, et al. (1989). "The natural course of supravalvar aortic stenosis and peripheral pulmonary artery stenosis in Williams's syndrome." Br Heart J 62(4): 315-9.
- Harikrishnan, S., S. R. Manohar, et al. (2003). "Supravalvar aortic stenosis: clinical and hemodynamic profile, and surgical outcome." Indian Heart J 55(1): 49-54.
- Hazekamp, M. G., A. P. Kappetein, et al. (1999). "Brom's three-patch technique for repair of supravalvular aortic stenosis." J Thorac Cardiovasc Surg 118(2): 252-8.
- Hickey, E. J., G. Jung, et al. (2008). "Congenital Supravalvular Aortic Stenosis: Defining Surgical and Nonsurgical Outcomes." Ann Thorac Surg 86 (6): 1919-1927.
- Imashuku, S., S. Hayashi, et al. (2000). "Sudden death of a 21-year-old female with Williams syndrome showing rare complications." Pediatr Int 42 (3): 322-4.
- Ishibashi, N., M. Aoki, et al. (2007). "Modified Myers and coronary artery bypass grafting using free internal thoracic artery graft for complicated supravalvular aortic stenosis." J Card Surg 22(1): 56-7.
- Kantharia, B. K. and R. S. Mittleman (1999). "Concomitant reentrant tachycardias from concealed accessory atrioventricular bypass tract and atrioventricular nodal reentry in a patient with Williams syndrome." Cardiology 91(4): 264-7.

Bibliography continued…

Cardiovascular continued…

- Kaplan, P., M. Levinson, et al. (1995). "Cerebral artery stenoses in Williams syndrome cause strokes in childhood." J Pediatr 126(6): 943-5.
- Kim, Y. M., S. J. Yoo, et al. (1999). "Natural course of supravalvar aortic stenosis and peripheral pulmonary arterial stenosis in Williams' syndrome." Cardiol Young 9(1): 37-41.
- Miyamura, H., H. Watanabe, et al. (1996). "Spontaneous regression of peripheral pulmonary artery stenosis in Williams syndrome." Jpn Circ J 60 (5): 311-4.
- Nakamoto, S., T. Saga, et al. (2003). "Williams syndrome associated with complete atrioventricular septal defect." Heart 89(5): e15.
- Park, J. H., H. S. Kim, et al. (2008). "Demonstration of peripheral pulmonary stenosis and supravalvular aortic stenosis by different cardiac imaging modalities in a patient with Williams syndrome--usefulness of noninvasive imaging studies." Int J Cardiol 128(3): e95-7.
- Pham, P. P., J. H. Moller, et al. (2008). "Cardiac Catheterization and Operative Outcomes from a Multicenter Consortium for Children with Williams Syndrome." Pediatr Cardiol.
- Sadler, L. S., R. Gingell, et al. (1998). "Carotid ultrasound examination in Williams syndrome." J Pediatr 132(2): 354-6.
- Sadler, L. S., B. R. Pober, et al. (2001). "Differences by sex in cardiovascular disease in Williams syndrome." J Pediatr 139(6): 849-53.
- Scheiber, D., G. Fekete, et al. (2006). "Echocardiographic findings in patients with Williams-Beuren syndrome." Wiener Klinische Wochenschrift 118(17): 538-542.
- Suarez-Mier, M. P. and B. Morentin (1999). "Supravalvular aortic stenosis, Williams syndrome and sudden death. A case report." Forensic Sci Int 106(1): 45-53.
- Takeda, K., G. Matsumiya, et al. (2007). "Successful reconstructive surgery for isolated mitral insufficiency associated with Williams syndrome: report of a case." Surg Today 37(3): 237-9.
- van Pelt, N. C., N. J. Wilson, et al. (2005). "Severe coronary artery disease in the absence of supravalvular stenosis in a patient with Williams syndrome." Pediatr Cardiol 26(5): 665-7.
- Vural, H., P. Vural, et al. (2008). "Surgical repair of supravalvular aortic stenosis in Williams syndrome." Anadolu Kardiyol Derg 8(3): 229-30.
- Wang, C. C., W. L. Hwu, et al. (2007). "Outcome of pulmonary and aortic stenosis in Williams-Beuren syndrome in an Asian cohort." Acta Paediatr 96(6): 906-9.
- Wessel, A., R. Pankau, et al. (1994). "Three decades of follow-up of aortic and pulmonary vascular lesions in the Williams-Beuren syndrome." Am J Med Genet 52(3): 297-301.
- Wessel, A., V. Gravenhorst, et al. (2004). "Risk of sudden death in the Williams-Beuren syndrome." Am J Med Genet A 127A(3): 234-7.
- Youn, H. J., W. S. Chung, et al. (2002). "Demonstration of supravalvar aortic stenosis by different cardiac imaging modalities in Williams syndrome." Heart 88(4): 438.

