

Metabolic Health in children and adolescents living with Perinatal HIV

Chiva Good Practice Guidance v1.1 16.10.26 C Foster

Introduction

Children and adolescents living with perinatally acquired HIV (CAPHIV) are at increased risk of adverse metabolic health when compared to aged-matched peers not living with HIV.¹ Risk factors include lifelong HIV exposure with chronic immune activation, side effects associated with certain antiretroviral therapy (ART) regimens and traditional risk factors including diet, body mass index (BMI), exercise and ethnicity.

Poor metabolic health in childhood is associated with increased morbidity and mortality in adult life.² Whilst clinical manifestations of adverse metabolic health such as type 2 diabetes (DM) and cardiovascular events may not be apparent until later adulthood emerging data in young adults with PHIV is of concern.³ The REPRIEVE study in adults living with HIV showed a reduction in all cause cardiovascular events with statin use, however data is not available for those under 40 years.⁴ However early optimisation of metabolic health, including traditional risk factors such as obesity is therefore important and should addressed within paediatric HIV care.

Favourable metabolic health⁵ is characterised by optimisation of:

1. Blood sugar
2. Blood pressure (BP)
3. Waist circumference
4. Triglycerides
5. High-density lipoprotein (HDL) cholesterol

Antiretroviral therapy and adverse metabolic health

Studies in adults with HIV have shown association between certain ART agents and an increased risk of adverse metabolic health including:

1. Abacavir and increased cardiovascular risk⁶
2. Boosted protease inhibitors (PI) and dyslipidaemia⁷
3. Second generation integrase inhibitors and weight gain⁸
4. Tenofovir alafenamide (TAF) and weight gain⁹

Data in children and adolescents are more limited and bar increased rates of dyslipidaemia with boosted lopinavir the associations seen in adults have not been replicated.^{9,10} Dyslipidaemia associated with boosted PIs in adults is less marked with darunavir or atazanavir compared to lopinavir and when boosted with cobicistat compared to ritonavir.^{7,11} When considering a tenofovir disoproxil fumarate (TDF)-based or TAF-based regimen, the lipid-lowering beneficial effect of TDF should be weighed against the potential for increased renal and bone toxicity. Concerns regarding the potential impact of an ART regimen on metabolic health should be discussed prior to ART initiation/switch with the Perinatal Virtual Clinic (PVC) (<https://www.chiva.org.uk/professionals/clinic-networks/>) or regional centre multidisciplinary team (MDT).

Obesity and metabolic health

10% of UK children aged 5 are obese (BMI >30) rising to 23% as they enter secondary school age 11.¹² 63.8% of UK adults are overweight (BMI 25-30; 37.9%) or obese (25.9%). Childhood obesity is

associated with an increased risk of dyslipidaemia, diabetes (type 2 and to a lesser extent type 1) and metabolic dysfunction-associated steatotic liver disease (MASLD).¹³⁻¹⁵ CAPHIV with obesity should be referred to dietetics/endocrinology/specialist weight loss services as for the general childhood population and the potential increased risk of end organ disease for those living with HIV highlighted.

Monitoring of metabolic health

- Children and adolescents living with HIV should have their weight, height, BMI and blood pressure monitored at each routine visit (<https://www.chiva.org.uk/wp-content/uploads/2024/10/Chiva-Baseline-Investigations-and-Monitoring-Toolkit.pdf>)
- A family history of dyslipidaemia, early onset cardiovascular disease (hypertension, myocardial infarction, stroke prior to age 60 in a first degree relative) and diabetes should be documented.
- Lipid profiles should be measured at baseline and following ART switch. For children and adolescents on stable suppressive ART with normal lipid profiles, repeat lipid profiles can be considered at 2 yearly intervals unless clinically indicated.
- Abnormal lipid profiles should be repeated, fasted >8 hours, with confirmatory sampling within 3 months with suggested investigation of abnormal lipid profiles detailed below.
- Liver function should be monitored at each routine visit with suggested investigation of abnormal liver function detailed below. Transaminitis is a feature of MASLD but requires exclusion of other causes with the diagnosis supported by a raised BMI and evidence of fatty infiltration on liver ultrasound or fibroscan. Unexplained persistent transaminitis should be discussed with paediatric hepatology/PVC/regional MDT as appropriate.

Baseline investigations for dyslipidaemia

Consider family history consistent with familial hyperlipidaemia. Exclude secondary causes: DM, alcohol, hypothyroidism, drugs (eg ciclosporin, corticosteroids), chronic renal disease, obstructive liver disease and storage disorders.

1. Height, weight, BMI, BP
2. Fasted lipid profile with confirmatory sample
3. Glucose, HbA1C, C-peptide
4. Liver and Thyroid Function
5. HBV, HCV serology
6. USS Liver and/or fibroscan if ALT raised

Baseline investigations for unexplained transaminitis

Consider uncontrolled HIV, obesity, drugs (ART, alcohol/ drug use, steroids, anti-tuberculosis medication, herbal and over the counter remedies).

1. Height, weight, BMI
2. HAV, HBV, HCV, HEV, CMV, EBV serology
3. LFTs with AST / GGT, alpha-feto protein
4. FBC and Clotting
5. Autoantibodies – mitochondrial, smooth muscle and L/K microsomal
6. Alpha-1 anti trypsin, Copper, Ceruloplasmin, Ferritin, CK, coeliac Ab
7. Glucose, HbA1C, Lipid profile, Thyroid Function
8. USS Liver/ biliary tract/spleen, fibroscan

Management

- ⇒ Lifestyle interventions addressing diet, exercise, avoidance of smoking and alcohol are the mainstay of treatment for dyslipidaemia, the metabolic syndrome, MASLD and obesity in childhood.
- ⇒ CAPHIV should be referred to dietetics/endocrinology/specialist weight loss services as for the general childhood population, however the potential increased risk of end organ disease for those living with HIV should be highlighted.
- ⇒ Dietetic advice addressing childhood obesity can be found at <https://www.bda.uk.com/specialist-groups-and-branches/paediatric-specialist-group/childhood-obesity-toolkit.html>
- ⇒ Early referral to paediatric endocrinology/lipid services if cholesterol >7.5 mmol/L or triglycerides >5.5 mmol/L or LDL-Cholesterol >6.5 mmol/L (confirmed 2 fasted samples >3 weeks apart)^{11,16}
- ⇒ The potential role of ART in metabolic health should be discussed at the PVC/regional MDT prior to switch.

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Appendix *(from NHLBI ¹⁷)*

Under 13

Normal bp <90%

Pre-hypertension 90-95%

Stage 1 hypertension >95% + <12mmHg

Stage 2 hypertension >95% + >12 mmHg

13+

Normal bp <120/80

High BP 120-129 systolic

Stage 1 hypertension 130-139

Stage 2 Hypertension 140+

Blood Pressure Levels for Boys by Age and Height Percentile

Age (Year)	BP Percentile ↓	Systolic BP (mmHg)							Diastolic BP (mmHg)						
		← Percentile of Height →							← Percentile of Height →						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	80	81	83	85	87	88	89	34	35	36	37	38	39	39
	90th	94	95	97	99	100	102	103	49	50	51	52	53	53	54
	95th	98	99	101	103	104	106	106	54	54	55	56	57	58	58
	99th	105	106	108	110	112	113	114	61	62	63	64	65	66	66
2	50th	84	85	87	88	90	92	92	39	40	41	42	43	44	44
	90th	97	99	100	102	104	105	106	54	55	56	57	58	58	59
	95th	101	102	104	106	108	109	110	59	59	60	61	62	63	63
	99th	109	110	111	113	115	117	117	66	67	68	69	70	71	71
3	50th	86	87	89	91	93	94	95	44	44	45	46	47	48	48
	90th	100	101	103	105	107	108	109	59	59	60	61	62	63	63
	95th	104	105	107	109	110	112	113	63	63	64	65	66	67	67
	99th	111	112	114	116	118	119	120	71	71	72	73	74	75	75
4	50th	88	89	91	93	95	96	97	47	48	49	50	51	51	52
	90th	102	103	105	107	109	110	111	62	63	64	65	66	66	67
	95th	106	107	109	111	112	114	115	66	67	68	69	70	71	71
	99th	113	114	116	118	120	121	122	74	75	76	77	78	78	79
5	50th	90	91	93	95	96	98	98	50	51	52	53	54	55	55
	90th	104	105	106	108	110	111	112	65	66	67	68	69	69	70
	95th	108	109	110	112	114	115	116	69	70	71	72	73	74	74
	99th	115	116	118	120	121	123	123	77	78	79	80	81	81	82
6	50th	91	92	94	96	98	99	100	53	53	54	55	56	57	57
	90th	105	106	108	110	111	113	113	68	68	69	70	71	72	72
	95th	109	110	112	114	115	117	117	72	72	73	74	75	76	76
	99th	116	117	119	121	123	124	125	80	80	81	82	83	84	84
7	50th	92	94	95	97	99	100	101	55	55	56	57	58	59	59
	90th	106	107	109	111	113	114	115	70	70	71	72	73	74	74
	95th	110	111	113	115	117	118	119	74	74	75	76	77	78	78
	99th	117	118	120	122	124	125	126	82	82	83	84	85	86	86
8	50th	94	95	97	99	100	102	102	56	57	58	59	60	60	61
	90th	107	109	110	112	114	115	116	71	72	72	73	74	75	76
	95th	111	112	114	116	118	119	120	75	76	77	78	79	79	80
	99th	119	120	122	123	125	127	127	83	84	85	86	87	87	88
9	50th	95	96	98	100	102	103	104	57	58	59	60	61	61	62
	90th	109	110	112	114	115	117	118	72	73	74	75	76	76	77
	95th	113	114	116	118	119	121	121	76	77	78	79	80	81	81
	99th	120	121	123	125	127	128	129	84	85	86	87	88	88	89
10	50th	97	98	100	102	103	105	106	58	59	60	61	61	62	63
	90th	111	112	114	115	117	119	119	73	73	74	75	76	77	78
	95th	115	116	117	119	121	122	123	77	78	79	80	81	81	82
	99th	122	123	125	127	128	130	130	85	86	86	88	88	89	90

Blood Pressure Levels for Boys by Age and Height Percentile (Continued)

Age	BP Percentile	Systolic BP (mmHg)							Diastolic BP (mmHg)						
		+- Percentile of Height							+- Percentile of Height						
11	50th	99	100	102	104	105	107	107	59	59	60	61	62	63	63
	90th	113	114	115	117	119	120	121	74	74	75	76	77	78	78
	95th	117	118	119	121	123	124	125	78	78	79	80	81	82	82
	99th	124	125	127	129	130	132	132	86	86	87	88	89	90	90
12	50th	101	102	104	106	108	109	110	59	60	61	62	63	63	64
	90th	115	116	118	120	121	123	123	74	75	75	76	77	78	79
	95th	119	120	122	123	125	127	127	78	79	80	81	82	82	83
	99th	126	127	129	131	133	134	135	86	87	88	89	90	90	91
13	50th	104	105	106	108	110	111	112	60	60	61	62	63	64	64
	90th	117	118	120	122	124	125	126	75	75	76	77	78	79	79
	95th	121	122	124	126	128	129	130	79	79	80	81	82	83	83
	99th	128	130	131	133	135	136	137	87	87	88	89	90	91	91
14	50th	106	107	109	111	113	114	115	60	61	62	63	64	65	65
	90th	120	121	123	125	126	128	128	75	76	77	78	79	79	80
	95th	124	125	127	128	130	132	132	80	80	81	82	83	84	84
	99th	131	132	134	136	138	139	140	87	88	89	90	91	92	92
15	50th	109	110	112	113	115	117	117	61	62	63	64	65	66	66
	90th	122	124	125	127	129	130	131	76	77	78	79	80	80	81
	95th	126	127	129	131	133	134	135	81	81	82	83	84	85	85
	99th	134	135	136	138	140	142	142	88	89	90	91	92	93	93
16	50th	111	112	114	116	118	119	120	63	63	64	65	66	67	67
	90th	125	126	128	130	131	133	134	78	78	79	80	81	82	82
	95th	129	130	132	134	135	137	137	82	83	83	84	85	86	87
	99th	136	137	139	141	143	144	145	90	90	91	92	93	94	94
17	50th	114	115	116	118	120	121	122	65	66	66	67	68	69	70
	90th	127	128	130	132	134	135	136	80	80	81	82	83	84	84

BP, blood pressure

• The 90th percentile is 1.28 SD, 95th percentile is 1.645 SD, and the 99th percentile is 2.326SD over the mean.

For research purposes, the standard deviations in Appendix Table B- 1 allow one to compute BP Z-scores and percentiles for boys with height percentiles given in Table 3 (i.e., the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles). These height percentiles must be converted to height Z-scores given by (5% = -1.645 ; 10% = -1.28 ; 25% = -0.68 ; 50% = 0 ; 75% = 0.68 ; 90% = 1.28 ; 95% = 1.645) and then computed according to the methodology in steps 2-4 described in Appendix B. For children with height percentiles other than these, follow steps 1-4 as described in Appendix B.

Blood Pressure Levels for Girls by Age and Height Percentile

Age (Year)	BP Percentile	Systolic BP (mm Hg)							Diastolic BP (mm Hg)						
		± Percentile of Height							± Percentile of Height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	83	84	85	86	88	89	90	38	39	39	40	41	41	42
	90th	97	97	98	100	101	102	103	52	53	53	54	55	55	56
	95th	100	101	102	104	105	106	107	56	57	57	58	59	59	60
	99th	108	108	109	111	112	113	114	64	64	65	65	66	67	67
2	50th	85	85	87	88	89	91	91	43	44	44	45	46	46	47
	90th	98	99	100	101	103	104	105	57	58	58	59	60	61	61
	95th	102	103	104	105	107	108	109	61	62	62	63	64	65	65
	99th	109	110	111	112	114	115	116	69	69	70	70	71	72	72
3	50th	86	87	88	89	91	92	93	47	48	48	49	50	50	51
	90th	100	100	102	103	104	106	106	61	62	62	63	64	64	65
	95th	104	104	105	107	108	109	110	65	66	66	67	68	68	69
	99th	111	111	113	114	115	116	117	73	73	74	74	75	76	76
4	50th	88	88	90	91	92	94	94	50	50	51	52	52	53	54
	90th	101	102	103	104	106	107	108	64	64	65	66	67	67	68
	95th	105	106	107	108	110	111	112	68	68	69	70	71	71	72
	99th	112	113	114	115	117	118	119	76	76	76	77	78	79	79
5	50th	89	90	91	93	94	95	96	52	53	53	54	55	55	56
	90th	103	103	105	106	107	109	109	66	67	67	68	69	69	70
	95th	107	107	108	110	111	112	113	70	71	71	72	73	73	74
	99th	114	114	116	117	118	120	120	78	78	79	79	80	81	81
6	50th	91	92	93	94	96	97	98	54	54	55	56	56	57	58
	90th	104	105	106	108	109	110	111	68	68	69	70	70	71	72
	95th	108	109	110	111	113	114	115	72	72	73	74	74	75	76
	99th	115	116	117	119	120	121	122	80	80	80	81	82	83	83
7	50th	93	93	95	96	97	99	99	55	56	56	57	58	58	59
	90th	106	107	108	109	111	112	113	69	70	70	71	72	72	73
	95th	110	111	112	113	115	116	116	73	74	74	75	76	76	77
	99th	117	118	119	120	122	123	124	81	81	82	82	83	84	84
8	50th	95	95	96	98	99	100	101	57	57	57	58	59	60	60
	90th	108	109	110	111	113	114	114	71	71	71	72	73	74	74
	95th	112	112	114	115	116	118	118	75	75	75	76	77	78	78
	99th	119	120	121	122	123	125	125	82	82	83	83	84	85	86
9	50th	96	97	98	100	101	102	103	58	58	58	59	60	61	61
	90th	110	110	112	113	114	116	116	72	72	72	73	74	75	75
	95th	114	114	115	117	118	119	120	76	76	76	77	78	79	79
	99th	121	121	123	124	125	127	127	83	83	84	84	85	86	87
10	50th	98	99	100	102	103	104	105	59	59	59	60	61	62	62
	90th	112	112	114	115	116	118	118	73	73	73	74	75	76	76
	95th	116	116	117	119	120	121	122	77	77	77	78	79	80	80
	99th	123	123	125	126	127	129	129	84	84	85	86	86	87	88

Blood Pressure Levels for Girls by Age and Height Percentile (Continued)

Age (Year)	BP Percentile	Systolic BP (mmHg)							Diastolic BP (mm Hg)						
		± Percentile of Height							± Percentile of Height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
11	50th	100	101	102	103	105	106	107	60	60	60	61	62	63	63
	90th	114	114	116	117	118	119	120	74	74	74	75	76	77	77
	95th	118	118	119	121	122	123	124	78	78	78	79	80	81	81
	99th	125	125	126	128	129	130	131	85	85	86	87	87	88	89
12	50th	102	103	104	105	107	108	109	61	61	61	62	63	64	64
	90th	116	116	117	119	120	121	122	75	75	75	76	77	78	78
	95th	119	120	121	123	124	125	126	79	79	79	80	81	82	82
	99th	127	127	128	130	131	132	133	86	86	87	88	88	89	90
13	50th	104	105	106	107	109	110	110	62	62	62	63	64	65	65
	90th	117	118	119	121	122	123	124	76	76	76	77	78	79	79
	95th	121	122	123	124	126	127	128	80	80	80	81	82	83	83
	99th	128	129	130	132	133	134	135	87	87	88	89	89	90	91
14	50th	106	106	107	109	110	111	112	63	63	63	64	65	66	66
	90th	119	120	121	122	124	125	125	77	77	77	78	79	80	80
	95th	123	123	125	126	127	129	129	81	81	81	82	83	84	84
	99th	130	131	132	133	135	136	136	88	88	89	90	90	91	92
15	50th	107	108	109	110	111	113	113	64	64	64	65	66	67	67
	90th	120	121	122	123	125	126	127	78	78	78	79	80	81	81
	95th	124	125	126	127	129	130	131	82	82	82	83	84	85	85
	99th	131	132	133	134	136	137	138	89	89	90	91	91	92	93
16	50th	108	108	110	111	112	114	114	64	64	65	66	66	67	68
	90th	121	122	123	124	126	127	128	78	78	79	80	81	81	82
	95th	125	126	127	128	130	131	132	82	82	83	84	85	85	86
	99th	132	133	134	135	137	138	139	90	90	90	91	92	93	93
17	50th	108	109	110	111	113	114	115	64	65	65	66	67	67	68
	90th	122	122	123	125	126	127	128	78	79	79	80	81	81	82
	95th	125	126	127	129	130	131	132	82	83	83	84	85	85	86
	99th	133	133	134	136	137	138	139	90	90	91	91	92	93	93

BP, blood pressure

• The 90th percentile is 1.28 SD, 95th percentile is 1.64 SD, and the 99th percentile is 2.32 SD over the mean.

For research purposes the standard deviations in Appendix Table B-1 allow one to compute BP Z-scores and percentiles for girls with height percentiles given in Table 4 (i.e., the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles). These height percentiles must be converted to height Z-scores given by (5% = -1.645; 10% = -1.28; 25% = -0.68; 50% = 0; 75% = 0.68; 90% = 1.28; 95% = 1.645) and then computed according to the methodology in steps 2-4 described in Appendix B. For children with height percentile other than the set of steps 1-4 as described in Appendix B.