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Body mass index during and early after therapy for pediatric acute lymphoblastic leukemia is associated with obesity in survivors

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KS, KKN, and HI conceived the study. KS, GCZ, DS, KKN, and HI contributed to the study design. KS, GCZ, NL, AN, KP, TY, JLB, PY, CLW, SBD, AD, YS, SCK, GTA, CHP, MMH, DS, KKN, and HI were involved in data acquisition, analysis, interpretation, manuscript editing, and review. GCZ and DS performed the statistical analysis. KS, NL, GCZ, DS, KKN, and HI prepared the manuscript. All authors reviewed and approved the final version of the manuscript.

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DATA-SHARING STATEMENT

The SJLIFE data that support the findings of this study are openly available at https://www.stjude.cloud/research-domains/cancer-survivorship. Data specific to this paper will be uploaded to https://zenodo.org concomitant with the publication of the manuscript.

CONFLICT OF INTEREST DISCLOSURE

The authors have declared no conflicts of interest.

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The current 5-year survival rate for childhood acute lymphoblastic leukemia (ALL) exceeds 90% with risk-adaptive therapy, effective central nervous system (CNS) control without cranial radiotherapy (CRT), and improved supportive care.[1] However, survivors remain vulnerable to chronic health conditions.[2] In recent protocols, the prevalences of obesity and musculoskeletal disorders have surpassed those of neurocognitive impairment and cardiopulmonary dysfunction.[2] Childhood obesity contributes to cardiometabolic disorders in adulthood, making it a key focus in survivorship research.[3] Disease risk classification, specific treatments such as glucocorticoids and CRT, genetics, unhealthy diet, and physical inactivity can contribute to obesity among survivors, and survivors with a high polygenic risk score (PRS) experience an increase of up to 53-fold in severe obesity.[4,5] A prior study of body mass index (BMI) in ALL used single-timepoint BMIs, which cannot capture dynamic treatment-related weight changes.[6] Moreover, survivors experience additional biological and therapy-related factors that may further modify obesity persistence into adulthood. Therefore, we modeled longitudinal BMI trajectories and calculated BMI areas under the curve (AUCs) above the overweight/obesity threshold with variable observation periods to characterize the dynamic and cumulative overweight/obesity burden, enabling early identification of high-risk patients for timely intervention during therapy. This study was approved by the St. Jude Institutional Review Board. Informed consent or assent was obtained from each patient or from their legal guardian, as appropriate to the patient's age.

Eligible survivors (n=881) were treated in St. Jude Total Therapy Studies X-XV (1980-2006)[1,7-12] and participated in the St. Jude Lifetime Cohort Study (SJLIFE) with a completed initial on-campus evaluation.[13] Data from the Total Therapy Studies and SJLIFE were sequentially linked for individual participants. Exclusion criteria

included age <2 years at ALL diagnosis (n=76) and having Down syndrome/Turner syndrome (n=10), relapsed disease (n=66), transplantation (n=37), secondary malignant neoplasms requiring treatment before the SJLIFE visit (n=5), and missing BMI data during therapy (n=9). Therefore, 678 patients were evaluated.

Patient demographics, treatment exposures, and lifestyle data were obtained from medical records and protocol databases.[13] The BMI-PRS included 2.09 million genome-wide common variants.[4] Genetic ancestry was determined by using *k*-means clustering implemented in Admixture,[14] based on genotype data and the 1000 Genomes reference populations. Height and weight were collected at diagnosis (±3 days), end of induction (±7 days), 6 months (±14 days), 12 months (±14 days), 18 months (±30 days), 24 months (±30 days), end of therapy (±30 days), and annually thereafter (±180 days) until 5 years off-therapy. Survivorship outcomes were obtained at the first SJLIFE visit. BMI was converted to an age- and sex-adjusted Z-score by using Centers for Disease Control and Prevention (CDC) growth charts. For patients aged >20 years, Z-scores were based on reference data for individuals aged 20 years. Survivors were categorized by BMI as follows: <18.5 kg/m^2: underweight; 18.5-24.9 kg/m^2: normal weight; 25.0-29.9 kg/m^2: overweight, and ≥30.0 kg/m^2: obese.

Latent classes were identified using a latent process mixed model, assigning each patient to the class with the highest posterior probability. Missing BMI values during treatment were imputed using the last observation carried forward (LOCF) method. The optimal number of latent classes was determined using Bayesian and Akaike Information Criteria and clinical relevance. Total AUC, representing exposure to overweight/obesity, was calculated as the area above a BMI Z-score of 1.036 (85th percentile) by integrating BMI Z-scores across measurement intervals. Analyses

were performed in R version 4.3.1. Latent profiles were modeled using BMI Z-scores from diagnosis to 5 years off-therapy and from diagnosis to 1 year post-diagnosis. AUCs were calculated for three periods: diagnosis to 5 years off-therapy, diagnosis to 1 year post-diagnosis, and diagnosis to end of induction therapy. A web application for predicting a patient's latent class and calculating the BMI AUC is available at https://sjbiostat.shinyapps.io/BMIzExplorer/. Associations of BMI latent classes and AUCs with weight status were evaluated using multinomial logistic regression. Statistical significance was set at $P<0.05$.

Characteristics of the 678 patients included in the analysis and their longitudinal changes in weight, height, and BMI Z-scores from diagnosis until 5 years off-therapy are shown in *Online Supplementary Tables S1* and *S2*, respectively. The median time from end of therapy to first SJLIFE evaluation was 17.47 years (range, 6.08-33.42 years). The percentage of overweight/obese patients increased from 16.4% at diagnosis to 35.2% at off-therapy and 44.6% at 5 years off-therapy, and it continued rising to 63.3% in survivors.

We identified four BMI trajectory classes from diagnosis to 5 years off-therapy (Fig. 1A). The low-slow group was characterized by persistently low BMI with a gradual increase (n=404, 59.6%). The medium-slow group showed mid-range BMI at diagnosis with a slow upward trend (n=180, 26.5%). The low-fast group began treatment with a lower BMI but experienced a rapid increase during and shortly after therapy (n=65, 9.6%). The high-slow group started with a higher BMI that gradually increased (n=29, 4.3%). These patterns may reflect differences in baseline nutritional status, treatment-related metabolic effects, or activity limitations during therapy. For BMI trajectories from diagnosis to 1 year post-diagnosis, most patients were in the

"normal" group (n=393, 58.0%), followed by the "medium" (n=151, 22.3%), "low" (n=108, 15.9%), and "high" (n=26, 3.8%) groups (Fig. 1B).

Multivariable models evaluating associations between BMI trajectories, host and treatment factors, and BMI Z-scores or weight-status categories in survivors included sex, race/ethnicity, attained age, and CRT (the only treatment factor significant in univariate analysis). BMI latent classes and BMI AUCs were significantly associated with BMI categories and BMI Z-scores at survivorship in all models (Tables 1 and 2). From diagnosis to 5 years off-therapy, the “high-slow” group had the highest risk of overweight and obesity, followed by the “low-fast” and “medium-slow” groups, when compared with the “low-slow” group ($P \leq 0.026$ for all). From diagnosis to 1 year post-diagnosis, the “high” group had the highest risk of obesity when compared to the “normal” group ($P < 0.001$). The “medium” group had an increased risk of both overweight and obesity in survivors ($P \leq 0.020$), whereas the “low” group exhibited protective effects ($P < 0.001$). For the association of overweight/obesity AUCs with overweight and obesity in survivors, a larger overweight/obesity AUCs derived from all models (from diagnosis to 5 years off-therapy, from diagnosis to 1 year post-diagnosis, and from diagnosis to end of induction therapy) showed a significantly increased risk of overweight and obesity in survivors ($P \leq 0.012$ for all) (Table 2). Across the BMI trajectory and AUC models, CRT and older age at SJLIFE assessment were significantly associated with an increased risk of both overweight and obesity ($P \leq 0.007$ for all) (Tables 1 and 2).

The BMI-PRS was available for 599 of the 678 survivors (88.4%). Higher PRS was associated with significantly greater odds of overweight and obesity in both trajectory models and all AUC models ($P \leq 0.007$ for all) (*Online Supplementary Table*

S3). Even after adjusting for PRS, the associations of BMI trajectories and AUC with overweight and obesity risk remained significant.

Our findings showed that the prevalence of overweight and obesity increased steadily over survival time, from 16.4% at diagnosis to 63.3% at the first SJLIFE visit, which is higher than that in a previous meta-analysis (34%-46% at ≥10 years off-therapy).[3] There were associations of BMI trajectories and overweight/obesity AUCs with the overweight and obesity categories and BMI Z-scores in long-term survivors across multiple timeframes. These associations, along with older age at SJLIFE assessment and CRT, remained significant even after adjustment for BMI-PRS, a powerful predictor of severe obesity. In the trajectory models, survivors in the "high-slow" and "high" categories, as compared with those in the "low-slow" and "normal" categories, respectively, had substantially higher obesity risks (odds ratios: 76.6 and 58.8, respectively) than were found in the healthy population, showing that obese children are approximately five times more likely than non-obese children to be obese adults.[6] Treatment factors, such as glucocorticoids, CNS-directed therapy, and a sedentary lifestyle may exacerbate weight gain during and after therapy.[3,15] AUC analysis further supported the trajectory models, showing that more extensive overweight/obesity—even during induction therapy alone—was associated with a higher risk of long-term obesity.

CRT, especially at a younger age, was a major contributor to reduced adult height and increased BMI resulting from growth hormone deficiency and central precocious puberty.[5] The shift away from CRT towards intrathecal therapy in modern protocols is expected to reduce these effects.[1,5] However, even survivors of ALL treated without CRT have demonstrated an increased obesity risk when compared to controls.[6] As the association between BMI AUC and survivorship obesity emerges as

early as induction, preventive interventions by a multidisciplinary team including a dietitian, a physical therapist, a pharmacist, a social worker, child life specialists, and clinicians should begin during this phase.

This study has limitations, including potential selection bias from evaluating only survivors who completed an on-site visit and missing socioeconomic, environmental, or lifestyle data during therapy. Nevertheless, effect directions remained consistent after adjustment for CRT and PRS. Further prospective studies are warranted to minimize these confounders.

In conclusion, BMI trajectories and overweight/obesity exposure during ALL treatment and early survivorship are independently associated with long-term obesity in survivors. These findings support the implementation of early, multidisciplinary interventions—including nutritional counseling, physical activity promotion, and behavioral support—beginning as early as induction therapy to prevent or treat obesity in this vulnerable population.

REFERENCES.

1. Pui C-H, Campana D, Pei D, et al. Treating childhood acute lymphoblastic leukemia without cranial irradiation. N Engl J Med. 2009;360(26):2730-2741.
2. Mulrooney DA, Hyun G, Ness KK, et al. The changing burden of long-term health outcomes in survivors of childhood acute lymphoblastic leukaemia: a retrospective analysis of the St Jude Lifetime Cohort Study. Lancet Haematol. 2019;6(6):e306-e316.
3. Zhang FF, Kelly MJ, Saltzman E, Must A, Roberts SB, Parsons SK. Obesity in pediatric ALL survivors: a meta-analysis. Pediatrics. 2014;133(3):e704-e715.
4. Sapkota Y, Qiu W, Dixon SB, et al. Genetic risk score enhances the risk prediction of severe obesity in adult survivors of childhood cancer. Nat Med. 2022;28(8):1590-1598.
5. Garmey EG, Liu Q, Sklar CA, et al. Longitudinal changes in obesity and body mass index among adult survivors of childhood acute lymphoblastic leukemia: a report from the Childhood Cancer Survivor Study. J Clin Oncol. 2008;26(28):4639-4645.
6. Browne EK, Zhou Y, Chemaitilly W, et al. Changes in body mass index, height, and weight in children during and after therapy for acute lymphoblastic leukemia. Cancer. 2018;124(21):4248-4259.
7. Rivera GK, Raimondi SC, Hancock ML, et al. Improved outcome in childhood acute lymphoblastic leukaemia with reinforced early treatment and rotational combination chemotherapy. Lancet. 1991;337(8733):61-66.
8. Abromowitch M, Ochs J, Pui CH, et al. High-dose methotrexate improves clinical outcome in children with acute lymphoblastic leukemia: St. Jude Total Therapy Study X. Med Pediatr Oncol. 1988;16(5):297-303.
9. Evans WE, Relling MV, Rodman JH, Crom WR, Boyett JM, Pui CH. Conventional compared with individualized chemotherapy for childhood acute lymphoblastic leukemia. N Engl J Med. 1998;338(8):499-505.
10. Pui CH, Mahmoud HH, Rivera GK, et al. Early intensification of intrathecal chemotherapy virtually eliminates central nervous system relapse in children with acute lymphoblastic leukemia. Blood. 1998;92(2):411-415.
11. Pui C-H, Sandlund JT, Pei D, et al. Improved outcome for children with acute lymphoblastic leukemia: results of Total Therapy Study XIIIB at St Jude Children's Research Hospital. Blood. 2004;104(9):2690-2696.
12. Kishi S, Griener J, Cheng C, et al. Homocysteine, pharmacogenetics, and neurotoxicity in children with leukemia. J Clin Oncol. 2003;21(16):3084-3091.
13. Howell CR, Bjornard KL, Ness KK, et al. Cohort Profile: The St. Jude Lifetime Cohort Study (SJLIFE) for paediatric cancer survivors. Int J Epidemiol. 2021;50(1):39-49.
14. Alexander DH, Novembre J, Lange K. Fast model-based estimation of ancestry in unrelated individuals. Genome Res. 2009;19(9):1655-1664.
15. Gibson TM, Ehrhardt MJ, Ness KK. Obesity and metabolic syndrome among adult survivors of childhood leukemia. Curr Treat Options Oncol. 2016;17(4):17.

TABLE 1. Association of host, treatment factors, and BMI trajectory pattern with overweight/obesity categories and BMI Z-score in survivors

Overweight/obesity categories in survivors							
		Overweight			**Obesity**		
Factor	***N***	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
BMI trajectory from diagnosis to 5 years off-therapy							
Sex							
Female	339	—	—		—	—	
Male	339	1.65	1.10, 2.48	**0.016**	1.22	0.79, 1.89	0.400
Attained age	678	1.07	1.03, 1.12	**<0.001**	1.15	1.10, 1.20	**<0.001**
Race/ethnicity							
Non-Hispanic White	566	—	—		—	—	
Non-Hispanic Black	77	1.48	0.74, 2.97	0.300	1.73	0.85, 3.51	0.130
Hispanic, Asian, or other	35	1.11	0.49, 2.48	0.800	0.31	0.09, 1.06	0.062
Cranial radiotherapy							
No	465	—	—		—	—	
Yes	213	2.00	1.21, 3.31	**0.007**	2.39	1.42, 4.04	**0.001**
Latent class profile							
Low-slow	404	—	—		—	—	
Medium-slow	180	2.71	1.59, 4.62	**<0.001**	14.20	8.26, 24.30	**<0.001**
Low-fast	65	5.18	1.92, 14.00	**0.001**	32.70	12.70, 84.30	**<0.001**
High-slow	29	6.70	1.26, 35.70	**0.026**	76.60	16.80, 349.00	**<0.001**
BMI trajectory from diagnosis to 1 year post-diagnosis							
Sex							
Female	339	—	—		—	—	
Male	339	1.63	1.09, 2.44	**0.019**	1.20	0.79, 1.81	0.400
Attained age	678	1.09	1.04, 1.13	**<0.001**	1.16	1.11, 1.21	**<0.001**
Race/ethnicity							
Non-Hispanic White	566	—	—		—	—	
Non-Hispanic Black	77	1.69	0.84, 3.39	0.140	2.31	1.17, 4.56	**0.016**
Hispanic, Asian, or other	35	1.06	0.48, 2.36	0.900	0.29	0.09, 0.94	**0.039**

Cranial radiotherapy							
No	465	—	—		—	—	
Yes	213	2.06	1.25, 3.41	**0.005**	2.54	1.54, 4.19	**<0.001**
Latent class profile							
Normal	393	—	—		—	—	
Low	108	0.38	0.22, 0.66	**<0.001**	0.12	0.06, 0.24	**<0.001**
Medium	151	1.90	1.10, 3.27	**0.020**	4.23	2.51, 7.13	**<0.001**
High	26	4.04	0.36, 45.90	0.300	58.8	7.54, 458.00	**<0.001**

BMI Z-score in survivors

Factor	***N***	**Beta**	**95% CI**	***P***
BMI trajectory from diagnosis to 5 years off-therapy				
Sex				
Female	339	—	—	
Male	339	−0.01	−0.15, 0.12	0.900
Attained age	678	0.04	0.03, 0.06	**<0.001**
Race/ethnicity				
Non-Hispanic White	566	—	—	
Non-Hispanic Black	77	0.13	−0.08, 0.35	0.200
Hispanic, Asian, or other	35	−0.24	−0.55, 0.06	0.120
Cranial radiotherapy				
No	465	—	—	
Yes	213	0.19	0.03, 0.35	**0.023**
Latent class profile				
Low-slow	404	—	—	
Medium-slow	180	1.00	0.86, 1.20	**<0.001**
Low-fast	65	1.30	1.00, 1.50	**<0.001**
High-slow	29	1.60	1.20, 1.90	**<0.001**
BMI trajectory from diagnosis to 1 year post-diagnosis				
Sex				
Female	339	—	—	

Male	339	0.00	−0.15, 0.14	>0.900
Attained age	678	0.05	0.04, 0.07	**<0.001**
Race/ethnicity				
Non-Hispanic White	566	—	—	
Non-Hispanic Black	77	0.27	0.05, 0.50	**0.018**
Hispanic, Asian, or other	35	−0.31	−0.63, 0.01	0.055
Cranial radiotherapy				
No	465	—	—	
Yes	213	0.24	0.07, 0.40	**0.006**
Latent class profile				
Normal	393	—	—	
Low	108	−0.87	−1.10, −0.67	**<0.001**
Medium	151	0.58	0.40, 0.76	**<0.001**
High	26	1.40	0.98, 1.70	**<0.001**

Abbreviations: BMI, body mass index; OR, odds ratio; CI, confidence interval

TABLE 2. Association of host, treatment factors, and overweight/obesity AUC with overweight/obesity categories and BMI Z-score in survivors

Overweight/obesity categories in survivors							
		Overweight			**Obesity**		
Factor	***N***	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Area under the curve (at diagnosis, end of induction, off-therapy, and 5 years off-therapy)							
Sex							
Female	328	—	—		—	—	
Male	329	1.41	0.94, 2.13	0.100	0.92	0.59, 1.44	0.700
Attained age	657	1.07	1.03, 1.12	**0.001**	1.15	1.10, 1.20	<0.001
Race/ethnicity							
Non-Hispanic White	550	—	—		—	—	
Non-Hispanic Black	73	1.41	0.69, 2.89	0.300	1.68	0.81, 3.49	0.200
Hispanic, Asian, or other	34	1.01	0.44, 2.31	>0.900	0.19	0.05, 0.72	**0.015**
Cranial radiotherapy							
No	451	—	—		—	—	
Yes	206	2.15	1.30, 3.57	**0.003**	3.04	1.82, 5.06	**<0.001**
Overweight/obesity AUC	657	1.28	1.15, 1.43	**<0.001**	1.65	1.48, 1.85	**<0.001**
Area under the curve (at diagnosis, end of induction, and 1 year post-diagnosis)							
Sex							
Female	338	—	—		—	—	
Male	339	1.47	0.98, 2.19	0.061	0.92	0.61, 1.39	0.700
Attained age	677	1.07	1.02, 1.11	**0.002**	1.12	1.07, 1.16	**<0.001**
Race/ethnicity							
Non-Hispanic White	565	—	—		—	—	
Non-Hispanic Black	77	1.45	0.73, 2.87	0.300	1.75	0.90, 3.39	0.100
Hispanic, Asian, or other	35	1.02	0.46, 2.27	>0.900	0.28	0.08, 0.90	**0.033**
Cranial radiotherapy							
No	464	—	—		—	—	
Yes	213	2.08	1.27, 3.41	**0.004**	2.90	1.80, 4.68	**<0.001**

Overweight/obesity AUC	677	2.34	1.47, 3.74	**<0.001**	4.55	2.90, 7.14	**<0.001**
Area under the curve (at diagnosis and end of induction)*							
Sex							
Female	339	—	—		—	—	
Male	339	1.54	1.04, 2.29	**0.033**	0.98	0.66, 1.46	>0.900
Attained age	678	1.06	1.02, 1.10	**0.005**	1.10	1.06, 1.14	**<0.001**
Race/ethnicity							
Non-Hispanic White	566	—	—		—	—	
Non-Hispanic Black	77	1.56	0.79, 3.06	0.200	2.04	1.07, 3.87	**0.030**
Hispanic, Asian, or other	35	1.06	0.48, 2.33	0.900	0.28	0.09, 0.92	**0.035**
Cranial radiotherapy							
No	465	—	—		—	—	
Yes	213	2.03	1.24, 3.31	**0.005**	2.73	1.70, 4.37	**<0.001**
Overweight/obesity AUC∟×∟10	678	1.22	1.05, 1.43	**0.012**	1.52	1.31, 1.76	**<0.001**

BMI Z-score in survivors				
Factor	***N***	**Beta**	**95% CI**	***P***
Area under the curve (at diagnosis, end of induction, off-therapy, and 5 years off-therapy)				
Sex				
Female	328	—	—	
Male	329	−0.10	−0.24, 0.05	0.200
Attained age	657	0.04	0.03, 0.06	**<0.001**
Race/ethnicity				
Non-Hispanic White	550	—	—	
Non-Hispanic Black	73	0.15	−0.08, 0.38	0.200
Hispanic, Asian, or other	34	−0.34	−0.66, −0.02	**0.038**
Cranial radiotherapy				
No	451	—	—	
Yes	206	0.33	0.16, 0.49	**<0.001**
Overweight/obesity AUC	657	0.14	0.12, 0.15	**<0.001**
Area under the curve (at diagnosis, end of induction, and 1 year post-diagnosis)				

Sex				
Female	338	—	—	
Male	339	−0.10	−0.24, 0.05	0.200
Attained age	677	0.04	0.02, 0.05	**<0.001**
Race/ethnicity				
Non-Hispanic White	565	—	—	
Non-Hispanic Black	77	0.20	−0.04, 0.43	0.100
Hispanic, Asian, or other	35	−0.32	−0.66, 0.01	0.059
Cranial radiotherapy				
No	464	—	—	
Yes	213	0.33	0.16, 0.51	**<0.001**
Overweight/obesity AUC	677	0.43	0.36, 0.51	**<0.001**
Area under the curve (at diagnosis and end of induction)*				
Sex				
Female	339	—	—	
Male	339	−0.07	−0.22, 0.08	0.300
Attained age	678	0.03	0.02, 0.05	**<0.001**
Race/ethnicity				
Non-Hispanic White	566	—	—	
Non-Hispanic Black	77	0.26	0.02, 0.49	**0.035**
Hispanic, Asian, or other	35	−0.32	−0.66, 0.02	0.062
Cranial radiotherapy				
No	465	—	—	
Yes	213	0.31	0.13, 0.49	**<0.001**
Overweight/obesity AUC∟×∟10	678	1.20	0.97, 1.50	**<0.001**

Abbreviations: BMI, body mass index; AUC, area under the curve; OR, odds ratio; CI, confidence interval
*****Because AUCs during induction were small, they were multiplied by 10 for analysis.
Footnotes:
The total cohort comprised 678 patients. Sample sizes varied because of missing BMI data at certain timepoints: for the AUC model from diagnosis to 5 years off-therapy (with BMI measured at diagnosis, end of induction, off-therapy, and 5 years off-therapy), n=657; for the AUC model from diagnosis to 1 year post-diagnosis (with BMI measured at diagnosis, end of induction, and 1 year post-diagnosis), n=677; and for the AUC model from diagnosis to end of induction therapy (with BMI measured at diagnosis and end of induction), n=678.

FIGURE LEGEND

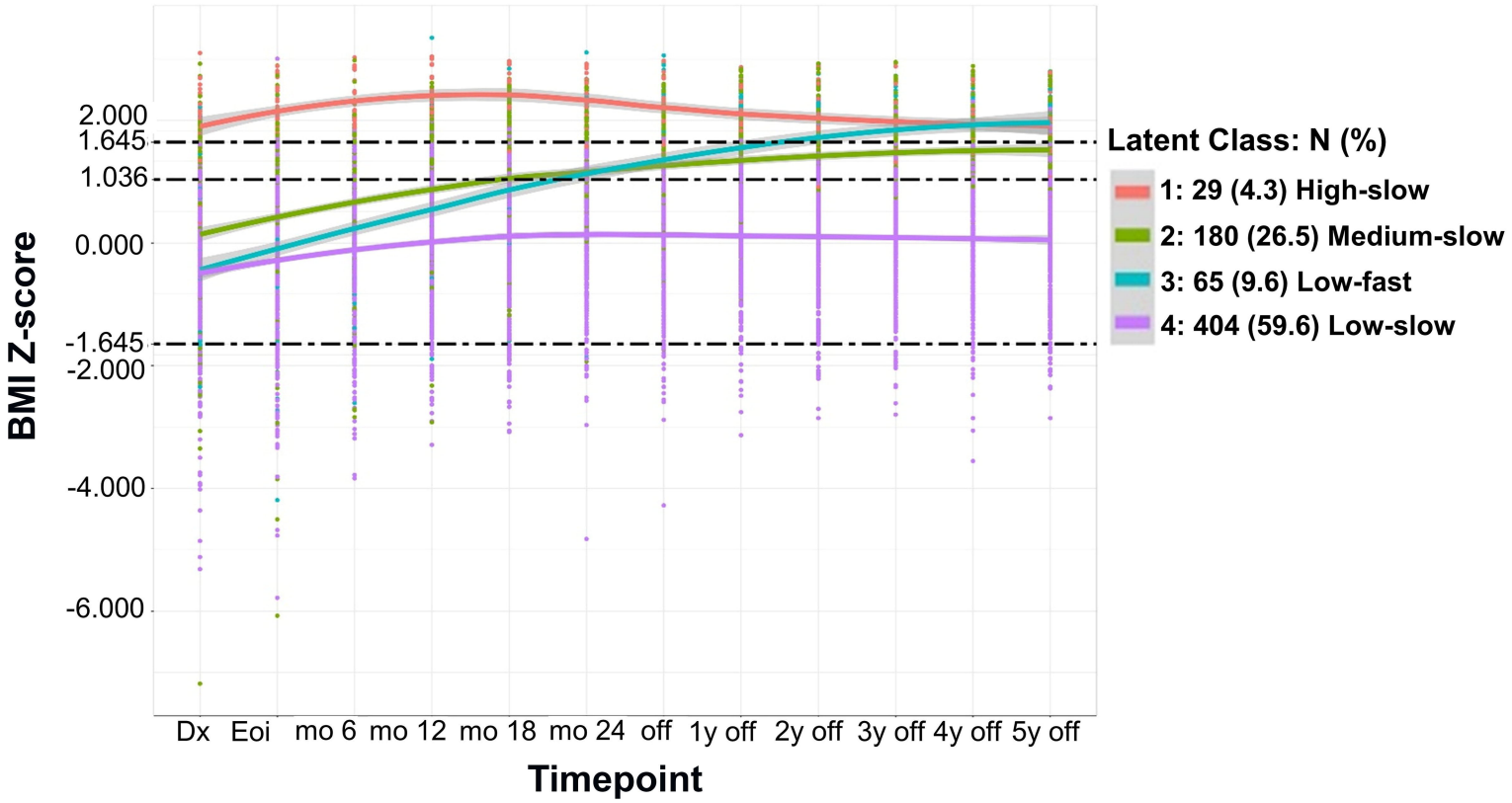
Figure 1. Longitudinal BMI trajectory patterns in childhood ALL survivors, showing trajectories from diagnosis to 5 years off-therapy and from diagnosis to 1 year post-diagnosis.

(A) Trajectories from diagnosis to 5 years off-therapy.