Dental

- Axelsson, S., T. Bjornland, et al. (2003). "Dental characteristics in Williams syndrome: a clinical and radiographic evaluation." Acta Odontol Scand 61(3): 129-36.
- Axelsson, S. (2005). "Variability of the cranial and dental phenotype in Williams syndrome." Swed Dent J Suppl(170): 3-67.
- Fearne, J. "Dental Advice for Children with Williams Syndrome." UNPUBLISHED - from Williams Syndrome Foundation website: www.williams-syndrome.org.uk
- Habersack, K., B. Grimaldi, et al. (2007). "Orthodontic orthognathic surgical treatment of a subject with Williams Beuren syndrome a follow-up from 8 to 25 years of age." Eur J Orthod 29(4): 332-7.
- Hertzberg, J., L. Nakisbendi, et al. (1994). "Williams syndrome--oral presentation of 45 cases." Pediatr Dent 16(4): 262-7.
- Joseph, C., M. M. Landru, et al. (2008). "Periodontal conditions in Williams Beuren syndrome: a series of 8 cases." Eur Arch Paediatr Dent 9(3): 142-7.

Bibliography continued…

Dental continued…

- Kashyap, A. S., H. S. Sharma, et al. (2000). "Dental anomalies in Williams syndrome." Postgrad Med J 76(901): 712.
- Moskovitz, M., D. Brener, et al. (2005). "Medical considerations in dental treatment of children with Williams syndrome." Oral Surg Oral Med Oral Pathol Oral Radiol Endod 99(5): 573-80.
- Tarjan, I., G. Balaton, et al. (2003). "Facial and dental appearance of Williams syndrome." Postgrad Med J 79(930): 241.

Development, Behaviour and Mental Health

- Cherniske, E. M., T. O. Carpenter, et al. (2004). "Multisystem study of 20 older adults with Williams syndrome." Am J Med Genet A 131(3): 255-64.
- Davies, M., H. Patricia, et al. (1997). "Independence and adaptive behavior in adults with Williams syndrome." American Journal of Medical Genetics 70(2): 188-195.
- Davies, M., O. Udwin, et al. (1998). "Adults with Williams syndrome. Preliminary study of social, emotional and behavioural difficulties." Br J Psychiatry 172: 273-6.
- Dykens, E. M. (2000). "Psychopathology in children with intellectual disability." J Child Psychol Psychiatry 41(4): 407-17.
- Dykens, E. M. (2003). "Anxiety, fears, and phobias in persons with Williams syndrome." Dev Neuropsychol 23(1-2): 291-316.
- Dykens, E. M. and Hodapp, R.M (1997). "Treatment Issues in Genetic Mental Retardation Syndromes." Professional Psychology: Research and Practice 28(3): 263-270.
- Einfeld, S. L., B. J. Tonge, et al. (1997). "Behavioral and emotional disturbance in individuals with Williams syndrome." Am J Ment Retard 102(1): 45-53.
- Gillberg, C. and P. Rasmussen (1994). "Brief report: four case histories and a literature review of Williams syndrome and autistic behavior." J Autism Dev Disord 24(3): 381-93.
- Jones, W., U. Bellugi, et al. (2000). "II. Hypersociability in Williams Syndrome." J Cogn Neurosci 12 Suppl 1: 30-46.
- Leyfer, O. T., J. Woodruff-Borden, et al. (2006). "Prevalence of psychiatric disorders in 4 to 16-year-olds with Williams syndrome." Am J Med Genet B Neuropsychiatr Genet 141B(6): 615-22.
- Metcalfe, K. (1999). "Williams syndrome: an update on clinical and molecular aspects." Arch Dis Child 81(3): 198-200.
- Santos, A. and C. Deruelle (2008). "Verbal Peaks and Visual Valleys in Theory of Mind Ability in Williams Syndrome." J Autism Dev Disord.
- Stinton, C., S. Elison, et al. (2008). "Physical and mental health of adults with Williams syndrome." J Intellect Disabil Res 52(10): 813.
- Vicari, S. (2004). "Memory development and intellectual disabilities." Acta Paediatr Suppl 93(445): 60-3; discussion 63-4.

