Empirically derived psychosocial states among adolescents diagnosed with cancer during the acute and extended phase of survival

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Background: To, during the acute and extended phase of survival, identify psychosocial states among adolescents diagnosed with cancer and to analyse these in relation to demographic and clinical characteristics and self-reported depression.

Patients and methods: Participants completed the Hospital Anxiety and Depression Scale and two subscales, Vitality and Mental Health, in the SF-36 4–8 weeks (T1) (n = 61), 6 (T2) (n = 57), 12 (T3) (n = 50), and 18 (T4) months (n = 48) after diagnosis. I-State as Object of Analysis was used to identify a finite set of states based on three dimensions. Cluster analysis was carried out using Ward’s method.

Results: Five states were obtained: psychosocial dysfunction (state A) and poor (B), incomplete (C), good (D), and excellent (E) psychosocial function. At T1, more adolescents than expected by chance were in states A (P < 0.05) and C (P < 0.01) and fewer in states D (P < 0.05) and E (P < 0.001). At T4, more adolescents than expected by chance were in state E (P < 0.001) and fewer in state C (P < 0.05). Female gender and being in late adolescence when diagnosed is related to worse psychosocial function.

Conclusion: The findings provide support for subgroups of adolescents whose level of vitality, mental health, and anxiety differ during the acute and extended phase of survival of cancer. Clinical interventions tailored to the level of impairment as determined by the clusters may result in better psychosocial outcomes.

Key words: adolescents, cancer, cluster analysis, HADS, psychosocial function, SF-36

introduction

Reviews concerning the psychosocial outcome after childhood/adolescent cancer comment upon the difficulty of drawing definite conclusions due to small and heterogeneous samples and a lack of longitudinal research [1–3]. We have tried to avoid these shortcomings by following a group of adolescents diagnosed with cancer longitudinally from diagnosis. Mean values on health-related quality of life (QoL), anxiety, and depression suggest that psychosocial function changes for the better over time during the acute and extended phase of survival [4]. A question that remains to be addressed is how to sort the adolescents in a clinically meaningful way according to psychosocial function. So far, most research has focused on analysing statistical trends across entire samples and comparing groups with and without cancer. Using cluster analysis, attempts have been made to sort individuals with cancer according to similarity on one or more psychosocial dimensions [5, 6]. Subgroups of women with breast cancer based on QoL were identified in a study by Nagel et al. [6]. By means of cluster analysis, four subgroups differing on intrusiveness of disease and treatments, view towards the future, age, body image, and sexual activity were identified. It was concluded that the patients would likely benefit from very different interventions following their treatment; with patients reporting high levels of intrusiveness from the treatment benefiting more from medical interventions and rehabilitation programmes and those reporting more psychic issues benefiting from psychological support. Trask and Griffith [5] carried out a study to determine whether there are subgroups of cancer patients who differ on coping, psychological, and QoL measures and to determine whether these subgroups have a different course of distress and health following diagnosis. The findings provide support for distinct subgroups of patients whose level of distress and general health vary greatly following a cancer diagnosis. The authors concluded that clinical
interventions tailored to the level of psychological or physical impairment as determined by the cluster may result in better outcomes following cancer treatment.

To the best of our knowledge, this is the first study to, by using cluster analysis, explore psychosocial states among individuals diagnosed with cancer during adolescence. We hypothesise that there are a finite number of psychosocial states that characterise these individuals during the acute and extended phase of survival and that the stability of the states can be analysed over time and in relation to demographic and clinical characteristics. The aims were to (among individuals diagnosed with cancer during adolescence): (i) identify psychosocial states, on the basis of self-reported vitality, mental health, and anxiety at 4–8 weeks (T1), 6 (T2), 12 (T3), and 18 (T4) months after diagnosis and (ii) analyse each state in relation to demographic and clinical characteristics: age at diagnosis, gender, family situation, diagnosis, and self-reported depression.

patients and methods

design and sample
Sixty-one adolescents (13–19 years) diagnosed with cancer (n=56) or with a recurrence of cancer (n=5) were included from 1999 to 2003 at three paediatric oncology centres in Sweden. Data were collected at 4–8 weeks (T1), 6 (T2), 12 (T3), and 18 (T4) months and 2 (T5), 3 (T6), and 4 (T7) years after diagnosis. Data collected at T1–T4 are presented in this report.