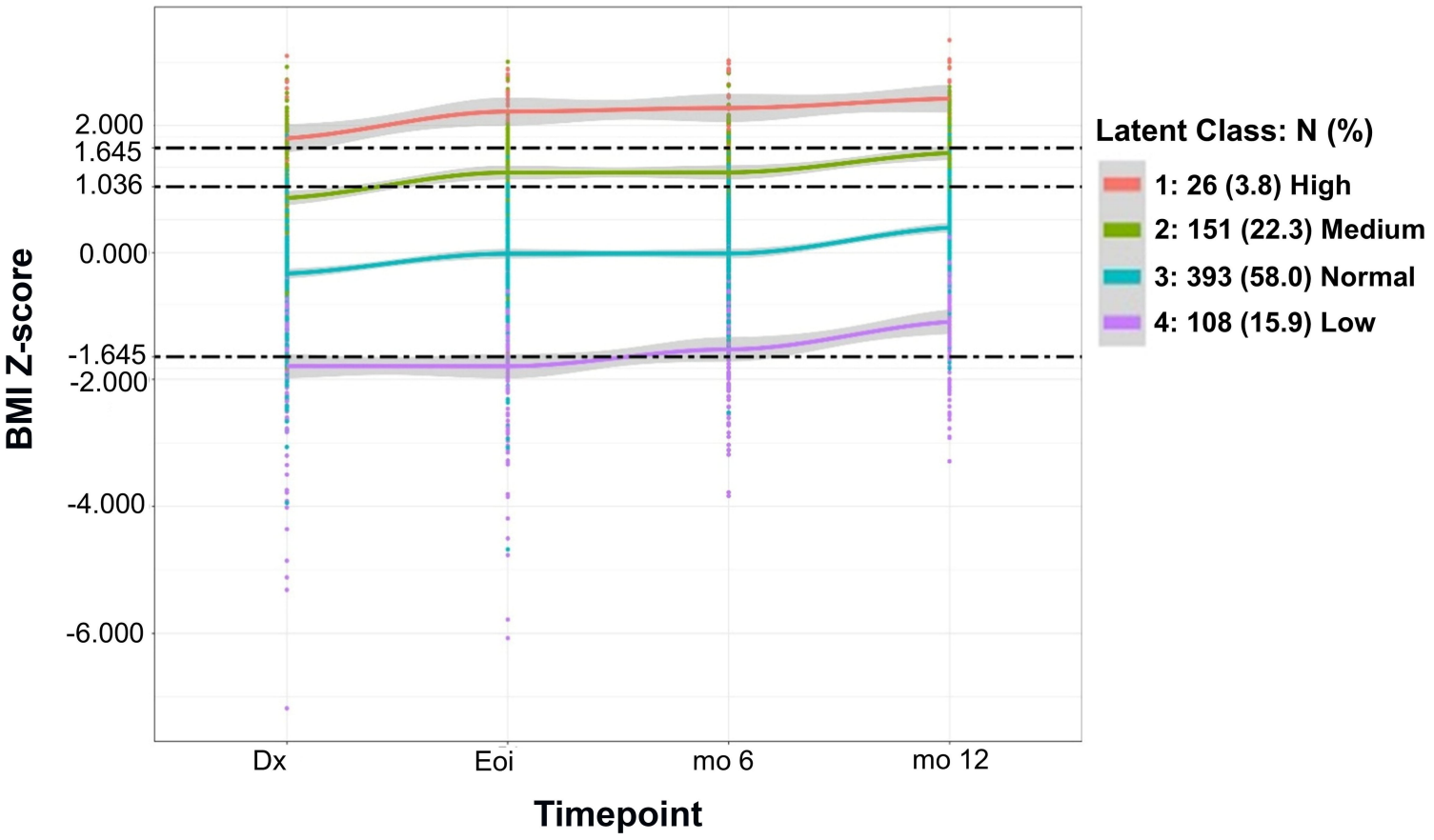
(B) Trajectories from diagnosis to 1 year post-diagnosis.

Abbreviations: ALL, acute lymphoblastic leukemia; BMI, body mass index; Dx, diagnosis; EOI, end of induction; mo, month; off, off-therapy

(A)


2.000
1.645
1.036
0.000
-1.645
-2.000
-4.000
-6.000
BMI Z-score
Dx
Eoi
mo 6
mo 12
mo 18
mo 24
off
1y off
2y off
3y off
4y off
5y off
Timepoint
Latent Class: N (%)
1: 29 (4.3) High-slow
2: 180 (26.5) Medium-slow
3: 65 (9.6) Low-fast
4: 404 (59.6) Low-slow

(B)


2.000
1.645
1.036
0.000
-1.645
-2.000
-4.000
-6.000
BMI Z-score
Dx
Eoi
mo 6
mo 12
Timepoint
Latent Class: N (%)
1: 26 (3.8) High
2: 151 (22.3) Medium
3: 393 (58.0) Normal
4: 108 (15.9) Low

Body mass index during and early after therapy for pediatric acute lymphoblastic leukemia is associated with obesity in survivors

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Supplemental Table 1. Clinical characteristics of survivor participants for the overall group and for each BMI category at the first SJLIFE visit

Clinical Characteristic	Overall *N* = 678	Normal/Underweight *N* = 249	Overweight *N* = 183	Obesity *N* = 246
Age at diagnosis in years, median (IQR)	6.1 (3.6, 10.5)	5.7 (3.5, 10.2)	7.2 (3.5, 10.4)	6.0 (3.9, 11.5)
Age at assessment in years, median (IQR)	26.9 (22.9, 31.4)	24.9 (21.4, 28.5)	27.2 (23.0, 32.4)	28.8 (25.1, 32.4)
Time since diagnosis in years, median (IQR)	20.0 (15.2, 24.9)	17.7 (14.6, 22.4)	20.9 (15.4, 25.8)	22.7 (16.3, 26.1)
Sex				
Male, No. (%)	339 (50.0)	112 (45.0)	105 (57.4)	122 (49.6)
Female, No. (%)	339 (50.0)	137 (55.0)	78 (42.6)	124 (50.4)
Race				
Non-Hispanic White, No. (%)	566 (83.5)	210 (84.3)	150 (82.0)	206 (83.7)
Non-Hispanic Black, No. (%)	77 (11.4)	20 (8.0)	21 (11.5)	36 (14.6)
Other, No. (%)	35 (5.1)	19 (7.7)	12 (6.4)	4 (1.7)
Risk classification				
Standard risk	378 (55.8)	146 (58.6)	97 (53.0)	135 (54.9)
High risk	300 (44.2)	103 (41.4)	86 (47.0)	111 (45.1)
Corticosteroids, No. (%)	676 (99.7)	248 (99.6)	183 (100)	245 (100)
Median (prednisolone equivalent dose), mg/m^2, (IQR)	9651 (2240, 11,986)	10,441 (9556, 12,010)	9656 (2240, 11,992)	9616 (2240, 10,922)
Corticosteroid types and cumulative dosage according to treatment protocol				
Total therapy X				
Standard risk	Prednisolone 1120 mg/m^2			
High risk	Prednisolone 1120 mg/m^2			
Total therapy XI				
Lower risk	Prednisolone 9520 mg/m^2			
Higher risk	Prednisolone 9520 mg/m^2			
Total therapy XII	Prednisolone 1120 mg/m^2			
Total therapy XIII				
Low risk	Prednisolone 9560 mg/m^2			
High risk	Prednisolone 9560 mg/m^2			
Total therapy XIIIB				
Low risk	Prednisolone 1120 mg/m^2, dexamethasone 1680 mg/m^2			
High risk	Prednisolone 1160 mg/m^2, dexamethasone 1680 mg/m^2			
Total therapy XIV				
Low risk	Prednisolone 1120 mg/m^2, dexamethasone 2016 mg/m^2 (girl) or 2520 mg/m^2 (boy)			
Standard/high risk	Prednisolone 1120 mg/m^2, dexamethasone 2464 mg/m^2 (girl) or 3080 mg/m^2 (boy)			
Total therapy XV				
Low risk	Prednisolone 1120 mg/m^2, dexamethasone 2160 mg/m^2 (girl) or 2600 mg/m^2 (boy)			
Standard/high risk	Prednisolone 1120 mg/m^2, dexamethasone 2520 mg/m^2 (girl) or 3060 mg/m^2 (boy)			
Cytarabine, No. (%)	627 (92.4)	232 (93.2)	171 (93.4)	224 (91.1)
Median dose, mg/m^2 (IQR)	5147 (2200, 10,379)	4,807 (1812, 10,237)	5136 (2510, 10,372)	7029 (2709, 10,554)
Epipodophyllotoxins, No. (%)	506 (74.6)	177 (71.1)	138 (75.4)	191 (77.6)
Median dose, mg/m^2 (IQR)	6589 (1353, 14,853)	4,258 (1231, 14,752)	6800 (1371, 14,955)	9978 (1378, 15,060)
Alkylating agents, No. (%)	434 (64.0)	148 (59.4)	125 (30.6)	161 (65.4)
Median dose (cyclophosphamide equivalent dose), mg/m^2 (IQR)	7970 (4508, 9500)	7841 (4208, 9406)	7398 (4327, 9462)	8219 (4764, 9632)
Asparaginase, No. (%)	678 (100.0)	249 (100.0)	183 (100.0)	246 (100.0)
Median dose, mg/m^2 (IQR)	4553 (2969, 10,123)	5988 (3000, 11,196)	4510 (2955, 10,485)	4337 (2932, 7916)
Anthracyclines, No. (%)	559 (82.4)	219 (88.0)	147 (80.3)	193 (78.5)
Median dose (doxorubicin equivalent dose), mg/m^2 (IQR)	52 (26, 87)	51 (26, 85)	52 (36, 89)	52 (25, 109)
Methotrexate, No. (%)	67 (100.0)	249 (100.0)	183 (100.0)	246 (100.0)