Endocrine & Thyroid

- Bini, R. and I. Pela (2004). "New case of thyroid dysgenesis and clinical signs of hypothyroidism in Williams syndrome." Am J Med Genet A 127A(2): 183-5.
- Cambiaso, P., C. Orazi, et al. (2007). "Thyroid morphology and subclinical hypothyroidism in children and adolescents with Williams syndrome." J Pediatr 150(1): 62-5.
- Cammareri, V., G. Vignati, et al. (1999). "Thyroid hemiagenesis and elevated thyrotropin levels in a child with Williams syndrome." Am J Med Genet 85(5): 491-4.
- Cherniske, E. M., T. O. Carpenter, et al. (2004). "Multisystem study of 20 older adults with Williams syndrome." Am J Med Genet A 131(3): 255-64.
- Hill, I. D., M. H. Dirks, et al. (2005). "Guideline for the diagnosis and treatment of celiac disease in children: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition." J Pediatr Gastroenterol Nutr 40(1): 1-19.
- Selicorni, A., A. Fratoni, et al. (2006). "Thyroid anomalies in Williams syndrome: investigation of 95 patients." Am J Med Genet A 140(10): 1098-101.
- Stagi, S., G. Bindi, et al. (2003). "Thyroid hypoplasia of the left lobe in two girls affected by Williams syndrome." Clin Dysmorphol 12(4): 267-8.

Bibliography continued…

Endocrine & Thyroid continued…

- Stagi, S., G. Bindi, et al. (2005). "Thyroid function and morphology in patients affected by Williams syndrome." Clin Endocrinol (Oxf) 63(4): 456-60.
- Stagi, S., C. Manoni, et al. (2008). "Thyroid Hypoplasia as a Cause of Congenital Hypothyroidism in Williams Syndrome." Horm Res 70(5): 316-318.

Gastrointestinal & Feeding

- Cherniske, E. M., T. O. Carpenter, et al. (2004). "Multisystem study of 20 older adults with Williams syndrome." Am J Med Genet A 131(3): 255-64.
- Giannotti, A., G. Tiberio, et al. (2001). "Coeliac disease in Williams syndrome." J Med Genet 38(11): 767-8.
- Hill, I. D., M. H. Dirks, et al. (2005). "Guideline for the diagnosis and treatment of celiac disease in children: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition." J Pediatr Gastroenterol Nutr 40(1): 1-19.
- Lashkari, A., A. K. Smith, et al. (1999). "Williams-Beuren syndrome: an update and review for the primary physician." Clin Pediatr (Phila) 38(4): 189-208.
- O'Reilly, M. F. and G. E. Lancioni (2001). "Treating food refusal in a child with Williams syndrome using the parent as therapist in the home setting." J Intellect Disabil Res 45(Pt 1): 41-6.
- Pankau, R., C. J. Partsch, et al. (1994). "Natural history of body mass index in Williams-Beuren syndrome." Am J Med Genet 52(1): 51-4.

