Cancer during adolescence

Psychological consequences and development of psychological treatment

MALIN ANDER
The overall aim of the present thesis was to examine long-term psychological distress following cancer during adolescence and to develop a tailored psychological intervention to reduce cancer-related distress experienced by young survivors of adolescent cancer that was feasible and acceptable.

Study I adopted a longitudinal design, assessing health-related quality of life (HRQOL) and symptoms of anxiety and depression among adolescents diagnosed with cancer from shortly after diagnosis (n=61) up to 10 years after diagnosis (n=28). Findings suggest that development of HRQOL and anxiety and depression is not linear and whilst the majority adjust well, a subgroup report long-term elevated distress. In Study II, experiences of cancer-related psychological distress were explored using unstructured interviews. Participants described cancer treatment as a mental challenge, felt marked and hindered by the cancer experience, and struggled with feelings of inadequacy and insecurity, existential issues, and difficulties handling emotions. Study III was a preliminary investigation of individualised cognitive behavioural therapy (CBT), alongside the identification and conceptualisation of cancer-related concerns using cognitive-behavioural theory. Significant difficulties with recruitment were encountered. Participants reported cancer-related concerns conceptualised as social avoidance, fear and avoidance of emotions and bodily symptoms, imbalance in activity, and worry and rumination. In Study IV, the acceptability and feasibility of an internet-administered CBT based self-help intervention (ICBT) for young persons diagnosed with cancer during adolescence was examined using an uncontrolled design and embedded process evaluation. The study protocol for Study IV was included in this thesis along with preliminary findings demonstrating significant difficulties with recruitment.

Overall, findings suggest that whilst the majority of survivors of adolescent cancer adjust well over time a subgroup report elevated levels of distress and a range of distressing cancer-related experiences. A number of cancer-related difficulties were identified in Study II and III, which may be used to inform the development of future psychological treatments for the population. Preliminary investigation of the psychological interventions examined within this thesis further highlights the need for future development work to enhance the feasibility and acceptability of psychological support for the population.

Keywords: cancer and oncology, adolescents, young adults, survivorship, anxiety, depression, psychological distress, health-related quality of life, cognitive behaviour therapy, guided self-help

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<td>AYA</td>
<td>Adolescent and young adult</td>
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<td>AYAs</td>
<td>Adolescents and young adults</td>
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<td>CBT</td>
<td>Cognitive behavioural therapy</td>
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<td>CNS</td>
<td>Central nervous system</td>
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<td>CONSORT</td>
<td>Consolidated Standards of Reporting Trials</td>
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<td>DSM</td>
<td>Diagnostic and Statistical Manual</td>
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<td>HRQOL</td>
<td>Health-related quality of life</td>
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<td>ICBT</td>
<td>Internet-administered cognitive behavioural therapy</td>
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<td>MRC</td>
<td>Medical Research Council</td>
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<td>PMTS</td>
<td>Pediatric medical traumatic stress</td>
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<td>PPI</td>
<td>Patient and public involvement</td>
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<td>PPPHM</td>
<td>Pediatric Psychosocial Preventative Health Model</td>
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<td>PTSD</td>
<td>Posttraumatic stress disorder</td>
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<td>PTSS</td>
<td>Posttraumatic stress symptoms</td>
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<td>RCT</td>
<td>Randomised controlled trial</td>
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Introduction

Cancer during adolescence

Each year approximately 80 adolescents are diagnosed with cancer in Sweden (Gustafsson, Kogner & Heyman, 2013; Official Statistics of Sweden, 2017). The most common diagnostic categories are leukemia, central nervous system (CNS) tumours, lymphoma, sarcomas and bone tumours (Gustafsson et al., 2013; Kaatsch, 2010). Cancer treatment follows standardised clinical protocols, with the type of treatment dependent on factors such as diagnosis, disease stage, histology, and/or tumour markers. Treatment may include chemotherapy, radiation therapy, and surgery, either alone or in combinations. Stem-cell transplantation is used for adolescents with high-risk leukemia and some types of lymphoma (Hayat, 2013).

Over the past decades, survival rates for children and adolescents diagnosed with cancer have risen dramatically with current data showing an overall five year-survival rate in excess of 80% (Gatta et al., 2009; Gustafsson et al., 2013). However, both cancer disease and its treatment are associated with significant stressors for adolescents and their families. During treatment, adolescents report a number of significant aspects of distress, including tiredness, lessened ability to get around, nausea, pain from diagnostic procedures, changed appearance, mucositis, feelings of alienation, and worry about not getting well (Hedström et al., 2005; Hinds, Quargnenti, & Wentz, 1992). After treatment completion, depending on the type of diagnosis and treatment received, adolescents are at risk for late effects (Landier, Armenian, & Bhatia, 2015; Oeffinger et al., 2006). Common late effects include cognitive impairments, sexual and reproductive problems, cardio-pulmonary failure, thyroid abnormalities, and visual and auditory problems (Landier, Armenian, & Bhatia, 2015; Oeffinger et al., 2006). Further, qualitative findings demonstrate survivors of adolescent cancer experience physical problems, bodily concerns, difficulties interacting with others, difficulties with school and paid employment, and psychological problems. Moreover, reported cancer-related consequences change with age and time from diagnosis (Lehmann et al., 2014).
Developmental considerations related to cancer during adolescence

In recent years, adolescents diagnosed with cancer have received increased attention in research (Epelman, 2013). Adolescence is a critical developmental period characterised by fast physical, psychological, and social changes associated with pubertal maturation and transition from childhood to adulthood (Ladouceur, Peper, Crone, & Dahl, 2012). Adolescence has been defined in several ways, for example by chronological age or developmental factors. However, no standard chronological age, development stage, or other definition for adolescence exists (American Psychological Association, 2002). For the purpose of the present thesis, adolescence is defined as the period between 13-19 years, corresponding to the language-based term “teen” commonly adopted in research within the field of psychology (e.g. Lakdawalla, Hankin, & Mermelstein, 2007). Indeed, these years involve a range of significant developmental experiences. For example, movement toward social and economic independence, development of reasoning ability, abstract thinking, reflection, and ability to plan for the future (Abrams, Hazen, & