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The long-term impact of cancer: evaluating psychological distress in adolescent and young adult cancer survivors in Switzerland

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Abstract

Objectives

Adolescents and young adults (AYA) are diagnosed with cancer during a critical life period full of psychosocial challenges. They may experience a significant impact of the cancer diagnosis on their psychological health, also in the long term. We aimed to (i) evaluate psychological distress in AYA cancer survivors, compare levels of distress with controls, and (ii) describe socio-demographic and cancer-related characteristics associated with psychological distress.

Methods

We sent a questionnaire to AYA cancer survivors (aged 16–25 years at diagnosis, survived ≥ 5 years) registered in the Cancer Registry Zurich and Zug, Switzerland. Psychological distress was measured using the Brief Symptom Inventory-18 (BSI-18) assessing anxiety, depression, somatization and a global severity index (GSI) (cut-off score indicating psychological distress: $T \geq 57$). Distress levels were compared between survivors and controls. We used logistic regression to determine associations of socio-demographic and cancer-related characteristics with distress.

Results

Of 160 AYA cancer survivors, 34 (21%) reported being distressed (27% in women, 17% in men, $p=0.129$). Compared to controls, survivors did not report higher levels of distress (all p -values > 0.05). Survivors with migration background and survivors with late effects reported higher levels on GSI, somatization, and anxiety. Higher levels of depression were associated with being female, not being in a partnership and having late effects.

Conclusions

A substantial subgroup of AYA cancer survivors reported psychological distress. Systematically screening for distress and providing psychological follow-up for survivors at risk may help to provide adequate psychological support.

Introduction

During the last decades, progress in cancer treatments have translated into increased survival rates and nowadays 87% of adolescent and young adult (AYA) cancer patients survive >5 years in Europe¹. Nevertheless, as more survivors reach long-term survivorship, cancer- and treatment-related adverse late outcomes (late effects) are increasing in frequency, requiring timely interventions during long-term follow-up care². AYAs are diagnosed with cancer during a unique and challenging period of their life³. We will focus on survivors having been diagnosed at age 16 to 25 covering an age range full of psychosocial developments. Therefore, late effects may be different from those in cancer survivors diagnosed at a younger or older age, especially regarding psychosocial difficulties, which are a major concern for long-term AYA cancer survivors⁴.

Psychological distress is a state of emotional suffering such as depression and anxiety, that can be associated with physiological symptoms, i.e. somatization⁵. Survivors of AYA cancer may be at high risk of experiencing psychological distress because of their diagnosis during a key time of consolidation of identity and social growth represented by multiple developmental transitions such as completing education, gaining independence, taking more responsibility in daily life decisions, establishing romantic relationships and entering into the labor market^{6,7}. AYA cancer survivors may face significant disruptions within their educational trajectory that might have an impact on their career development, thereby increasing the risk for financial burden in the long term^{6,8}. Furthermore, awareness about possible late effects, relapse or second malignancies represent stressors that may have a stronger impact on psychological health of AYA cancer survivors than in younger patients^{9,10}. So far, most research on late effects has focused on somatic complications or have been addressed in childhood cancer survivors.

Recent studies found that AYA cancer survivors reported poorer psychological health compared to cancer-free persons¹¹⁻¹³ and compared to persons diagnosed at a younger or older age^{6,12}. More than a quarter of AYA cancer patients and survivors reported psychological distress¹⁴⁻¹⁶ and more than 80% of AYA cancer survivors had not spoken to a health care professional about their problems¹¹. Due to the fact that a substantial proportion of distressed survivors may remain unrecognized and at risk of serious consequences, more research in this specific cancer survivor population is needed. We aimed to gain knowledge about the psychological health of long-term AYA cancer survivors in Switzerland by (i) describing psychological distress in AYA cancer survivors and comparing them with a control population, and (ii) describing socio-demographic and cancer-related characteristics associated with psychological distress in survivors.

Methods

Sample and procedure

AYA cancer survivors in the Canton Zurich, Switzerland were identified through the population-based Cancer Registry Zurich and Zug. Eligible survivors were aged 16-25 years at diagnosis (1990-2005) and had survived cancer for ≥ 5 years. Cancer diagnoses were restricted to leukemia, lymphoma, germ cell tumor, central nervous system tumor (CNS), neuroblastoma, renal tumors, hepatic tumors, bone tumors, and soft tissue sarcoma to enable comparison with a cohort of childhood cancer survivors¹⁷. Addresses of eligible survivors were made available by the cancer registry and updated by contacting the communities, if necessary. Each survivor received a cover letter, study information, questionnaire, informed consent form and pre-paid return envelope between August 2010 and January 2012. Non-responders received a reminder letter and another copy of the questionnaire about four weeks later.

The study was approved by the Cantonal Ethics Committee of Zurich (Ref No. EK: 2010-0228/2) and participants gave informed consent.

Control group

We used a sample of Swiss adults consisting of 358 persons aged 21-46 years from the Swiss general population (Table S1). Data were collected between May 2015 and June 2016. The control group was weighted according to the gender distribution in AYA cancer survivors.