Growth, Puberty and Sexual Health

- Bahadori, B., E. Uitz, et al. (2008). "Successful treatment of a morbidly obese and growth-retarded adolescent with Williams-Beuren Syndrome by combining the medication of growth hormone and sibutramine." Singapore Med J 49(1): e15-6.
- Cherniske, E. M., L. S. Sadler, et al. (1999). "Early puberty in Williams syndrome." Clin Dysmorphol 8(2): 117-21.
- Douchi, T., K. Maruta, et al. (1999). "Precocious puberty in a Williams syndrome patient." Obstet Gynecol 94(5 Pt 2): 860.
- Kaplan, A. S., V. A. Stallings, et al. (1998). "Body composition, energy expenditure, and energy intake in patients with Williams syndrome." J Pediatr 132(2): 223-7.
- Kotzot, D., F. Bernasconi, et al. (1995). "Phenotype of the Williams-Beuren syndrome associated with hemizygosity at the elastin locus." Eur J Pediatr 154(6): 477-82.
- Kuijpers, G. M., M. De Vroede, et al. (1999). "Growth hormone treatment in a child with Williams-Beuren syndrome: a case report." Eur J Pediatr 158(6): 451-4.
- Martin, N. D. T., W. R. Smith, et al. (2007). "New height, weight and head circumference charts for British children with Williams syndrome." Arch Dis Child 92(7): 598-601.
- Nicholson, W. R. and K. A. Hockey (1993). "Williams syndrome: a clinical study of children and adults." J Paediatr Child Health 29(6): 468-72.
- Pankau, R., C. J. Partsch, et al. (1994). "Natural history of body mass index in Williams-Beuren syndrome." Am J Med Genet 52(1): 51-4.
- Pankau, R., C. J. Partsch, et al. (1994). "Head circumference of children with Williams-Beuren syndrome." Am J Med Genet 52(3): 285-90.
- Partsch, C. J., R. Pankau, et al. (1994). "Hormonal regulation in children and adults with Williams-Beuren syndrome." Am J Med Genet 51(3): 251-7.
- Partsch, C. J., G. Dreyer, et al. (1999). "Longitudinal evaluation of growth, puberty, and bone maturation in children with Williams syndrome." J Pediatr 134(1): 82-9.
- Partsch, C. J., I. Japing, et al. (2002). "Central precocious puberty in girls with Williams syndrome." J Pediatr 141(3): 441-4.
- Scothorn, D. J. and M. G. Butler (1997). "How common is precocious puberty in patients with Williams syndrome?" Clin Dysmorphol 6(1): 91-3.
- Utine, G. E., A. Alikasifoglu, et al. (2006). "Central precocious puberty in a girl with Williams syndrome: the result of treatment with GnRH analogue." Eur J Med Genet 49(1): 79-82.
- Yau, E. K., I. F. Lo, et al. (2004). "Williams-Beuren syndrome in the Hong Kong Chinese population: retrospective study." Hong Kong Med J 10(1): 22-7.

Bibliography continued…

Hearing

- Gallo, F. J., B. P. Klein-Tasman, et al. (2008). "Expecting the worst: observations of reactivity to sound in young children with Williams syndrome." Res Dev Disabil 29(6): 567-81.
- Gothelf, D., N. Farber, et al. (2006). "Hyperacusis in Williams syndrome: characteristics and associated neuroaudiologic abnormalities." Neurology 66(3): 390-5.
- Levitin, D. J., V. Menon, et al. (2003). "Neural correlates of auditory perception in Williams syndrome: an fMRI study." Neuroimage 18(1): 74-82.
- Levitin, D. J., K. Cole, et al. (2005). "Aversion, awareness, and attraction: investigating claims of hyperacusis in the Williams syndrome phenotype." J Child Psychol Psychiatry 46(5): 514-23.
- Miani, C., P. Passon, et al. (2001). "Treatment of hyperacusis in Williams syndrome with bilateral conductive hearing loss." Eur Arch Otorhinolaryngol 258(7): 341-4.
- Mobbs, D., M. A. Eckert, et al. (2007). "Reduced parietal and visual cortical activation during global processing in Williams syndrome." Dev Med Child Neurol 49(6): 433-8.
- Nigam, A. and P. R. Samuel (1994). "Hyperacusis and Williams syndrome." J Laryngol Otol 108(6): 494-6.
- O'Reilly, M. F., C. Lacey, et al. (2000). "Assessment of the influence of background noise on escape-maintained problem behavior and pain behavior in a child with Williams syndrome." J Appl Behav Anal 33(4): 511-4.
- Van Borsel, J., L. M. Curfs, et al. (1997). "Hyperacusis in Williams syndrome: a sample survey study." Genet Couns 8(2): 121-6.

