Supplementary Information

CARDIOMETABOLIC RISK FACTORS IN CHILDHOOD, ADOLESCENT AND YOUNG ADULT SURVIVORS OF ACUTE LYMPHOBLASTIC LEUKEMIA SURVIVORS – A PETALE COHORT

Emile Levy[1], Mariia Samoilenko[3], Sophia Morel[1], Jade England[2], Devendra Amre[2], Laurence Bertout[2], Simon Drouin[2], Caroline Laverdière[2], Maja Krajinovic[2], Daniel Sinnett[2], Geneviève Lefebvre[3], Valérie Marcil[1*]

Research Centre, Sainte-Justine University Health Center, Departments of [1]Nutrition and [2]Pediatrics, Université de Montréal, Montreal, Quebec, Canada, H3T 1C5, [3]Department of Mathematics, Université du Québec à Montréal, Montreal, Quebec, Canada, H3C 3P8.

Supplementary Table 1. Cut-off values for cardiometabolic outcomes

Risk factor	Adults	Children
BMI		
Overweight	>25 and <30 kg/m^2	>85th and <97th percentile
Obesity	≥30 kg/m^2	≥97th percentile
Waist circumference		
Borderline	≥94 and <102 cm (men); ≥80 and <88 cm (women)	≥90th and <95th percentile
High	≥102 cm (men) and ≥88 cm (women)	≥95th percentile
Hypertension		
Pre-hypertension	≥130/85 and <140/90 mmHg	≥90th and <95th percentile for age and height
Hypertension	≥140/90 mmHg	≥95th percentile for age and height
Blood fasting glucose		
At risk	≥5.6 and <6.1 mmol/L	≥5.6 and <6.1 mmol/L
Prediabetes	≥6.1 mmol/L	≥6.1 mmol/L
Glycated hemoglobin		
At risk	≥5.5 and <6%	≥5.5 and <6%
Prediabetes	≥6% and <6.5%	≥6% and <6.5%
Triglycerides		
Borderline	≥1.3 and <1.7 mmol/L	≥1.00 and <1.47 mmol/L
High	≥1.7 mmol/L	≥1.47 mmol/L
LDL-cholesterol		
Borderline	≥2.6 and <3.4 mmol/L	≥2.85 and <3.36 mmol/L
High	≥3.4 mmol/L	≥3.36 mmol/L
HDL-cholesterol		
Low	<1.03 (men) and <1.3 mmol/L (women)	<1.03 mmol/L

BMI, body mass index; HOMA-IR, homeostasis model assessment; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

Supplementary Table 2. Distribution of cardiometabolic outcomes according to cut-off values of survivors of childhood acute lymphoblastic leukemia from the PETALE cohort

	Total (N=247)	**Adults** (N=162)	**Men** (N=80)	**Women** (N=82)	**Children** (N=85)	**Boys** (N=42)	**Girls** (N=43)
				N (%)			
BMI							
Normal	152 (61.5)	92 (56.8)	49 (61.2)	43 (52.4)	60 (70.6)	26 (61.9)	34 (79.1)
Overweight	60 (24.3)	42 (25.9)	21 (25.3)	21 (25.6)	18 (21.2)	11 (26.2)	7 (16.2)
Obesity	35 (14.2)	28 (17.3)	10 (12.50)	18 (22.0)	7 (8.2)	5 (11.9)	2 (4.7)
Waist circumference							
Normal	131 (53.0)	80 (50.0)	56 (70.00)	25 (30.5)	50 (58.8)	24 (57.1)	26 (60.5)
Borderline	38 (15.4)	32 (19.7)	13 (16.2)	19 (23.2)	6 (7.1)	2 (4.8)	4 (9.3)
High	78 (31.6)	49 (30.3)	11 (13.8)	38 (46.3)	29 (34.1)	16 (38.1)	13 (30.2)
Systolic blood pressure							
Normal	222 (89.9)	145 (89.5)	66 (82.5)	79 (96.3)	77 (90.6)	35 (83.3)	42 (97.7)
Pre-hypertension	21 (8.5)	14 (8.6)	11 (13.7)	3 (3.7)	7 (8.2)	6 (14.3)	1 (2.3)
Hypertension	4 (1.6)	3 (1.9)	3 (3.8)	0 (0)	1 (1.2)	1 (2.4)	0 (0)
Diastolic Blood pressure							
Normal	239 (96.8)	155 (95.7)	76 (95.0)	79 (96.3)	84 (98.8)	41 (97.6)	43 (100)
Pre-hypertension	7 (2.8)	6 (3.7)	3 (3.7)	3 (3.7)	1 (1.2)	1 (2.4)	0 (0)
Hypertension	1 (0.4)	1 (0.6)	1 (1.3)	0 (0)	0 (0)	0 (0)	0 (0)
Fasting blood glucose							
Optimal	217 (87.9)	136 (84.0)	63 (78.7)	73 (89.0)	81 (95.3)	39 (92.9)	42 (97.7)
At risk	23 (9.3)	19 (11.7)	15 (18.8)	4 (4.9)	4 (4.7)	3 (7.1)	1 (2.3)
Prediabetes	7 (2.8)	7 (4.3)	2 (2.5)	5 (6.1)	0 (0.0)	0 (0.0)	0 (0.0)
HbA1c							
Optimal	210 (85.0)	142 (87.6)	71 (88.8)	71 (86.6)	68 (80.0)	33 (78.6)	35 (81.4)
At-risk	33 (13.4)	17 (10.5)	8 (10.0)	9 (11.0)	16 (18.8)	9 (21.4)	7 (16.3)
Prediabetes	4 (1.6)	3 (1.9)	1 (1.2)	2 (2.4)	1 (1.2)	0 (0.00)	1 (2.3)
HOMA-IR							
Normal	207 (83.8)	133 (82.1)	69 (86.2)	64 (78.0)	74 (87.1)	37 (88.10)	37 (86.0)
High	40 (16.2)	29 (17.9)	11 (13.8)	18 (22.0)	11 (12.9)	5 (11.90)	6 (14.0)
Triglycerides							
Optimal	175 (70.8)	120 (74.0)	64 (80.0)	56 (68.3)	55 (64.7)	27 (64.3)	28 (65.1)
Borderline	42 (17.0)	21 (13.0)	6 (7.5)	15 (18.3)	21 (24.7)	12 (28.6)	9 (20.9)
High	30 (12.2)	21 (13.0)	10 (12.5)	11 (13.4)	9 (10.6)	3 (7.1)	6 (14.0)
LDL-cholesterol							
Optimal	139 (56.3)	73 (45.1)	33 (41.2)	40 (48.8)	66 (77.7)	34 (81.0)	32 (74.4)
Borderline	65 (26.3)	53 (32.7)	27 (33.8)	26 (31.7)	12 (14.1)	4 (9.5)	8 (18.6)
High	43 (17.4)	36 (22.2)	20 (25.00)	16 (19.5)	7 (8.2)	4 (9.5)	3 (7.0)
HDL-cholesterol							
Optimal	190 (76.9)	119 (73.5)	66 (82.5)	53 (64.6)	71 (83.5)	31 (73.8)	40 (93.0)
Low	57 (23.1)	43 (26.5)	14 (17.5)	29 (35.4)	14 (16.5)	11 (26.2)	3 (7.0)

BMI, body mass index; HOMA-IR, homeostasis model assessment; LDL, low-density lipoprotein; HDL, high-density lipoprotein; HbA1c: glycated hemoglobin.