Measurements

Participants received a questionnaire covering the following topics: health status, psychological distress, quality of life, and preferences for the organization and content of long-term follow-up care¹⁸⁻²⁰.

Psychological distress

To evaluate psychological distress we used the German version of the Brief Symptom Inventory-18 (BSI-18)²¹. The BSI-18 is a reliable and valid standardized self-report inventory containing three six-item scales (somatization, anxiety, and depression) and a global severity index (GSI) for *overall distress*²². Participants were asked to report their degree of distress over the past 7 days using a five-point Likert scale (0="not at all" to 4="extremely"). By summing up the items of the respective scales, raw scores for each scale (range 0-24), and for the GSI (sum of all items, range 0-72), were calculated. Higher scores indicate higher psychological distress. Survivors with more than three missing items per scale were not included in the analyses²². For those participants with no more than two missing items per scale, the rounded averages of the remaining items of the respective scale were imputed

in order to obtain the scale scores. Since no corresponding normative data were available we used sex-specific American normative data²² to transform raw scores of the three scales and the GSI into T scores (mean=50, standard deviation=10). To identify distressed participants, we used the standard case rule²² and the cut-off score of T=57 proposed by Zabora et al.²³ and previously used in Swiss⁹ and American²⁴ survivors: persons with at least two scales with T≥57 or GSI: T≥57 were considered *distressed*².

Socio-demographic characteristics

We assessed sex, age at study (20-29 years/30-39 years/>40 years), employment status (employed/not employed), highest educational achievement (primary education: compulsory schooling only/secondary education: vocational training or high school degree/tertiary education: college or university degree)²⁵, being in a partnership (yes/no), and migration background (yes/no). We classified participants as having a migration background if they were not Swiss citizen, not Swiss citizen since birth or not born in Switzerland (yes/no).

Cancer-related characteristics

Information on diagnosis and treatment was obtained from the cancer registry. Diagnoses were classified according to the International Classification of Childhood Cancer, third edition (ICCC-3)²⁶. For analyses, we grouped participants into: leukemia, lymphoma, germ cell tumors, CNS tumors, and other solid tumors. Treatment was hierarchically coded as surgery only, chemotherapy (may have had surgery), and radiotherapy (may have had surgery and/or chemotherapy). We also obtained information on age at diagnosis (16-20 years/21-25 years) and time since diagnosis (5-10 years/11-15 years/>16 years). In the questionnaire, we collected information on the presence of late effects (yes/no). Participants who answered yes, were asked to self-report the type of late effects they are suffering from, and we classified the nature as somatic, psychological or both. Further, survivors were asked whether they had had a cancer relapse (yes/no) or a second cancer (yes/no).

Statistical analysis

We applied descriptive statistics, t-tests (continuous variables) and chi-square tests (categorical variables) to compare participants and non-participants of the study. For aim 1, we used chi-square tests to compare proportions and adjusted Wald tests to compare T scores of AYA cancer survivors and controls. For aim 2, we analyzed associations between the three BSI-18 scales and the GSI with socio-demographic and cancer-related characteristics applying logistic regression. Variables significantly associated ($p \leq 0.05$) with the scales or the GSI in the univariable regression were included in the respective multivariable regression model. All analyses were performed using Stata 15.1 (College Station, TX).

Results

Study sample

The cancer registry identified 469 eligible AYA cancer survivors for our study, of whom we were able to contact 389 (82.9%, Figure S1). Of those, 160 (41.1%) survivors participated and completed the BSI-18 (61.3% men). Participants and non-participants were similar regarding socio-demographic and cancer-related characteristics (Table 1). Mean age at study was 34.0 years (SD=5.6, range:20.9-46.5) with a mean time since diagnosis of 12.4 years (SD=4.8, range:5.0-21.6). Most survivors were diagnosed with lymphomas (37.5%) and germ cell tumors (28.8%). Among the 45 participants reporting late effects, we found that frequent somatic late effects were infertility (n=15), endocrine complications (n=6), and treatment-induced cardiovascular issues (n=2). Regarding psychological late effects, anxiety (n=6) and depression (n=6) were the most frequently reported late effects.

Aim 1: Psychological distress in survivors and controls

A total of 34 survivors (21.3%) were considered distressed. We found more distressed women (27.4%) than men (17.4%, $p=0.129$) among survivors (Figure 1). Among controls, 16.6% were considered distressed ($p=0.209$ for comparison between survivors and controls). A similar number of men ($p=0.939$) but more women ($p=0.036$) were considered distressed among survivors compared to controls. Mean T scores of the BSI-18 in survivors were: somatization=47.0, depression=48.7, anxiety=47.3, GSI=46.9 (Table 2).

Aim 2: Characteristics associated with psychological distress in survivors

Regarding overall distress (GSI), those survivors with a migration background (OR=4.2, 95%CI:1.8-9.6, $p=0.001$; Table 3) and unemployed survivors (OR=4.6, 95%CI:1.5-14.2, $p=0.008$) were more likely to be distressed. Common risk factors for somatization, depression, and anxiety were having a migration background (somatization: OR=4.1, 95%CI:1.6-10.8, $p=0.004$; depression: OR=4.2, 95%CI:1.6-10.8, $p=0.004$; anxiety: OR=3.7, 95%CI:1.6-8.6, $p=0.002$; Tables S2, S3, and S4) and being unemployed (somatization: OR=4.8, 95%CI:1.4-16.3, $p=0.011$; depression: OR=5.0, 95%CI:1.6-15.7, $p=0.005$; anxiety: OR=3.4, 95%CI:1.1-10.7, $p=0.034$). Additionally, women (OR=2.9, 95%CI:1.6-6.4, $p=0.008$; Table S3) and survivors not being in a partnership (OR=3.0, 95%CI:1.3-6.8, $p=0.012$) were more likely to be depressed.

Applying multivariable regression, having a migration background was associated with risk for overall distress, somatization, and anxiety (Tables 3, S2, and S4). Risk for depression was associated with being a woman and not being in a partnership (Table S3).

The only cancer-related risk factor for psychological distress was the presence of late effects in both, univariable and multivariable regressions (multivariable regressions: overall distress:

OR=6.0,95%CI:2.5-14.6,p<0.001, somatization: OR=3.7,95%CI:1.3-10.4,p=0.012, depression: OR=3.0,95%CI:1.2-7.7,p=0.021, anxiety: OR=3.1,95%CI:1.3-7.3,p=0.010; Tables 3, S2, S3, and S4). Risk for distress was especially pronounced in survivors reporting both types of late effects.

Conclusions

We found the majority of long-term AYA cancer survivors not being distressed. However, 21% of survivors reported being distressed. Risk factors for psychological distress were having a migration background, not being in a partnership, and the presence of late effects.

In line with our findings in AYA cancer survivors, previous studies in childhood cancer survivors showed that the majority of survivors function well psychologically, although a subgroup may be at risk for psychological distress^{9,10,27,28}. We found similar levels of distress compared to controls. Other studies in AYA cancer survivors have reported higher psychological distress compared to cancer-free persons¹¹⁻¹³. Reasons for similar levels of distress in Swiss AYA cancer survivors compared to controls might be the well-functioning health care system in Switzerland providing survivors with needed support to function well psychologically and an in general good (re-)integration into work and social life after having been cured from cancer as indicated by another study in the same sample of Swiss AYA cancer survivors where we have found no significant differences for employment and marital status²⁹.

In our sample, survivors with migration background were more likely to report overall distress compared to survivors without migration background. This is in line with findings in Swiss adult survivors of childhood cancer¹⁰. A study in Norwegian adults found that immigrants from low- and middle-income countries showed higher levels of distress compared to immigrants from high-income countries and persons born in Norway, because they face more difficulties entering the labor market and a lack of social support³⁰. Survivors with migration background might be less familiar with the Swiss health care system and therefore experience more barriers to needed support. More research is needed to understand the support needs of survivors with different migration backgrounds in the context of cancer survivorship in order to support them adequately.

We found that survivors not being in a partnership were more likely to report depression. This is in line with findings from a US study¹¹.

We did not find a significant association between age at diagnosis and distress, but the risk was slightly elevated for survivors who were older at diagnosis. Among survivors of childhood and adolescent cancer, those diagnosed at older age have shown greater

psychological distress than those diagnosed at younger age^{10,27}. Among survivors of AYA cancer (age at diagnosis 15-39 years), survivors who were younger at diagnosis reported higher psychological distress^{11,31}. This indicates a higher risk for distress for survivors diagnosed during late adolescence or early young adulthood. In our study, the age range at diagnosis was relatively narrow (16-25 years), covering the period when survivors might experience most distress. Thus, survivors in our study might have been more equally affected, and therefore age at diagnosis did not play a differentiating role. Time since diagnosis was not significantly associated with distress in our study. Compared to US AYA cancer patients, levels of distress were lower in our study¹⁴ (Table S5).

In our study we did not find a direct association of psychological distress with either type of cancer nor treatment. However, late effects were a major correlate of psychological distress. Coping with treatment-related adverse outcomes and being aware of possible late effects in the long term might be an overwhelming experience for AYA cancer survivors³². Despite the scarcity of studies in long-term survivors of AYA cancer, the association between late effects and psychological distress is consistently found. Comorbidities in US AYA cancer survivors¹¹ were found being associated with psychological distress. A recent study found that AYA cancer survivors' perceptions of the impact of cancer was related to psychological distress⁶. Interestingly, they found that by additionally considering survivors' negative and positive perceptions of their disease, the effects of health problems on distress decreased. These findings are in line with our findings on self-reported late effects being associated with distress while we did not find associations of registry-based cancer and treatment information. Survivors' perceptions should thus be taken into consideration in future research, interventions, and support services.

In a recent study, we found the presence of late effects being associated with unemployment²⁹. Being unemployed might have a negative impact on psychological health. This might indicate another pathway of late effects being associated with psychological distress.

The prevalence of late effects in our study (28%) was lower compared to other studies⁴. This might be due to self-report of late effects and survivors not being aware of health problems being late sequelae of their cancer diagnosis and treatment.

Clinical implications

Our findings show the need for a subgroup of distressed AYA cancer survivors to be adequately followed-up and supported. Small but vulnerable subgroups may remain unrecognized in daily clinical practice resulting in deleterious consequences for their psychological health in the long term¹¹. Survivors of AYA cancer may benefit from regular

screening to detect those at risk for psychological distress³³, and provide adequate support or psychotherapy if needed¹⁴. The subjective perception of the disease impact may be relevant for the experience of psychological distress^{6,34}. Supporting a positive re-interpretation of the disease experience e.g. through cognitive behavioral interventions⁶, may help survivors to experience personal growth³⁴. Survivors may value the use of social media as an additional support strategy^{7,9}. Internet-based interventions may overcome accessibility barriers to psychological care, and they might also be more accepted than other approaches³⁵.

Future longitudinal studies in long-term AYA cancer survivors are needed to detect and better understand which characteristics influence their psychological health along the cancer trajectory and what type of support services help to improve their psychological health.

Study limitations

A limitation of this study is the relatively small sample size and relatively low response rate. Some larger 95% CIs indicate that these results should be interpreted with caution. Low response rates are common in studies in AYA cancer patients and survivors^{36,37}. A main reason for lower response rates in young adults compared to younger or older persons is that they are a mobile population difficult to localize, reach and recruit for studies³⁶. Self-selection may lead to biased results as distressed survivors and survivors with late effects might be less willing to participate resulting in underestimation of distress and underreporting of late effects. The inclusion of only a selected group of diagnoses might limit generalizability of our findings. Survivors with migration background might have been underrepresented since the questionnaire was only available in German and French what might have biased the risk of distress in survivors with migration background. Self-report questionnaire may cause social desirability bias³⁸. Data in survivors have been collected between 2010 and 2012. However, we do not expect that results would have been different in more recent years since the health care system has not changed much in the past few years in Switzerland. Furthermore, we used American normative data to standardize the BSI-18 scores²², because no Swiss normative data exist to date. Similarly to previous studies^{9,24}, we used a cut-off score of T=57 to define distress.

A major strength of our study is the population-based sample of AYA cancer survivors in a large and diverse region of Switzerland. Furthermore, our participants were representative of the entire sample of eligible AYA cancer survivors. We used the widely applied, valid and reliable BSI-18 to assess psychological distress. Furthermore, we considered a wide range of possible socio-demographic and cancer-related risk factors. Another strength is the use of

a control group from the Swiss general population instead of siblings, as siblings cannot be considered independent observations due to their related disease experience.

Even though the majority of participating AYA cancer survivors did not report psychological distress, we found a subgroup suffering from symptoms of somatization, depression or anxiety. Survivors with migration background, not being in a partnership and those suffering from late effects were at higher risk for psychological distress. These vulnerable subgroups of survivors could benefit from support services providing an environment able to detect and treat existing psychological distress.

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Conflict of interest statement

The authors declare that they have no conflict of interest.

References

1. Gatta G, Zigon G, Capocaccia R, et al. Survival of European children and young adults with cancer diagnosed 1995-2002. *Eur J Cancer*. 2009;45(6):992-1005.
2. Kinahan KE, Sanford S, Sadak KT, Salsman JM, Danner-Koptik K, Didwania A. Models of Cancer Survivorship Care for Adolescents and Young Adults. *Semin Oncol Nurs*. 2015;31(3):251-259.
3. Epelman CL. The adolescent and young adult with cancer: state of the art -- psychosocial aspects. *Curr Oncol Rep*. 2013;15(4):325-331.
4. Ahmad SS, Reinius MA, Hatcher HM, Ajithkumar TV. Anticancer chemotherapy in teenagers and young adults: managing long term side effects. *Bmj*. 2016;354:i4567.
5. Mirowsky J, Ross CE. Measurement for a human science. *J Health Soc Behav*. 2002;43(2):152-170.
6. Husson O, Zebrack BJ. Perceived impact of cancer among adolescents and young adults: Relationship with health-related quality of life and distress. *Psychooncology*. 2016;26(9):1307-1315.
7. Warner EL, Kent EE, Trevino KM, Parsons HM, Zebrack BJ, Kirchhoff AC. Social well-being among adolescents and young adults with cancer: A systematic review. *Cancer*. 2016;122(7):1029-1037.
8. Zebrack BJ, Corbett V, Embry L, et al. Psychological distress and unsatisfied need for psychosocial support in adolescent and young adult cancer patients during the first year following diagnosis. *Psychooncology*. 2014;23(11):1267-1275.
9. Gianinazzi ME, Rueegg CS, Wengenroth L, et al. Adolescent survivors of childhood cancer: are they vulnerable for psychological distress? *Psychooncology*. 2013;22(9):2051-2058.
10. Michel G, Rebholz CE, von der Weid NX, Bergstraesser E, Kuehni CE. Psychological distress in adult survivors of childhood cancer: the Swiss Childhood Cancer Survivor Study. *J Clin Oncol*. 2010;28(10):1740-1748.
11. Kaul S, Avila JC, Mutambudzi M, Russell H, Kirchhoff AC, Schwartz CL. Mental distress and health care use among survivors of adolescent and young adult cancer: A cross-sectional analysis of the National Health Interview Survey. *Cancer*. 2017;123(5):869-878.
12. Lang MJ, Giese-Davis J, Patton SB, Campbell DJT. Does age matter? Comparing post-treatment psychosocial outcomes in young adult and older adult cancer survivors with their cancer-free peers. *Psychooncology*. 2017;27(5):1404-1411.
13. Seitz DC, Besier T, Debatin KM, et al. Posttraumatic stress, depression and anxiety among adult long-term survivors of cancer in adolescence. *Eur J Cancer*. 2010;46(9):1596-1606.
14. Kwak M, Zebrack BJ, Meeske KA, et al. Trajectories of psychological distress in adolescent and young adult patients with cancer: a 1-year longitudinal study. *J Clin Oncol*. 2013;31(17):2160-2166.
15. Kwak M, Zebrack BJ, Meeske KA, et al. Prevalence and predictors of post-traumatic stress symptoms in adolescent and young adult cancer survivors: a 1-year follow-up study. *Psychooncology*. 2013;22(8):1798-1806.
16. Lang MJ, David V, Giese-Davis J. The Age Conundrum: A Scoping Review of Younger Age or Adolescent and Young Adult as a Risk Factor for Clinical Distress, Depression, or Anxiety in Cancer. *J Adolesc Young Adult Oncol*. 2015;4(4):157-173.
17. Kuehni CE, Rueegg CS, Michel G, et al. Cohort profile: the Swiss childhood cancer survivor study. *Int J Epidemiol*. 2012;41(6):1553-1564.