Orthopaedic

- Cohen, D. B. and M. R. Quigley (2006). "Thoracolumbar syrinx in association with Williams syndrome." Pediatrics 118(2): e522-5.
- Ferrero, G. B., E. Biamino, et al. (2007). "Presenting phenotype and clinical evaluation in a cohort of 22 Williams-Beuren syndrome patients." Eur J Med Genet 50(5): 327-37.
- Franceschini, P., A. Guala, et al. (1996). "The Williams syndrome: an Italian collaborative study." Minerva Pediatr 48(10): 421-8.
- Hocking, D. R., N. J. Rinehart, et al. (2008). "Gait function in adults with Williams syndrome." Exp Brain Res.
- Kaplan, P., M. Kirschner, et al. (1989). "Contractures in Patients With Williams Syndrome." Pediatrics 84(5): 895-899.
- Nicholson, W. R. and K. A. Hockey (1993). "Williams syndrome: a clinical study of children and adults." J Paediatr Child Health 29(6): 468-72.
- Osebold, W. R. and H. A. King (1994). "Kyphoscoliosis in Williams syndrome." Spine 19(3): 367-71.

Renal & Hypertension

- Aggoun, Y., D. Sidi, et al. (2000). "Mechanical properties of the common carotid artery in Williams syndrome." Heart 84(3): 290-3.
- Amenta, S., C. Sofocleous, et al. (2005). "Clinical manifestations and molecular investigation of 50 patients with Williams syndrome in the Greek population." Pediatr Res 57(6): 789-95.
- Bastianon, V. (1996). "Pseudohypertension and Williams syndrome." Pediatr Cardiol 17(2): 132.
- Broder, K., E. Reinhardt, et al. (1999). "Elevated ambulatory blood pressure in 20 subjects with Williams syndrome." Am J Med Genet 83(5): 356-60.
- Cherniske, E. M., T. O. Carpenter, et al. (2004). "Multisystem study of 20 older adults with Williams syndrome." Am J Med Genet A 131(3): 255-64.
- De Ferrari, M. E., G. Colussi, et al. (1997). "Type IV renal tubular acidosis and uric acid nephrolithiasis in William's syndrome--an unusual mode of renal involvement." Nephrol Dial Transplant 12(7): 1484-6.
- Del Campo, M., A. Antonell, et al. (2006). "Hemizygosity at the NCF1 gene in patients with Williams-Beuren syndrome decreases their risk of hypertension." Am J Hum Genet 78(4): 533-42.
- Ferrero, G. B., E. Biamino, et al. (2007). "Presenting phenotype and clinical evaluation in a cohort of 22 Williams-Beuren syndrome patients." Eur J Med Genet 50(5): 327-37.