Clinical Characteristic	Overall *N* = 678	Normal/Underweight *N* = 249	Overweight *N* = 183	Obesity *N* = 246
Median dose, mg/m^2 (IQR)	17,174 (4110, 22,575)	18,827 (7992, 23,048)	15,748 (4,040, 22,914)	14,005 (4000, 21,524)
Vincristine, No. (%)	678 (100)	249 (100)	183 (100)	246 (100)
Median dose, mg/m^2 (IQR)	52 (7, 59)	55 (37, 60)	52 (8, 59)	44 (6, 57)
Cranial radiotherapy	213 (31.4)	44 (17.7)	66 (36.1)	103 (41.9)
None	465 (68.6)	205 (82.3)	117 (63.9)	143 (58.1)
≤18 Gy, No. (%)	168 (24.8)	33 (13.3)	52 (28.4)	83 (33.7)
>18 Gy, No. (%)	45 (6.6)	11 (4.4)	14 (7.7)	20 (8.2)
Physical activity, No. (%)	655 (96.6)	241 (96.8)	175 (95.6)	239 (97.2)
Active	384 (58.6)	143 (59.3)	116 (66.3)	125 (52.3)
Inactive	271 (41.4)	98 (40.7)	59 (34.7)	114 (47.7)
History of smoking, No. (%)	643 (94.8)	235 (94.4)	171 (93.4)	237 (96.3)
Current	126 (19.6)	45 (19.1)	40 (23.4)	41 (17.3)
Past	79 (12.3)	26 (11.1)	26 (15.2)	27 (11.4)
Never	438 (68.1)	164 (69.8)	105 (61.4)	169 (71.3)
BMI Z-score at diagnosis, median (IQR)	−0.15 (−0.95, 0.57)	−0.47 (−1.46, 0.11)	−0.23 (−0.89, 0.39)	0.34 (−0.45, 1.20)
BMI Z-score at end of induction, median (IQR)	0.21 (−0.67, 0.98)	−0.32 (−1.05, 0.49)	0.08 (−0.73, 0.86)	0.78 (0.05, 1.52)
BMI Z-score at off-therapy, median (IQR)	0.63 (−0.06, 1.43)	0.27 (−0.56, 0.77)	0.48 (−0.06, 1.30)	1.12 (0.51, 1.94)
BMI Z-score at 5 years off-therapy, median (IQR)	0.82 (−0.01, 1.58)	−0.02 (−0.79, 0.50)	0.82 (0.18, 1.27)	1.63 (1.08, 1.99)

Abbreviations: BMI, body mass index; Gy, Gray; IQR, interquartile range

Supplemental Table 2. BMI, weight, and height Z-scores at each timepoint

	Dx (*N*=678)	EOI (*N*=678)	Mo 6 (*N*=678)	Mo 12 (*N*=677)	Mo 18 (*N*=675)	Mo 24 (*N*=674)	Off (*N*=673)	1y off (*N*=658)	2y off (*N*=633)	3y off (*N*=630)	4y off (*N*=602)	5y off (*N*=657)	Survivors (*N*=678)
Age (years)													
Mean (SD)	7.46 (4.51)	7.58 (4.51)	7.95 (4.51)	8.45 (4.51)	8.95 (4.52)	9.45 (4.51)	10.0 (4.56)	11.0 (4.57)	12.0 (4.54)	13.0 (4.58)	14.0 (4.55)	15.0 (4.57)	27.6 (5.85)
Median [min, max]	6.07 [2.01, 18.8]	6.18 [2.13, 18.9]	6.56 [2.49, 19.3]	7.06 [2.97, 19.8]	7.58 [3.34, 20.4]	8.07 [4.00, 20.8]	8.57 [4.47, 21.7]	9.54 [5.15, 22.7]	10.5 [6.31, 23.7]	11.5 [7.18, 24.8]	12.6 [8.18, 25.8]	13.6 [8.36, 27.0]	26.9 [18.3, 44.9]
Weight Z-score													
Mean (SD)	0.08 (1.09)	0.18 (1.14)	0.14 (1.11)	0.35 (1.10)	0.31 (1.12)	0.34 (1.09)	0.30 (1.12)	0.46 (1.10)	0.52 (1.13)	0.55 (1.14)	0.59 (1.15)	0.60 (1.15)	0.95 (1.21)
Median [min, max]	0.04 [−3.20, 3.52]	0.23 [−3.81, 3.59]	0.08 [−3.71, 3.67]	0.35 [−3.34, 3.75]	0.28 [−2.69, 3.75]	0.29 [−3.10, 3.52]	0.24 [−3.03, 3.37]	0.46 [−3.66, 3.52]	0.52 [−3.37, 3.62]	0.55 [−4.35, 3.54]	0.59 [−4.66, 3.65]	0.62 [−3.45, 3.72]	1.08 [−3.81, 3.99]
Weight Z-score (male)													
Mean (SD)	0.19 (1.08)	0.30 (1.16)	0.28 (1.08)	0.48 (1.10)	0.41 (1.10)	0.43 (1.07)	0.36 (1.10)	0.51 (1.08)	0.55 (1.15)	0.60 (1.16)	0.62 (1.19)	0.66 (1.18)	1.01 (1.21)
Median [min, max]	0.091 [−2.91, 3.52]	0.37 [−3.81, 3.32]	0.24 [−2.21, 3.32]	0.43 [−2.52, 3.35]	0.35 [−2.37, 3.23]	0.37 [−2.29, 3.35]	0.26 [−2.54, 3.32]	0.49 [−2.16, 3.52]	0.50 [−3.11, 3.62]	0.56 [−3.13, 3.54]	0.60 [−3.33, 3.65]	0.68 [−3.26, 3.72]	1.06 [−2.17, 3.99]
Weight Z-score (female)													
Mean (SD)	−0.03 (1.08)	0.06 (1.11)	−0.00 (1.12)	0.23 (1.09)	0.21 (1.12)	0.25 (1.11)	0.24 (1.13)	0.40 (1.12)	0.48 (1.11)	0.50 (1.11)	0.56 (1.12)	0.54 (1.12)	0.89 (1.21)
Median min, max]	−0.02 [−3.20, 3.46]	0.08 [−3.36, 3.59]	−0.02 [−3.71, 3.67]	0.24 [−3.34, 3.75]	0.21 [−2.69, 3.75]	0.25 [−3.10, 3.52]	0.18 [−3.03, 3.37]	0.39 [−3.66, 3.41]	0.52 [−3.37, 3.29]	0.54 [−4.35, 3.19]	0.58 [−4.66, 3.22]	0.58 [−3.45, 3.28]	1.10 [−3.81, 3.22]
Height Z-score													
Mean (SD)	0.32 (0.98)	0.20 (0.96)	0.06 (0.96)	−0.08 (0.97)	−0.12 (0.98)	−0.23 (0.98)	−0.31 (0.99)	−0.10 (1.01)	−0.15 (1.02)	−0.11 (1.03)	−0.09 (1.02)	−0.05 (1.01)	−0.17 (1.09)
Median [min, max]	0.27 [−2.97, 3.40]	0.15 [−3.10, 3.14]	0.03 [−3.10, 2.97]	−0.09 [−2.97, 2.84]	−0.21 [−3.26, 2.83]	−0.27 [−3.43, 3.10]	−0.36 [−3.63, 3.30]	−0.24 [−3.34, 3.92]	−0.21 [−3.75, 3.86]	−0.13 [−3.38, 3.85]	−0.13 [−3.46, 3.99]	−0.08 [−2.97, 3.99]	−0.18 [−4.36, 5.15]