To be eligible, the adolescents had to be: Swedish speaking, diagnosed with cancer for the first time or after having been disease free and off treatment for at least 1 year, treated with chemotherapy, and cognitively, emotionally, and physically able to participate. A coordinating nurse at each centre was responsible for recruitment and assessed, in collaboration with a physician, each adolescent’s ability to participate. Of 90 adolescents diagnosed with cancer for the first time and of 10 diagnosed with a recurrence, 11 were not asked about participation as they did not speak Swedish well enough to participate and/or were considered too cognitively or physically affected by the disease or by a neurological comorbidity to participate. Of 89 eligible adolescents, 61 adolescents were included (56 newly diagnosed and five with a recurrence). Reasons for nonparticipation, reasons for attrition at T2–T4, and participants’ demographic and clinical characteristics at T1–T4 are presented in Table 1.

instruments
health-related QoL. Health-related QoL (HRQL) was measured by two subscales, valid for use separately [7] from the SF-36: Vitality (four items) and Mental Health (five items). Responses are provided on a six-grade verbal scale (coded 1–6). The SF-36 is scored by coding raw scores for each question and recalibrating, summing, and transforming scores into a scale from 0 (worst possible HRQL) to 100 (best possible HRQL) [7]. Normative data for the general Swedish population ages 13–23 are available [8]. In telephone interviews, the Cronbach’s alpha values for the Vitality and Mental Health subscales were 0.81 and 0.82, respectively, for healthy Swedish adolescents and young adults [8].

anxiety and depression. Anxiety and depression was measured by the Hospital Anxiety and Depression Scale (HADS) [9]. The HADS embraces two subscales, one measuring anxiety and the other depression, each consisting of seven items, rated from 0 to 3. Subscale scores range from 0 (no distress) to 21 (maximum distress). The HADS has been used in a sample aged 12–16 years [10]. Normative data for the general Swedish population ages 13–23 are available [8]. In telephone interviews, the Cronbach’s alpha values for the HADS anxiety and depression subscales were 0.75 and 0.54, respectively, for healthy Swedish adolescents and young adults [8].

Table 1. Reasons for nonparticipation, reasons for attrition at T2–T4 and participants’ demographic and clinical characteristics at T1–T4

<table>
<thead>
<tr>
<th>Eligible</th>
<th>T1, n</th>
<th>T2, n</th>
<th>T3, n</th>
<th>T4, n</th>
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<tr>
<td>Reasons for nonparticipation</td>
<td></td>
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<tr>
<td>Chose not to participate</td>
<td>89</td>
<td>61</td>
<td>58</td>
<td>51</td>
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<tr>
<td>Became too ill before interview</td>
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<tr>
<td>Missed due to administrative reasons</td>
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<tr>
<td>Reasons for attrition</td>
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<tr>
<td>Chose to withdraw from the study</td>
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<tr>
<td>Chose not to participate at the particular time</td>
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<tr>
<td>Death</td>
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<tr>
<td>Participants’ characteristics</td>
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<tr>
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<td>53/4</td>
<td>46/4</td>
<td>42/6</td>
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<tr>
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<tr>
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<tr>
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<td>Age at diagnosis</td>
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<tr>
<td>13–15</td>
<td>38</td>
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<td>16–19</td>
<td>23</td>
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<td>Mean age (SD)</td>
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<tr>
<td>CNS tumour</td>
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<td>3</td>
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<tr>
<td>ALL</td>
<td>16</td>
<td>13</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>AML</td>
<td>4</td>
<td>4</td>
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<tr>
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<td>1</td>
<td>1</td>
<td>0</td>
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<td>43/14</td>
<td>14/36</td>
<td>11/37</td>
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</table>

ALL, acute lymphoblastic leukaemia; AML, acute myeloid leukaemia; CML, chronic myeloid leukaemia; CNS, central nervous system.

Results were 0.75 and 0.54, respectively, for healthy Swedish adolescents and young adults [8].

procedure
The study was approved by the local ethics committee at the faculty of medicine at the respective centre. A coordinating nurse at each centre provided eligible adolescents and their parents with oral and written information about the study ~3 weeks after the diagnosis. If the adolescent was <18 years, parental consent was obtained. Adolescents who agreed to participate were contacted by telephone by a doctoral student. A structured interview guide was used to collect data at T1–T4. The guide included questions about background data, prevalence and levels of disease- and treatment-related aspects of distress and coping strategies, the Vitality and Mental Health subscales of the SF-36, and the HADS subscales. The interviewer read the questions and response alternatives aloud to the participant and recorded the participant’s
responses. At the end of the interviews, the participant was asked whether he/she agreed to be contacted for another interview at the following assessment. All data were collected via telephone.