18. Christen S, Vetsch J, Mader L, et al. Preferences for the organization of long-term follow-up in adolescent and young adult cancer survivors. *Support Care Cancer*. 2016;24(8):3425-3436.
19. Harju E, Roser K, Dehler S, Michel G. Health-related quality of life in adolescent and young adult cancer survivors. *Support Care Cancer*. 2018.
20. Roser K, Baenziger J, Mader L, Christen S, Dehler S, Michel G. Attendance to follow-up care in survivors of adolescent and young adult cancer: application of the theory of planned behaviour. *J Adolesc Young Adult Oncol*. accepted.
21. Franke GH. *Brief Symptom Inventory von L. R. Derogatis (Kurzform der SCL -90 - R) - Deutsche Version - Manual*. Beltz Test GmbH; 2000.
22. Derogatis LR. *BSI 18 - Brief Symptom Inventory 18 - Administration, Scoring, and Procedures Manual*. NCS Pearson Inc.; 2000.
23. Zabora J, BrintzenhofeSzoc K, Jacobsen P, et al. A new psychosocial screening instrument for use with cancer patients. *Psychosomatics*. 2001;42(3):241-246.
24. Recklitis CJ, Rodriguez P. Screening childhood cancer survivors with the brief symptom inventory-18: classification agreement with the symptom checklist-90-revised. *Psychooncology*. 2007;16(5):429-436.
25. Kuehni CE, Strippoli MP, Rueegg CS, et al. Educational achievement in Swiss childhood cancer survivors compared with the general population. *Cancer*. 2012;118(5):1439-1449.
26. Steliarova-Foucher E, Stiller C, Lacour B, Kaatsch P. International Classification of Childhood Cancer, third edition. *Cancer*. 2005;103(7):1457-1467.
27. Kazak AE, Derosa BW, Schwartz LA, et al. Psychological outcomes and health beliefs in adolescent and young adult survivors of childhood cancer and controls. *J Clin Oncol*. 2010;28(12):2002-2007.
28. Zeltzer LK, Recklitis C, Buchbinder D, et al. Psychological status in childhood cancer survivors: a report from the Childhood Cancer Survivor Study. *J Clin Oncol*. 2009;27(14):2396-2404.
29. Mader L, Vetsch J, Christen S, et al. Education, employment and marriage in long-term survivors of teenage and young adult cancer compared with healthy controls. *Swiss Med Wkly*. 2017;147:w14419.
30. Dalgard OS, Thapa SB, Hauff E, McCubbin M, Syed HR. Immigration, lack of control and psychological distress: findings from the Oslo Health Study. *Scand J Psychol*. 2006;47(6):551-558.
31. Salsman JM, Garcia SF, Yanez B, Sanford SD, Snyder MA, Victorson D. Physical, emotional, and social health differences between posttreatment young adults with cancer and matched healthy controls. *Cancer*. 2014;120(15):2247-2254.
32. Zebrack BJ. Psychological, social, and behavioral issues for young adults with cancer. *Cancer*. 2011;117(10 Suppl):2289-2294.
33. Michel G, Vetsch J. Screening for psychological late effects in childhood, adolescent and young adult cancer survivors: a systematic review. *Curr Opin Oncol*. 2015;27(4):297-305.
34. Wenninger K, Helmes A, Bengel J, Lauten M, Volkel S, Niemeyer CM. Coping in long-term survivors of childhood cancer: relations to psychological distress. *Psychooncology*. 2013;22(4):854-861.
35. Leykin Y, Thekdi SM, Shumay DM, Munoz RF, Riba M, Dunn LB. Internet interventions for improving psychological well-being in psycho-oncology: review and recommendations. *Psychooncology*. 2012;21(9):1016-1025.