Bibliography continued…

Renal & Hypertension continued…

- Giordano, U., A. Turchetta, et al. (2001). "Exercise testing and 24-hour ambulatory blood pressure monitoring in children with Williams syndrome." Pediatr Cardiol 22(6): 509-11.
- Ichinose, M., K. Tojo, et al. (1996). "Williams syndrome associated with chronic renal failure and various endocrinological abnormalities." Intern Med 35(6): 482-8.
- Lacolley, P., P. Boutouyrie, et al. (2002). "Disruption of the elastin gene in adult Williams syndrome is accompanied by a paradoxical reduction in arterial stiffness." Clin Sci (Lond) 103(1): 21-9.
- Mathias, R. S. (2000). "Rickets in an infant with Williams syndrome." Pediatr Nephrol 14(6): 489-92.
- Narasimhan, C., T. Alexander, et al. (1993). "Pseudohypertension in a child with Williams syndrome." Pediatr Cardiol 14(2): 124-6.
- Panayiotopoulos, Y. P., M. R. Tyrrell, et al. (1996). "Mid-aortic syndrome presenting in childhood." Br J Surg 83(2): 235-40.
- Pankau, R., C. J. Partsch, et al. (1996). "Incidence and spectrum of renal abnormalities in Williams-Beuren syndrome." Am J Med Genet 63(1): 301-4.
- Pober, B. R., R. V. Lacro, et al. (1993). "Renal findings in 40 individuals with Williams syndrome." Am J Med Genet 46(3): 271-4.
- Pober, B. R., M. Johnson, et al. (2008). "Mechanisms and treatment of cardiovascular disease in Williams-Beuren syndrome." J Clin Invest 118(5): 1606-15.
- Radford, D. J. and P. G. Pohlner (2000). "The middle aortic syndrome: an important feature of Williams' syndrome." Cardiol Young 10(6): 597-602.
- Rose, C., A. Wessel, et al. (2001). "Anomalies of the abdominal aorta in Williams-Beuren syndrome--another cause of arterial hypertension." Eur J Pediatr 160(11): 655-8.
- Salaymeh, K. J. and A. Banerjee (2001). "Evaluation of arterial stiffness in children with Williams syndrome: Does it play a role in evolving hypertension?" Am Heart J 142(3): 549-55.
- Sammour, Z. M., C. M. Gomes, et al. (2006). "Voiding dysfunction and the Williams-Beuren syndrome: a clinical and urodynamic investigation." J Urol 175(4): 1472-6.
- Scheiber, D., G. Fekete, et al. (2006). "Echocardiographic findings in patients with Williams-Beuren syndrome." Wiener Klinische Wochenschrift 118(17): 538-542.
- Schulman, S. L., S. Zderic, et al. (1996). "Increased prevalence of urinary symptoms and voiding dysfunction in Williams syndrome." J Pediatr 129 (3): 466-9.
- Sever, P., G. Beevers, et al. (1993). "Management guidelines in essential hypertension: report of the second working party of the British Hypertension Society." BMJ 306(6883): 983-7.
- Sforzini, C., D. Milani, et al. (2002). "Renal tract ultrasonography and calcium homeostasis in Williams-Beuren syndrome." Pediatr Nephrol 17(11): 899-902.
- Sugayama, S. M., V. H. Koch, et al. (2004). "Renal and urinary findings in 20 patients with Williams-Beuren syndrome diagnosed by fluorescence in situ hybridization (FISH)." Rev Hosp Clin Fac Med Sao Paulo 59(5): 266-72.
- Sylos, C., A. C. Pereira, et al. (2002). "Arterial hypertension in a child with Williams-Beuren syndrome (7q11.23 chromosomal deletion)." Arq Bras Cardiol 79(2): 173-80.

Vision

- Atkinson, J., S. Anker, et al. (2001). "Visual and visuospatial development in young children with Williams syndrome." Dev Med Child Neurol 43(5): 330-7.
- Bohning, M., R. Campbell, et al. (2002). "Audiovisual speech perception in Williams syndrome." Neuropsychologia 40(8): 1396-406.
- Castelo-Branco, M., M. Mendes, et al. (2007). "Visual phenotype in Williams-Beuren syndrome challenges magnocellular theories explaining human neurodevelopmental visual cortical disorders." J Clin Invest 117(12): 3720-9.