	Dx (*N*=678)	EOI (*N*=678)	Mo 6 (*N*=678)	Mo 12 (*N*=677)	Mo 18 (*N*=675)	Mo 24 (*N*=674)	Off (*N*=673)	1y off (*N*=658)	2y off (*N*=633)	3y off (*N*=630)	4y off (*N*=602)	5y off (*N*=657)	Survivors (*N*=678)
Height Z-score (male)													
Mean (SD)	0.32 (0.97)	0.20 (0.96)	0.08 (0.97)	−0.02 (0.96)	−0.08 (0.96)	−0.16 (0.97)	−0.24 (0.99)	−0.14 (1.02)	−0.13 (1.01)	−0.11 (1.06)	−0.13 (1.04)	−0.06 (1.03)	−0.07 (1.06)
Median [min, max]	0.25 [−2.51, 3.13]	0.18 [−2.51, 3.12]	0.04 [−2.76, 2.97]	−0.12 [−2.56, 2.84]	−0.25 [−2.54, 2.58]	−0.27 [−2.57, 3.10]	−0.37 [−2.83, 3.30]	−0.26 [−2.78, 3.92]	−0.25 [−2.60, 3.86]	−0.18 [−2.63, 3.85]	−0.19 [−3.46, 3.99]	−0.14 [−2.57, 3.99]	−0.12 [−3.22, 5.15]
Height Z-score (female)													
Mean (SD)	0.32 (0.99)	0.20 (0.96)	0.04 (0.95)	−0.10 (0.97)	−0.17 (0.99)	−0.30 (0.99)	−0.38 (1.00)	−0.24 (0.99)	−0.16 (1.03)	−0.11 (0.99)	−0.05 (1.00)	−0.05 (1.00)	−0.26 (1.10)
Median [min, max]	0.29 [−2.97, 3.40]	0.12 [−3.10, 3.14]	0.03 [−3.10, 2.75]	−0.07 [−2.97, 2.73]	−0.14 [−3.26, 2.83]	−0.27 [−3.43, 2.75]	−0.36 [−3.63, 2.62]	−0.18 [−3.34, 2.46]	−0.19 [−3.75, 3.15]	−0.09 [−3.38, 2.81]	−0.06 [−2.98, 2.90]	−0.04[−2 .97, 2.88]	−0.19 [−4.36, 3.21]
BMI Z-score													
Mean (SD)	−0.22 (1.29)	0.07 (1.34)	0.12 (1.18)	0.50 (1.14)	0.49 (1.16)	0.61 (1.09)	0.60 (1.11)	0.68 (1.05)	0.69 (1.07)	0.70 (1.07)	0.72 (1.09)	0.70 (1.10)	0.96 (1.09)
Median [min, max]	−0.15 [−7.18, 3.10]	0.21 [−6.07, 3.00]	0.11 [−3.84, 3.02]	0.56 [−3.29, 3.35]	0.48 [−3.08, 2.96]	0.67 [−4.82, 3.11]	0.63 [−4.28, 3.06]	0.74 [−3.13, 2.87]	0.75 [−2.85, 2.93]	0.72 [−2.80, 2.95]	0.84 [−3.55, 2.88]	0.82 [−2.85, 2.80]	1.09 [−3.51, 3.26]
BMI Z-score (male)													
Mean (SD)	−0.11 (1.32)	0.20 (1.36)	0.24 (1.19)	0.58 (1.19)	0.55 (1.19)	0.65 (1.10)	0.62 (1.12)	0.71 (1.05)	0.70 (1.14)	0.72 (1.12)	0.73 (1.16)	0.74 (1.16)	0.97 (1.18)
Median [min, max]	−0.07 [−7.18, 2.92]	0.42 [−5.78, 2.77]	0.25 [−3.84, 3.02]	0.66 [−3.29, 3.35]	0.58 [−3.06, 2.96]	0.72 [−2.97, 3.11]	0.64 [−2.59, 3.06]	0.78 [−2.39, 2.84]	0.77 [−2.85, 2.93]	0.73 [−2.80, 2.95]	0.88 [−3.55, 2.88]	0.84 [−2.85, 2.80]	1.10 [−3.51, 3.26]
BMI Z-score (female)													
Mean (SD)	−0.33 (1.25)	−0.06 (1.31)	−0.01 (1.17)	0.42 (1.09)	0.43 (1.13)	0.58 (1.08)	0.59 (1.11)	0.65 (1.05)	0.69 (1.01)	0.68 (1.01)	0.71 (1.01)	0.66 (1.03)	0.96 (0.99)
Median [min, max]	−0.30 [−5.32, 3.10]	0.05 [−6.07, 3.00]	−0.03 [−3.78, 2.98]	0.46 [−2.90, 3.00]	0.42 [−3.08, 2.94]	0.60 [−4.82, 2.91]	0.61 [−4.28, 2.97]	0.69 [−3.13, 2.87]	0.72 [−2.21, 2.92]	0.71 [−2.61, 2.88]	0.78 [−3.06, 2.81]	0.74 [−2.34, 2.72]	1.07 [−2.52, 2.54]
BMI category													
Underweight	88 (13.0)	68 (10.0)	49 (7.2)	31 (4.6)	32 (4.7)	19 (2.8)	23 (3.4)	13 (2.0)	13 (2.0)	13 (2.1)	13 (2.1)	17 (2.6)	18 (2.7)

	Dx (*N*=678)	EOI (*N*=678)	Mo 6 (*N*=678)	Mo 12 (*N*=677)	Mo 18 (*N*=675)	Mo 24 (*N*=674)	Off (*N*=673)	1y off (*N*=658)	2y off (*N*=633)	3y off (*N*=630)	4y off (*N*=602)	5y off (*N*=657)	Survivors (*N*=678)
Normal weight	479 (70.6)	453 (66.8)	485 (71.6)	428 (63.2)	410 (60.7)	414 (61.4)	413 (61.4)	388 (58.9)	360 (56.9)	354 (56.2)	323 (53.7)	347 (52.8)	231 (34.1)
Overweight	60 (8.9)	91 (13.4)	72 (10.6)	107 (15.8)	120 (17.8)	116 (17.2)	112 (16.7)	131 (19.9)	131 (20.7)	127 (20.1)	119 (19.8)	141 (21.4)	183 (27.0)
Obesity	51 (7.5)	66 (9.8)	72 (10.6)	111 (16.4)	113 (16.8)	125 (18.6)	125 (18.5)	126 (19.2)	129 (20.4)	136 (21.6)	147 (24.4)	152 (23.2)	246 (36.3)

Abbreviations: BMI, body mass index; Dx, diagnosis; EOI, end of induction; Mo, month; off, off-therapy; SD, standard deviation; y, years

Supplemental Table 3. Association of BMI trajectory pattern, overweight/obesity AUC, and host, genetic, and treatment factors with overweight/obesity in survivors