36. Harlan LC, Lynch CF, Keegan TH, et al. Recruitment and follow-up of adolescent and young adult cancer survivors: the AYA HOPE Study. *J Cancer Surviv.* 2011;5(3):305-314.
37. Rosenberg AR, Bona K, Wharton CM, et al. Adolescent and Young Adult Patient Engagement and Participation in Survey-Based Research: A Report From the "Resilience in Adolescents and Young Adults With Cancer" Study. *Pediatr Blood Cancer.* 2016;63(4):734-736.
38. Logan DE, Claar RL, Scharff L. Social desirability response bias and self-report of psychological distress in pediatric chronic pain patients. *Pain.* 2008;136(3):366-372.

Table 1: Comparison of participating and non-participating Swiss AYA cancer survivors.

| Swiss AYA cancer survivors(n=469) | | | |
|--|---------------------|-------------------------|----------------------|
| | Participants(n=160) | Non-participants(n=309) | |
| | n(%) | n(%) | p-value [†] |
| Socio-demographic characteristics | | | |
| Sex | | | 0.110 |
| Male | 98(61.3) | 210(67.9) | |
| Female | 62(38.7) | 96(31.1) | |
| Unknown‡ | 0(0) | 3(1.0) | |
| Age at study(years) | | | 0.569 |
| 20-29 | 43(26.9) | 74(23.9) | |
| 30-39 | 85(53.1) | 180(58.3) | |
| 40+ | 32(20) | 55(17.8) | |
| Migration background | | | n.a. |
| No | 125(78.1) | | |
| Yes | 35(21.9) | | |
| Partnership | | | n.a. |
| Yes | 123(76.9) | | |
| No | 37(23.1) | | |
| Education | | | n.a. |
| Primary | 13(8.1) | | |
| Secondary | 74(46.3) | | |
| Tertiary | 72(45) | | |
| Unknown‡ | 1(0.6) | | |
| Employment status | | | n.a. |
| Employed | 145(90.6) | | |
| Not employed | 14(8.8) | | |
| Unknown‡ | 1(0.6) | | |
| Cancer-related characteristics | | | |
| Diagnosis(ICCC3) | | | 0.138 |
| Leukemia | 13(8.1) | 28(9.1) | |
| Lymphoma | 60(37.5) | 91(29.4) | |
| CNS tumor | 15(9.4) | 36(11.7) | |
| Neuroblastoma | 2(1.2) | 2(0.6) | |
| Renal tumor | 3(1.9) | 1(0.3) | |
| Hepatic tumor | 0(0) | 2(0.6) | |
| Bone tumor | 6(3.7) | 15(4.9) | |
| Soft tissue sarcoma | 15(9.4) | 17(5.5) | |
| Germ cell tumors | 46(28.8) | 117(37.9) | |
| Treatments§ | | | 0.428 |
| Surgery only | 57(35.6) | 109(35.3) | |
| Chemotherapy | 36(22.5) | 75(24.3) | |
| Radiotherapy | 41(25.6) | 60(19.4) | |
| Unknown‡ | 26(16.3) | 65(21.0) | |

| | | | | |
|-----------------------------|-----------------|-----------------|--|-----------------|
| Age at diagnosis(years) | | | | 0.373 |
| 16-20 | 70(43.7) | 122(39.5) | | |
| 21-25 | 90(56.3) | 187(60.5) | | |
| Time since diagnosis(years) | | | | 0.976 |
| 5-10 | 59(36.9) | 111(36.0) | | |
| 11-15 | 51(31.8) | 99(32.0) | | |
| 16+ | 50(31.3) | 99(32.0) | | |
| Relapse | | | | n.a. |
| No | 136(85.0) | | | |
| Yes | 24(15.0) | | | |
| Second cancer | | | | n.a. |
| No | 148(92.5) | | | |
| Yes | 12(7.5) | | | |
| Late effects | | | | n.a. |
| No | 111(69.4) | | | |
| Yes | 45(28.1) | | | |
| Unknown‡ | 4(2.5) | | | |
| Type of late effects | | | | n.a. |
| No late effects | 111(69.4) | | | |
| Psychological | 6(3.7) | | | |
| Somatic | 27(16.9) | | | |
| Both | 12(7.5) | | | |
| Unknown‡ | 4(2.5) | | | |
| | Mean(SD) | Mean(SD) | | p-value¶ |
| Age at study(years) | 34.0(5.8) | 34.2(5.6) | | 0.754 |
| Age at diagnosis(years) | 21.6(2.8) | 21.7(2.9) | | 0.706 |
| Time since diagnosis(years) | 12.4(4.8) | 12.4(4.8) | | 0.884 |

Abbreviations: ICC3,International Classification of Childhood Cancer-Third Edition; CNS,central nervous system; SD,standard deviation; n.a.,not available

†p-value from chi-square test for categorical variables

‡Unknown; not included in p-value calculation

§Chemotherapy (may have had surgery but not radiotherapy);Radiotherapy (may have had surgery and/or chemotherapy)

¶p-value from t-test for continuous variables

Table 2: Comparison of levels of psychological distress (T scores) measured by the Brief Symptom Inventory-18 (BSI-18) in adolescent and young adult (AYA) cancer survivors (n=160) and controls (n=358).

