

## Introduction

Abnormalities in metabolic parameters and body composition are frequently reported among survivors of childhood leukemias treated with cranial or total body irradiation. Data regarding the occurrence of metabolic impairments among survivors following abdominal and pelvic radiation are lacking.

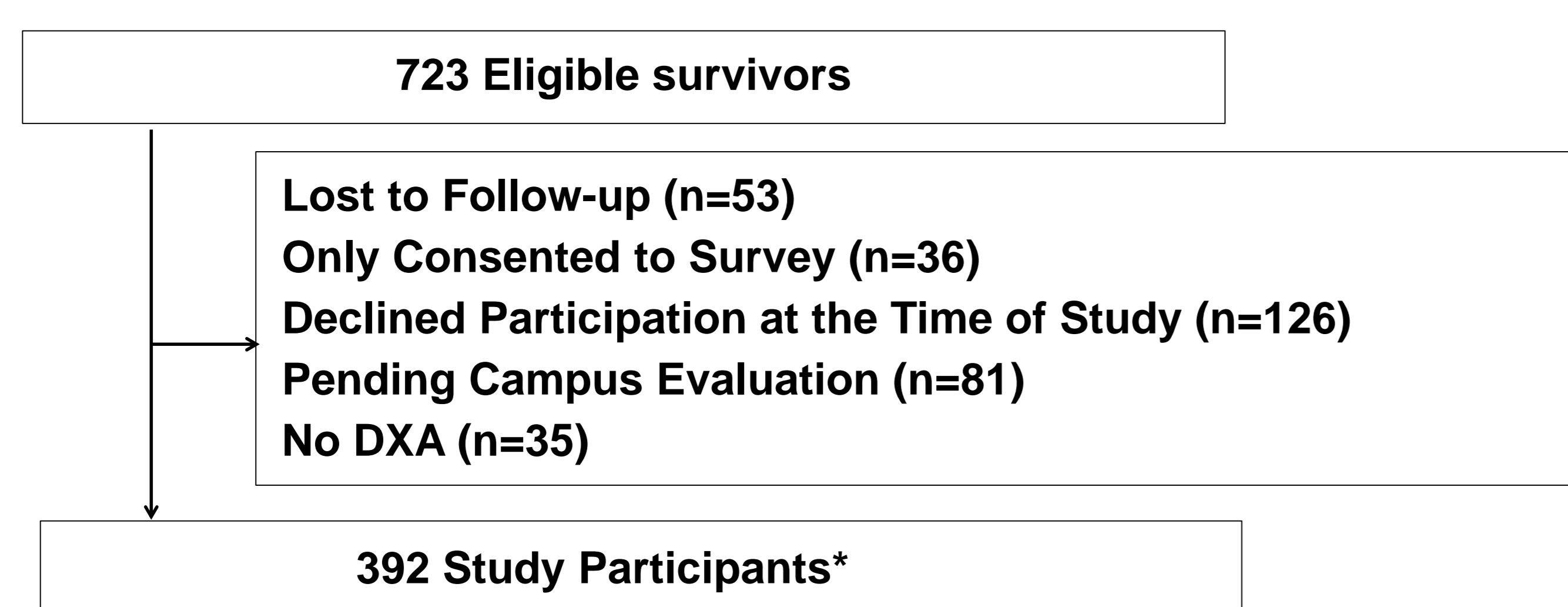
## Objective

To define the prevalence of metabolic impairments (diabetes mellitus, insulin resistance and dyslipidaemia) among survivors of paediatric abdominal and pelvic solid tumours and to assess the contribution of treatment exposures, lifestyle factors and body composition to metabolic impairments.

## Patients and Methods

- Participants included 392 10+ year survivors of paediatric abdominal and pelvic tumors who were ≥18 years of age at study, and who underwent dual X-ray absorptiometry.
- Participants underwent evaluation for the following conditions
  - Insulin resistance - defined as HOMA-IR > 2.86.
  - Diabetes mellitus - defined by the presence of either: a fasting blood glucose level ≥126 mg/dL on two separate tests; or by hemoglobin (Hgb) A1C ≥ 6.5%; random glucose ≥ 200 mg/dL; or by the use of glucose lowering medications.
  - Dyslipidemia - defined by the presence of either: a fasting total cholesterol ≥ 200 mg/dL; LDL ≥ 130 mg/dL; HDL < 40 mg/dL among males or < 50 among females); and/or triglycerides ≥ 150 mg/dL; or by the use of cholesterol lowering medications.
- Relative lean mass Z-score (LM) and total body fat Z-score were determined using dual X-ray absorptiometry.
- Poisson regression was used to evaluate associations between treatment exposures, lifestyle factors and body composition and metabolic impairments.