**Analysis**

A person-oriented method called I-States as Objectives of Analyses (ISOA) [11] was used to identify a finite set of psychosocial states based on three dimensions: vitality, mental health, and anxiety. Correlations between vitality, mental health, and anxiety based on data from T1–T4 were as follows: vitality and mental health, r = 0.69; vitality and anxiety, r = -0.32, and mental health and anxiety, r = -0.51. The HADS depression subscale was excluded from the cluster analysis due to low reliability when used in telephone interviews with healthy Swedish adolescents and young adults [8]. However, the subscale was used as an external validation variable to discriminate between the clusters [12]. The rationale and the methodology underlying person-oriented methodology and ISOA in particular are presented elsewhere [11, 13]. When short-term development is in focus, an individual may be described on a certain measurement occasion using one of a finite set of states. These are based on vectors of measures taken from the specific time period. The available variable value profiles from all occasions are used to define a finite set of states, called I-states. Because each profile (belonging to a distinct individual and to a distinct occasion) is included in the analysis, the individual can be characterised by a sequence of I-states which he/she may share with other individuals. A set of longitudinal profiles expressed in terms of state sequences is obtained for each individual.

Each individual contributed a number of data vectors, each corresponding to one occasion. A total of 215 vectors were obtained. One vector was imputed for missing values and one was excluded from the analysis as it was found to be an outlier. Cluster analysis was carried out on 214 vectors using Ward’s method. The established rationale for obtaining a well-functioning [14, 15] and trustworthy classification was followed [12]. The explained error sum of squares for the cluster solution was 68%. Validation by replication analysis was carried out to ensure the stability of the clustering [12] and the result was tested against a null hypothesis of no relationships by simulation [16]. All analyses were conducted using procedures in SLEIPNER 2.1 [13].

Because each individual is characterised by one state on a given occasion, this allows for an analysis of state frequencies per occasion. For this analysis, exact analyses of single cells in a contingency table using EXACON were carried out [17]. EXACON was also used to compare the obtained states with regard to extraneous categorical variables: age at diagnosis, gender, family situation, diagnosis, and self-reported depression.

One-way analysis of variance was used to compare the clusters with regard to the HADS depression subscale. *Post hoc* tests were carried out (Tamhane, Dunnett T3, Games-Howell and Dunett C).

**Results**

The cluster analysis resulted in five psychosocial states, see Figure 1. The mean values of the dimensions (vitality, mental health, anxiety) were $z$ transformed to show potential deviations from the mean value of the total sample of states ($N = 214$). One unit on the $y$-axis in Figure 1 corresponds to one standard deviation (SD). The mean values for the three dimensions in the total sample of states are presented as a straight line in the graphs. A score of $\pm 0.5$ SD from the straight line is considered as average, a score of $>0.5$–1.0 SD from the straight line is considered as above/below average, whereas a score of $>1$ SD from the straight line is considered as low/high.

State A is characterised by a below average score on vitality, a low score on mental health, and a high score on anxiety (psychosocial dysfunction); state B is characterised by low scores on vitality and mental health and an average score on anxiety (poor psychosocial function); state C is characterised by a below average score on vitality and average scores on mental health and anxiety (incomplete psychosocial function); state D is characterised by average scores on vitality and anxiety and an above average score on mental health (good psychosocial function); and state E is characterised by high scores on vitality and mental health and a below average score on anxiety (excellent psychosocial function).

The characteristics of the cluster solutions, including mean values and SDs, the total number of individuals in each state, and the number of individuals in each state at T1–T4, are presented in Table 2.

Significant differences between the observed and the expected number of individuals in each state at T1–T4 are presented in Table 3. At T1, more adolescents than expected by chance are found in states A and C, i.e. psychosocial dysfunction and incomplete psychosocial function; fewer are found in state D, i.e. good psychosocial function; and nobody is found in state E, i.e. excellent psychosocial function. Over time, a different pattern emerges. At T3, fewer adolescents than expected by chance are found in state C, i.e. incomplete psychosocial function and more in state D, i.e. good psychosocial function. At T4, fewer adolescents than expected by chance are found in state C, i.e. incomplete psychosocial function and more in state E, i.e. excellent psychosocial function.

Significant differences between the observed and the expected number of individuals in each state with regard to clinical and demographic characteristics are presented in Table 4. More females and fewer males than expected by chance are found in state A, i.e. psychosocial dysfunction and more males and fewer females than expected by chance are found in state C, i.e. incomplete psychosocial function. More adolescents who are 16–19 years at diagnosis, than expected by chance, are found in state B, i.e. poor psychosocial function, whereas less adolescents 13–15 years at diagnosis, than expected by chance, are found in state B.

Significant differences between the observed and the expected number of males and females in each state at T1–T4 are presented in Table 5.