| | AYA cancer survivors(n=160) | Controls(weighted) | |
|---------------------|-----------------------------|--------------------|----------------------|
| | Mean(95%CI) | Mean(95%CI) | p-value ^a |
| Somatization | | | |
| All | 47(45.9-48.2) | 47.5(46.7-48.2) | 0.535 |
| Men | 46.7(45.2-48.2) | 46.9(45.9-48.0) | 0.823 |
| Women | 47.6(45.6-49.5) | 48(46.9-49.0) | 0.719 |
| Depression | | | |
| All | 48.7(47.2-50.2) | 47.9(47.1-48.8) | 0.373 |
| Men | 47.9(46.3-49.6) | 48.7(47.3-50.1) | 0.486 |
| Women | 49.9(47.2-52.7) | 47.3(46.2-48.4) | 0.079 |
| Anxiety | | | |
| All | 47.3(45.9-48.6) | 47.4(46.6-48.2) | 0.85 |
| Men | 48.1(46.4-49.7) | 47.4(46.2-48.7) | 0.486 |
| Women | 46(43.7-48.3) | 47.4(46.4-48.4) | 0.276 |
| GSI | | | |
| All | 46.9(45.4-48.5) | 47.3(46.5-48.2) | 0.659 |
| Men | 47.1(45.2-49.0) | 48.2(46.8-49.5) | 0.359 |
| Women | 46.7(44.0-49.4) | 46.6(45.4-47.8) | 0.967 |

Abbreviations: CI, confidence interval; GSI, global severity index

[†]p-values calculated with adjusted Wald test for differences between survivors and controls

Table 3: Characteristics of distressed survivors (GSI with T \geq 57 or at least two scales with T \geq 57) and associations of overall distress with socio-demographic and cancer-related characteristics.

| | | Distressed AYA cancer survivors n(%) | Univariable regression | | | Multivariable regression | | |
|--|------------------|--|------------------------|------------|--------------|--------------------------|-----------|--------------|
| | | | OR | 95%CI | p-value | OR | 95%CI | p-value |
| Whole sample | | 34(21) | - | - | - | - | - | - |
| Socio-demographic characteristics | | | | | | | | |
| Sex | | | | | 0.132 | | | |
| | Male | 17(17) | 1.00 | | | | | |
| | Female | 17(27) | 1.80 | 0.84-3.87 | | | | |
| Age at study(years) | | | | | 0.299 | | | |
| | 20-29 | 6(14) | 1.00 | | | | | |
| | 30-39 | 19(22) | 1.78 | 0.65-4.84 | | | | |
| | 40+ | 9(28) | 2.41 | 0.76-7.67 | | | | |
| Migration background | | | | | 0.001 | | | 0.005 |
| | No | 19(15) | 1.00 | | | | | |
| | Yes | 15(43) | 4.18 | 1.83-9.58 | | 3.82 | 1.50-9.73 | |
| Partnership | | | | | 0.162 | | | |
| | Yes | 23(19) | 1.00 | | | | | |
| | No | 11(30) | 1.84 | 0.80-4.25 | | | | |
| Education | | | | | | | | |
| | Primary | 4(31) | 1.00 | | 0.669 | | | |
| | Secondary | 15(20) | 0.57 | 0.15-2.11 | | | | |
| | Tertiary | 14(19) | 0.54 | 0.15-2.02 | | | | |
| Employment status | | | | | 0.008 | | | 0.294 |
| | Employed | 26(18) | 1.00 | | | | | |
| | Not employed | 7(50) | 4.58 | 1.48-14.17 | | 2.03 | 0.54-7.61 | |
| Cancer-related characteristics | | | | | | | | |
| Diagnosis | | | | | 0.683 | | | |
| | Leukemia | 4(31) | 1.00 | | | | | |
| | Lymphoma | 15(25) | 0.75 | 0.20-2.79 | | | | |
| | CNS tumors | 3(20) | 0.56 | 0.10-3.17 | | | | |
| | Germ cell tumors | 7(15) | 0.40 | 0.10-1.68 | | | | |
| | Other† | 5(19) | 0.54 | 0.12-2.47 | | | | |
| Treatment | | | | | 0.607 | | | |
| | Surgery | 14(25) | 1.00 | | | | | |
| | Chemotherapy | 9(25) | 1.02 | 0.39-2.69 | | | | |
| | Radiotherapy | 7(17) | 0.63 | 0.23-1.74 | | | | |
| Age at diagnosis(years) | | | | | 0.463 | | | |
| | 16-20 | 13(19) | 1.00 | | | | | |
| | 21-25 | 21(23) | 1.33 | 0.61-2.90 | | | | |
| Time since diagnosis(years) | | | | | 0.348 | | | |
| | 5-10 | 9(15) | 1.00 | | | | | |
| | 11-15 | 13(25) | 1.90 | 0.74-4.91 | | | | |