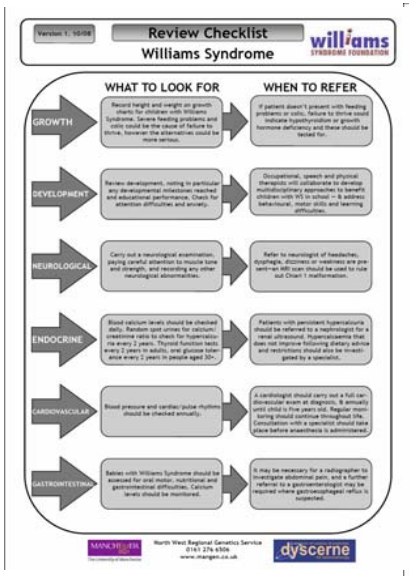
Bibliography continued…

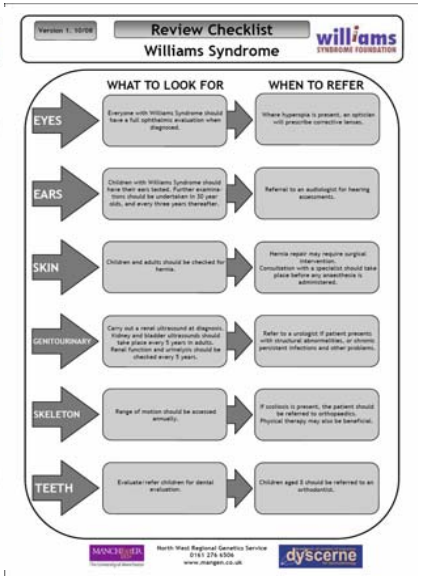
Vision continued…

- Eckert, M. A., A. M. Galaburda, et al. (2006). "The neurobiology of Williams syndrome: cascading influences of visual system impairment?" Cell Mol Life Sci 63(16): 1867-75.
- Kapp, M. E., G. K. von Noorden, et al. (1995). "Strabismus in Williams syndrome." Am J Ophthalmol 119(3): 355-60.
- Olitsky, S. E., L. S. Sadler, et al. (1997). "Subnormal binocular vision in the Williams syndrome." J Pediatr Ophthalmol Strabismus 34(1): 58-60.
- Sadler, L. S., S. E. Olitsky, et al. (1996). "Reduced stereoacuity in Williams syndrome." Am J Med Genet 66(3): 287-8.
- Sarpal, D., B. R. Buchsbaum, et al. (2008). "A Genetic Model for Understanding Higher Order Visual Processing: Functional Interactions of the Ventral Visual Stream in Williams Syndrome." Cereb. Cortex 18(10): 2402-2409.
- Van der Geest, J. N., G. C. Lagers-van Haselen, et al. (2005). "Visual depth processing in Williams-Beuren syndrome." Exp Brain Res 166(2): 200-9.
- Winter, M., R. Pankau, et al. (1996). "The spectrum of ocular features in the Williams-Beuren syndrome." Clin Genet 49(1): 28-31.

Other Resources

- **Williams Syndrome Review Checklist**





This has been developed as part of the same project as this guideline document, and is aimed at clinicians who see Williams Syndrome patients in follow-up clinics.
It contains clear instructions on why, when and who to refer patients to when they present with specific complications, and is available from Kay Metcalfe, Consultant Geneticist at St Mary's Hospital in Manchester (kay.metcalfe@cmft.nhs.uk).

- **Orphanet (www.orpha.net)**

Orphanet is an online database of rare diseases and related services provided throughout Europe. It contains information on over 5,000 conditions, including Williams Syndrome, and lists specialised clinics, diagnostic tests, patient organisations, research projects, clinical trials and patient registries relating specifically to Williams Syndrome.

Resources for Patients

- **Personal Health Record for Williams Syndrome (Blue Book)**

All babies in the UK are issued with a red book to record their health, growth and development. We have previously designed similar Blue Books for several rare conditions requiring multi-disciplinary management, including 22q11 Deletion Syndrome, Achondroplasia and Neurofibromatosis Type 1.
As part of this project a Blue Book has been designed for people with Williams Syndrome.
The primary aim of the Blue Book is to empower patients and their families, giving them more information about and ultimately more control over their health. It will also benefit the healthcare professionals involved in managing these patients, by facilitating inter-speciality communication, educating non-specialists and allied healthcare professionals, providing a readily 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 (see below), or from Kate Strong, Guidelines Developer at the Nowgen Centre in Manchester (kate.strong@cmft.nhs.uk).

- **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.

Acknowledgements

- **The Williams Syndrome Guideline Development Group**
  Dr Jane Ashworth, Dr Susmito Biswas, Professor Bruno Dallapiccola, Dr Mark Dalzell, Dr Jane Deal, Professor Dian Donnai, Pam Griffiths, Dr Kay Hood, Professor Pat Howlin, Dr Ed Ladusans, Dr Ralph MacKinnon, Dr Josephine Marriage, Dr Neil Martin, Dr Kay Metcalfe, Dr Zulf Mughal, Dr Ramanlal Patel, Dr Alison Pike, Dr Christopher Stinton, Kate Strong, Dr Rajat Verma, Dr Mike Wolfman

- **DYSCERNE: A Network of Centres of Expertise in Dysmorphology (www.dyscerne.org)**

- **The Williams Syndrome Foundation (www.williams-syndrome.org.uk)**
  Regional Coordinators
  Professional Advisory Panel

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

These guidelines were produced thanks to funding from DYSCERNE: A Network of Centre of Expertise for Dysmorphology (funded by the European Commission Public Health Executive Agency (DG Sanco) Project: 2006122), and the Williams Syndrome Foundation UK.

Document Title: Management of Williams Syndrome: A Clinical Guideline
Version: 1
Created: 08/05/2009
Reviewed: 02/10/2009
Review Date: 01/06/2010

Author and contact details: Kate Strong: kate.strong@cmft.nhs.uk