No one is found in state E, i.e. excellent psychosocial function at T1, whereas more females and males than expected by chance are found in that state at T4. At T1, more females than expected by chance are found in state A, i.e. psychosocial dysfunction, whereas more males than expected by chance are found in state C, i.e. incomplete psychosocial function. At T3, more females than expected by chance are found in state D, i.e. good psychosocial function and no female is found in state B, i.e. poor psychosocial function. At T3 and T4, fewer males than expected by chance are found in state C, i.e. incomplete psychosocial function.

The HADS depression subscale discriminated between the five states. States A–C have higher scores on the subscale than states D and E (A > D, $P < 0.001$; A > E, $P < 0.001$; B > D, $P < 0.001$; B > E, $P < 0.001$; C > D, $P < 0.01$; and C > E, $P < 0.001$), and State D has a higher score on the subscale than state E ($P < 0.01$).
Five states of psychosocial function were identified using cluster analysis applied to a combination of vitality, mental health, and anxiety measures. The findings indicate a shift over time during the first 18 months after a cancer diagnosis from poor to better psychosocial function. Female gender and being in late adolescence when diagnosed with cancer is related to worse psychosocial function than expected by chance.

Thirty-eight percent were found in excellent psychosocial function 18 months after diagnosis. All these individuals, except two (both on oral chemotherapy treatment), were off treatment at this time. However, two of them experienced sequel following operation in knee and femur, respectively, one was bone marrow transplanted and one had recently been diagnosed with a recurrence. In addition, another individual suffered from diabetes mellitus. The result as well as the fact that no differences were found between the observed and the expected number of individuals in any state with regard to diagnosis suggest that not only medical parameters influence psychosocial function among persons during the first phases of survival after a cancer diagnosis.

Five adolescents diagnosed with a recurrence were included in the study and four participants were diagnosed with a recurrence during the study period. Due to the small number of persons diagnosed with a recurrence, a comparison between those with versus without a recurrence with regard to distribution over states cannot be done. However, a visual inspection of data reveals that no one who was in good psychosocial function at T1 was in a state indicating worse

**Figure 1.** The cluster solution describing five psychosocial states.
Further research should examine whether this finding is replicable.

Table 4. Significant differences between the observed and the expected number of individuals in each state at T1–T4

Table 5. Significant differences between the observed and the expected number of males/females in each state at T1–T4

Table 2. Mean values, SDs, total number of individuals in each state, and number of individuals in each state at T1–T4

Table 3. Significant differences between the observed and the expected number of individuals in each state at T1–T4

Table 5. Significant differences between the observed and the expected number of males/females in each state at T1–T4

supports previous findings demonstrating that females report more psychosocial distress than males [18]. However, 18 months after diagnosis, not only more males but also more females, than expected by chance, were found in state E indicating excellent psychosocial function.

More adolescents who were 16–19 years at diagnosis than expected by chance were found in state B characterised by low levels of vitality and mental health and an average level of anxiety. The Mental Health subscale has been shown to detect depression [19] and it can be speculated whether being diagnosed with cancer during late adolescence is related to an increased risk for depression. The finding corresponds with findings demonstrating a decrease in life satisfaction during the course of adolescence [20].

The findings illustrate that it, by means of cluster analysis, is possible to identify time-independent meaningful states of psychosocial functioning in a moderately large group of adolescents during the acute and extended phase of survival after a cancer diagnosis. However, the successful identification of these psychosocial states and how they change or remain stable for different characterised individuals is only beneficial to the extent that they are utilised and subsequently lead to a change in the treatment of those individuals who share trajectories and other individual characteristics. The next step is clearly to create a study that characterises patients and provides matched and unmatched treatments to determine their efficacy.
methodological discussion

The prospective, longitudinal design and the homogeneity of the sample with regard to age and time since diagnosis are methodological strengths even in an international perspective. However, the sample may be considered too small, too heterogeneous with regard to diagnoses and other medical characteristics and too homogeneous with regard to socio-economic status, treatment, and care. Some of these circumstances were difficult, whereas others were impossible to overcome as the Swedish adolescent population diagnosed with cancer is very small and as the treatment of paediatric cancer in Sweden follows standardised treatment protocols for almost all childhood cancer diagnoses [21]. In spite of this, it is reasonable to assume that the findings can be generalised to the population of adolescents during the acute and extended phase of survival of cancer in Sweden and in other comparable countries. The structural validity of the cluster solution was shown to hold by means of statistical data simulation and the external validity was strengthened by comparing the identified clusters with respect to the HADS depression subscale.

conclusions

The findings provide support for subgroups of adolescents whose level of vitality, mental health, and anxiety differs during the acute and extended phase of survival of cancer. Clinical interventions tailored to the level of impairment as determined by the clusters may result in better psychosocial outcomes.

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references