| | | | | | | | |
|----------------------|--------|-------|-------------|--|------|------------|--------|
| 16+ | 12(24) | 1.75 | 0.67-4.59 | | | | |
| Relapse | | | | | | | 0.133 |
| No | 26(19) | 1.00 | | | | | |
| Yes | 8(33) | 2.12 | 0.82-5.47 | | | | |
| Second cancer | | | | | | | 0.212 |
| No | 33(22) | 1.00 | | | | | |
| Yes | 1(8) | 0.32 | 0.04-2.54 | | | | |
| Late effects | | | | | | | <0.001 |
| No | 12(11) | 1.00 | | | | | <0.001 |
| Yes | 20(44) | 6.60 | 2.85-15.28 | | 6.01 | 2.47-14.62 | |
| Type of late effects | | | | | | | <0.001 |
| No late effects | 12(11) | 1.00 | | | | | |
| Psychological | 2(33) | 4.13 | 0.68 -24.95 | | | | |
| Somatic | 9(33) | 4.13 | 1.52-11.21 | | | | |
| Both | 9(75) | 24.75 | 5.88-104.20 | | | | |

Abbreviations: GSI,global severity index; OR,odds ratio; CI,confidence interval

†Others includes other solid tumors (neuroblastoma, renal tumors, hepatic tumors, bone tumors, and soft tissue sarcoma)

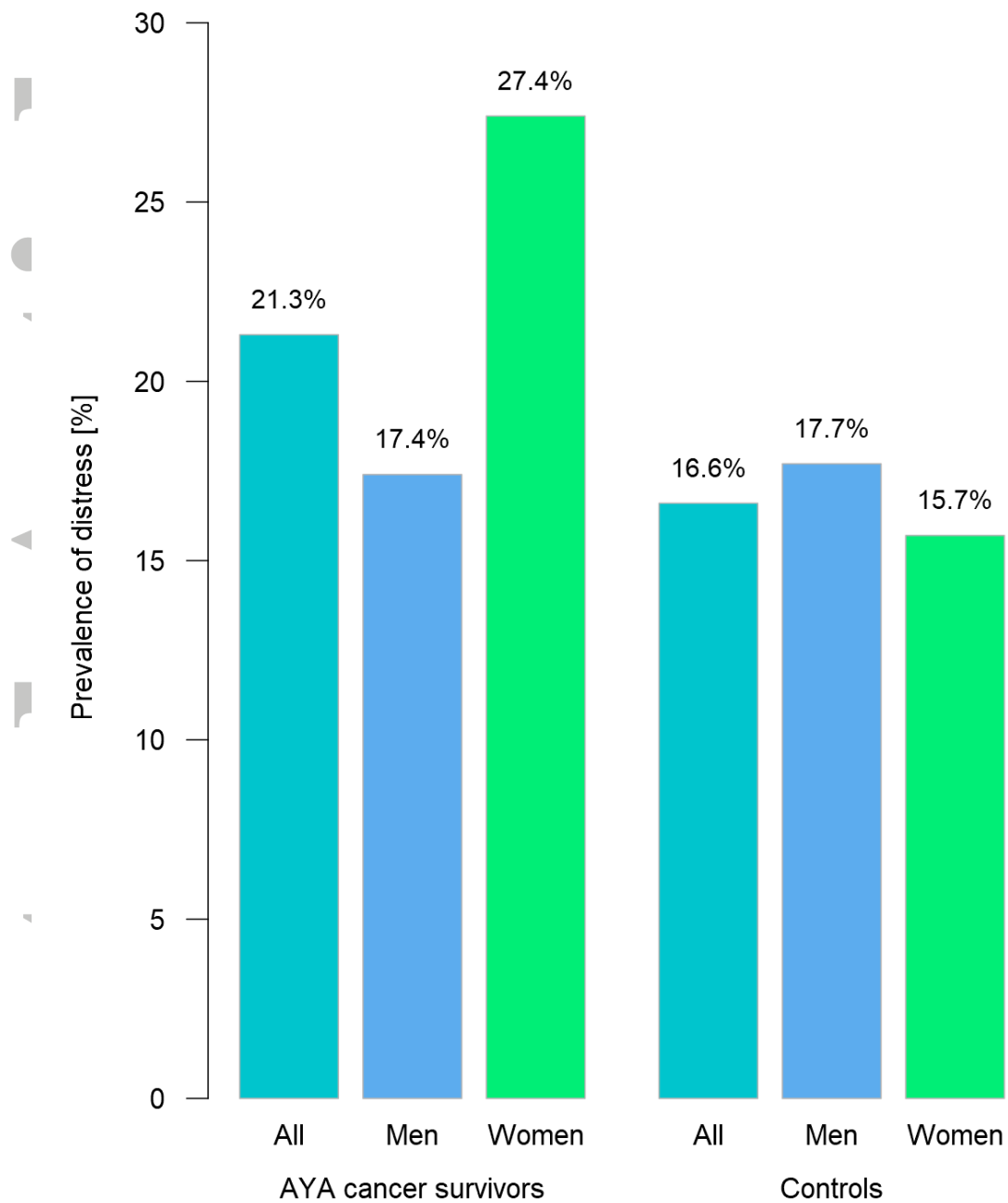


Figure 1: Proportion of male (n = 98) and female (n = 62) Swiss AYA cancer survivors and male and female controls (weighted) with psychological distress measured by the BSI-18.

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