		Overweight			Obesity		
Factor	***N***	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
BMI trajectory from diagnosis to 5 years off-therapy							
Sex							
Female	304	—	—		—	—	
Male	295	1.41	0.90, 2.18	0.130	1.01	0.63, 1.62	>0.900
Attained age	599	1.07	1.03, 1.12	**0.001**	1.15	1.10, 1.21	**<0.001**
Genetic admixture							
EAS	599	0.85	0.08, 8.70	0.900	0.03	0.00, 4.47	0.200
AMR	599	0.97	0.26, 3.56	>0.900	0.18	0.04, 0.90	**0.037**
SAS	599	0.14	0.00, 18.40	0.400	0.00	0.00, 35.00	0.200
AFR	599	0.53	0.18, 1.59	0.300	0.23	0.08, 0.70	**0.010**
BMI-PRS	599	1.17	1.05, 1.30	**0.004**	1.37	1.22, 1.54	**<0.001**
Cranial radiotherapy							
No	403	—	—		—	—	
Yes	196	2.23	1.30, 3.80	**0.003**	2.77	1.57, 4.88	**<0.001**
Latent class profile							
Low-slow	367	—	—		—	—	
Medium-slow	151	2.26	1.27, 4.00	**0.005**	9.81	5.50, 17.50	**<0.001**
Low-fast	59	5.78	1.95, 17.10	**0.002**	34.40	11.90, 99.30	**<0.001**
High-slow	22	6.59	0.66, 65.60	0.110	81.40	10.10, 653.00	**<0.001**
BMI trajectory from diagnosis to 1 year post-diagnosis							
Sex							
Female	304	—	—		—	—	
Male	295	1.47	0.94, 2.29	0.088	1.10	0.70, 1.74	0.700
Attained age	599	1.09	1.04, 1.14	**<0.001**	1.15	1.10, 1.21	**<0.001**

Genetic admixture							
EAS	599	1.05	0.11, 9.60	>0.900	0.07	0.00, 5.22	0.200
AMR	599	0.87	0.24, 3.13	0.800	0.14	0.03, 0.66	**0.013**
SAS	599	0.16	0.00, 42.30	0.500	0.00	0.00, 4.66	0.083
AFR	599	0.60	0.20, 1.80	0.400	0.27	0.09, 0.80	**0.018**
BMI-PRS	599	1.17	1.05, 1.30	**0.004**	1.38	1.24, 1.54	**<0.001**
Cranial radiotherapy							
No	403	—	—		—	—	
Yes	196	2.38	1.39, 4.08	**0.002**	3.10	1.80, 5.34	**<0.001**
Latent class profile							
Normal	356	—	—		—	—	
Low	95	0.36	0.19, 0.65	**<0.001**	0.14	0.07, 0.30	**<0.001**
Medium	127	1.90	1.06, 3.44	**0.032**	3.27	1.83, 5.86	**<0.001**
High	21	840.00	301.00, 2347.00	**<0.001**	17,298.00	6186.00, 48,371.00	**<0.001**
Area under the curve (at diagnosis, end of induction, off-therapy, and 5 years off-therapy)							
Sex							
Female	295	—	—		—	—	
Male	287	1.25	0.80, 1.95	0.300	0.83	0.51, 1.34	0.400
Attained age	582	1.08	1.03, 1.12	**0.002**	1.15	1.09, 1.20	**<0.001**
Genetic admixture							
EAS	582	1.00	0.11, 9.13	>0.900	0.04	0.00, 8.13	0.200
AMR	582	0.86	0.23, 3.27	0.800	0.11	0.02, 0.66	**0.016**
SAS	582	0.09	0.00, 15.30	0.400	0.00	0.00, 54.60	0.200
AFR	582	0.51	0.16, 1.58	0.200	0.22	0.07, 0.68	**0.009**
BMI-PRS	582	1.16	1.04, 1.29	**0.007**	1.36	1.21, 1.53	**<0.001**
Cranial radiotherapy							
No	393	—	—		—	—	

Yes	189	2.47	1.44, 4.23	**0.001**	3.66	2.09, 6.40	**<0.001**
Overweight/obesity AUC	582	1.24	1.10, 1.39	**<0.001**	1.58	1.41, 1.78	**<0.001**
Area under the curve (at diagnosis, end of induction, off-therapy, and 1 year post-diagnosis)							
Sex							
Female	303	—	—		—	—	
Male	295	1.31	0.85, 2.03	0.200	0.86	0.55, 1.35	0.500
Attained age	598	1.07	1.02, 1.12	**0.003**	1.11	1.06, 1.16	**<0.001**
Genetic admixture							
EAS	598	1.11	0.13, 9.69	>0.900	0.05	0.00, 6.43	0.200
AMR	598	0.84	0.23, 3.02	0.800	0.12	0.02, 0.57	**0.008**
SAS	598	0.09	0.00, 14.60	0.400	0.00	0.00, 6.71	0.092
AFR	598	0.51	0.17, 1.50	0.200	0.21	0.07, 0.60	**0.004**
BMI-PRS	598	1.17	1.06, 1.30	**0.003**	1.39	1.25, 1.55	**<0.001**
Cranial radiotherapy							
No	402	—	—		—	—	
Yes	196	2.45	1.44, 4.16	**<0.001**	3.64	2.14, 6.18	**<0.001**
Overweight/obesity AUC	598	2.71	1.53, 4.80	**<0.001**	5.16	2.95, 9.04	**<0.001**
Area under the curve (at diagnosis and end of induction)							
Sex							
Female	304	—	—		—	—	
Male	295	1.38	0.90, 2.13	0.140	0.93	0.59, 1.44	0.700
Attained age	599	1.06	1.02, 1.11	**0.008**	1.10	1.05, 1.14	**<0.001**
Genetic admixture							
EAS	599	1.01	0.12, 8.70	>0.900	0.04	0.00, 5.62	0.200
AMR	599	0.91	0.26, 3.23	0.900	0.13	0.03, 0.62	**0.011**
SAS	599	0.09	0.00, 14.70	0.400	0.00	0.00, 11.20	0.110
AFR	599	0.57	0.19, 1.66	0.300	0.27	0.10, 0.76	**0.013**

BMI-PRS	599	1.17	1.06, 1.30	**0.002**	1.38	1.24, 1.54	**<0.001**
Cranial radiotherapy							
No	403	—	—		—	—	
Yes	196	2.37	1.40, 4.00	**0.001**	3.37	2.00, 5.67	**<0.001**
Overweight/obesity AUC × 10	599	1.26	1.03, 1.53	**0.024**	1.54	1.28, 1.86	**<0.001**

Abbreviations: AMR, admixed American; AFR, African; BMI, body mass index; BMI-PRS, body mass index polygenic risk score; CI, confidence interval; EAS, East Asian; OR, odds ratio; SAS, South Asian
*Because AUCs during induction were small, they were multiplied by 10 for analysis.

Footnotes:
The total cohort comprised 678 patients. Analyses including genetic admixture and BMI-PRS were limited to those patients with genotype data (n = 599). Sample sizes varied because of missing BMI or genetic data: for the AUC model from diagnosis to 5 years off-therapy (with BMI measured at diagnosis, end of induction, off-therapy, and 5 years off-therapy), n = 582; for the AUC model from diagnosis to 1 year post-diagnosis (with BMI measured at diagnosis, end of induction, and 1 year post-diagnosis), n = 598; and for the AUC model from diagnosis to end of induction therapy (with BMI measured at diagnosis and end of induction), n = 599.