Figure 1: Consort diagram of study participation



\*Study participants were more likely to be male, have received treatment with anthracyclines (p=0.01) or pancreatic radiation (p=0.03) than non-participants. No differences were noted in terms of race, age at cancer diagnosis, or type of cancer.

## Results

- Median age at evaluation was 29.9 (range: 18.7-55.1) years.
- Overall, 36%, 41% and 32% of participants received radiation to the abdomen (mean 18.4Gy, standard deviation ± 14.2), pelvis (21.2Gy ± 17.2) or pancreatic tail (11.6Gy ± 11.8), respectively.

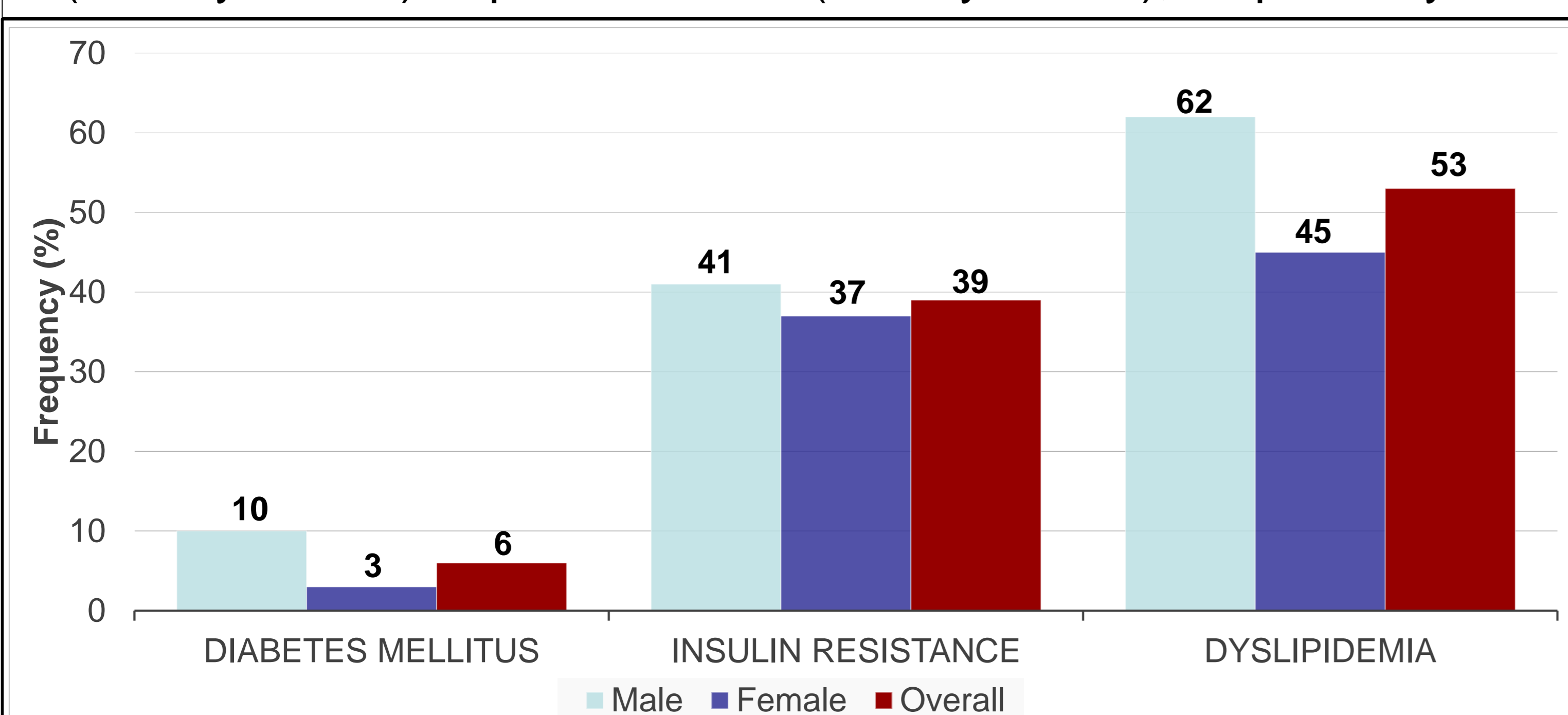


Figure 2: Frequency of metabolic impairments, overall and by sex

## Results continued

- There were 26 cases of diabetes mellitus. In univariate analysis, radiation to the pancreatic tail was associated with an increased risk of diabetes (RR=1.60, 95%CI = 1.26-2.03, p<0.001).

Table 1: Factors associated with Insulin Resistance

Characteristic		RR	95% CI	P-value
<b>Sex</b>	<b>Male vs. female</b>	<b>1.29</b>	<b>1.01-1.65</b>	<b>0.040</b>
Age at diagnosis, years		1.01	0.98-1.03	0.66
Age at evaluation, years		1.01	0.99-1.03	0.36
Abdomen dose (10Gy)		1.03	0.93-1.14	0.59
Pelvic dose (10Gy)		1.05	0.95-1.15	0.33
Anthracyclines	1-250 mg/m <sup>2</sup> vs. None	1.25	0.95-1.64	0.10
	>250 mg/m <sup>2</sup> vs. None	0.93	0.62-1.39	0.72
Alkylating agent	1-8000 mg/m <sup>2</sup> vs. None	0.99	0.68-1.44	0.97
	>8000 mg/m <sup>2</sup> vs. None	0.87	0.59-1.29	0.50
Platinum	1-400 mg/m <sup>2</sup> vs. None	0.95	0.63-1.45	0.82
	>400 mg/m <sup>2</sup> vs. None	0.87	0.56-1.34	0.51
Smoking	Current vs. Non-smoker	1.03	0.77-1.38	0.84
	Past vs. Non-smoker	0.98	0.71-1.35	0.90
Physically active	Yes vs. No	1.01	0.79-1.29	0.84
<b>Lean mass Z-score</b>		<b>1.43</b>	<b>1.26-1.61</b>	<b>&lt;0.001</b>
<b>Total body fat Z-score</b>		<b>1.38</b>	<b>1.19-1.60</b>	<b>&lt;0.001</b>

Survivors who expended >450 METs in moderate or vigorous physical activity were considered active

Table 2: Factors associated with Dyslipidemia

Characteristic		RR	95% CI	P-value
<b>Sex</b>	<b>Female vs. Male</b>	<b>1.47</b>	<b>1.23-1.75</b>	<b>&lt;0.001</b>
Age at diagnosis, years		1.01	0.99-1.02	0.34
Age at evaluation, years		1.01	1.00-1.03	0.07
Abdomen dose (10Gy)		1.03	0.96-1.11	0.43
Pelvic dose (10Gy)		1.03	0.96-1.10	0.46
Anthracyclines	1-250 mg/m <sup>2</sup> vs. None	1.21	0.98-1.48	0.08
	>250 mg/m <sup>2</sup> vs. None	1.09	0.81-1.46	0.56
Alkylating agent	1-8000 mg/m <sup>2</sup> vs. None	1.08	0.83-1.40	0.55
	>8000 mg/m <sup>2</sup> vs. None	0.90	0.68-1.20	0.48
Platinum	1-400 mg/m <sup>2</sup> vs. None	1.21	0.87-1.67	0.25
	>400 mg/m <sup>2</sup> vs. None	0.89	0.65-1.22	0.48
<b>Smoking</b>	<b>Current vs. Non-smoker</b>	<b>1.30</b>	<b>1.08-1.57</b>	<b>0.005</b>
	Past vs. Non-smoker	0.95	0.70-1.28	0.71
Physically active	Yes vs. No	0.88	0.73-1.06	0.16
Lean mass Z-score		1.06	0.98-1.15	0.16
<b>Total body fat Z-score</b>		<b>1.21</b>	<b>1.09-1.33</b>	<b>&lt;0.001</b>

Survivors who expended >450 METs in moderate or vigorous physical activity were considered active

## Conclusions

- Insulin resistance and dyslipidaemia are frequent among survivors.
- Data suggest pancreatic radiation may increase the risk of diabetes mellitus among survivors, however; further analysis are required in larger samples.
- Body composition changes, particularly increased body fat, influences metabolic health among solid tumour survivors. Accordingly, interventions aimed at reducing total body fat may improve metabolic health in this population.



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