Survivors of childhood acute lymphoblastic leukaemia (ALL) are at increased risk of metabolic dysfunction as a long-term side effect of cancer treatment. They have higher rates of adiposity, dyslipidaemia, arterial hypertension and insulin resistance and are therefore more likely to suffer from cardiovascular diseases (CVD). Unhealthy behaviour may further exacerbate morbidity.

The aim of this study is to evaluate the modifiable factors of metabolic risk in survivors of childhood acute lymphoblastic leukaemia (ALL) treated in a single Bulgarian pediatric hematology center.

**Patients and methods:**
- 47 patients in long-term remission
  - Mean age 20.6 ± 6.2 y (9 – 32 y) (M/F 53.2%:46.8%)
  - 19 survivors < 18 years (40.4%), 28 survivors ≥ 18 years
- Treatment between 1990 – 2012 according to 2 ALL protocols: Dana Farber Cancer Institute Consortium (DFCI) protocol 87-01 and BFM protocols: BFM 1998, BFM 2002
- ≥ 5 years after completion of therapy, FU period: mean 11.4 ± 4.4 y (5 - 25 y)
- 35 age- and sex-matched healthy controls

ALL survivors’ initial disease characteristics, treatment exposure and follow-up period are summarized in Table 1.

**Results:**
- The BMI, the SDS, the WC and the A/G ratio were higher in younger ALL survivors and in adult male survivors than among matched controls. Female survivors and female controls ≥ 18 y had n.s. difference (Table 2).

Survivors, especially children and male survivors, had significantly higher body fat mass than healthy controls (Figures 1 and 2). 57% of the adult female survivors had normal weight obesity (as defined by the BMI and the DEXA result).

The prevalence of dyslipidaemia was higher among survivors (Figure 3), and multiple abnormalities were more frequent in male than in female survivors. Similarly, the prevalence of MS components and their clustering was higher among ALL survivors than among controls (Figure 4).

The rate of modifiable factors of metabolic risk in survivors < 18 y is presented on Figure 5.

**Conclusions:**
- At a relatively young age survivors of childhood ALL develop an unfavorable metabolic profile and increased clustering of traditional CVD risk factors.
- Continuous monitoring, early identification and aggressive management of modifiable risk factors would reduce the overall metabolic burden.
- Physical activity is an important tool for the prevention of premature metabolic complications in this high-risk group.

<table>
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<th><strong>Age at diagnosis (years)</strong></th>
<th><strong>ALL survivors (n=47)</strong></th>
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<tr>
<td>≥ 18 y</td>
<td>33 ± 14.5</td>
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<tr>
<td>&lt; 18 y</td>
<td>22.9 ± 13.4</td>
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**Risk group**
- Body mass index (BMI)
- Waist circumference
- Central body adiposity
- Treatment protocol
- Follow-up period

**Clinical assessment**
- Weight, height, BMI, WC, blood pressure, pulse rate
- Biochemistry: fasting Cholesterol, HDL-C, LDL-C, TG and BGL
- Body composition evaluation (Dual-Energy X-ray Absorptiometry, Lunar Prodigy): Fat mass, Fat mass Index (BMI), % Fat, Android % Fat, Gynoid % Fat, A/G ratio

**Questionnaires and interviews**
- Traditional cardiovascular risk factors (treatment for diabetes, arterial hypertension, hyperlipidaemia, current smoking and sedentary lifestyle habits)
- Physical activity (PA): PA adequate to WHO healthy PA recommendations; modified Gansin Leisure-Time Activity Questionnaire

The metabolic syndrome (MS) was measured according to the International Diabetes Federation consensus. Dyslipidaemia was determined by presenting at least one of three factors: high LDL-C ≥ 3.36 mmol/l, high TG ≥ 1.7 mmol/l and/or low HDL-C (< 1.03/1.29 mmol/l in children and men, and in women, respectively).

**Table 1. Disease characteristics and treatment exposure in ALL survivors**

**Table 2. Anthropometric characteristics of participants**

**Figure 1. Fat mass parameters (DEXA) in survivors and controls by age group**

**Figure 2. Fat mass parameters (DEXA) in male and female survivors ≥ 18 years compared to controls.**

**Figure 3. Prevalence of lipidaemia abnormalities among ALL survivors and controls**

**Figure 4. MS components clustering among ALL survivors in comparison with controls**

**Figure 5. Cardiovascular risk factors among ALL survivors and controls < 18 years**

**References:**