Supplementary Table 3. Predictors of cardiometabolic complications in survivors of childhood acute lymphoblastic leukemia: simple log-binomial regression univariate analyses

	High BMI	High waist circumference	High TG	High LDL-cholesterol	Low HDL-cholesterol	High glucose	High HbA1c
	Relative Risk (95% CI)						
CRT (yes vs. none)	1.30 (0.68-2.50)	1.29 (0.87-1.90)	1.18 (0.58-2.36)	5.17* (2.11-12.68)	1.17 (0.73-1.87)	4.08 (0.50-33.39)	2.04 (0.22-19.34)
Gender (males vs. females)	0.77 (0.41-1.43)	0.54 (0.37-0.80)	0.78 (0.40-1.54)	1.29 (0.75-2.24)	0.80 (0.51-1.27)	0.41 (0.08-2.07)	0.34 (0.04-3.24)
Age at diagnosis (per unit of year)	1.01 (0.95-1.08)	1.01 (0.97-1.05)	1.05 (0.98-1.12)	0.98 (0.92-1.05)	1.01 (0.96-1.06)	1.13 (0.98-1.29)	1.04 (0.86-1.27)
Age at interview (per unit of year)	1.08* (1.03-1.12)	1.02 (0.99-1.05)	1.04 (0.99-1.09)	1.06* (1.02-1.09)	1.03 (0.99-1.06)	1.14* (1.03-1.26)	1.08 (0.94-1.24)
Obesity at the end of treatment (yes vs. none)	2.90* (1.40-5.54)	2.23* (1.50-3.30)	1.93 (0.78-4.02)	0.84 (0.37-1.88)	1.09 (0.60-2.01)	CP	4.05 (0.27-63.37)
Δ Percentile BMI (unit=5%)	1.01 (0.94-1.08)	1.03 (0.99-1.07)	0.96 (0.89-1.04)	0.96 (0.90-1.03)	0.99 (0.94-1.04)	1.07 (0.89-1.30)	0.90 (0.68-1.19)

Simple log-binomial regression analysis for each cardiometabolic complication as a function of each predictor was performed. CRT: cranial radiotherapy; BMI: body mass index; RR: relative risk; CI: confidence interval; TG: triglycerides; LDL: low-density lipoprotein; HDL: high-density lipoprotein. Δ BMI percentile = percentile BMI at end of treatment - percentile BMI at diagnosis. CP: This analysis could not be performed because of convergence problems. *P<0.05.

Supplementary Table 4. Predictors of cardiometabolic complications in survivors of childhood acute lymphoblastic leukemia: multiple log-binomial univariate analyses

	High BMI	High waist circumference	High TG	High LDL-cholesterol	Low HDL-cholesterol
	Relative Risk (95% CI)				
CRT (yes vs. none)	1.07 (0.49-2.36)	1.36 (0.87-2.15)	1.29 (0.55-3.01)	4.78* (1.72-13.28)	1.22 (0.70, 2.13)
Gender (males vs. females)	0.95 (0.48-1.90)	0.65 (0.41-1.03)	0.80 (0.37-1.75)	1.12 (0.64-1.94)	0.80 (0.48, 1.33)
Age at diagnosis (per unit of year)	0.97 (0.88-1.07)	1.04 (0.99-1.11)	1.06 (0.96-1.17)	0.87 (0.81-0.95)	0.97 (0.90, 1.05)
Age at interview (per unit of year)	1.11* (1.02-1.20)	1.00 (0.95-1.05)	0.98 (0.91-1.07)	1.11* (1.04-1.19)	1.05 (0.99, 1.10)
Obesity at the end of treatment (yes vs. none)	2.73* (1.32-5.63)	2.14* (1.36-3.38)	1.94 (0.84-4.49)	0.74 (0.34-1.58)	1.00 (0.53, 1.88)
Δ Percentile BMI (unit=5%)	0.99 (0.92-1.06)	1.01 (0.97-1.05)	0.97 (0.89-1.05)	0.96 (0.90-1.01)	0.99 (0.94, 1.04)

Multiple log-binomial regression analysis was performed with a model including the predictors: gender, exposure to CRT, age at diagnosis, age at interview, obesity at end of treatment and delta BMI percentile. CRT: cranial radiotherapy; BMI: body mass index; RR; CI: confidence interval; TG: triglycerides; LDL: low-density lipoprotein; HDL: high-density lipoprotein. Δ BMI percentile = percentile BMI at end of treatment - percentile BMI at diagnosis. *P<0.05.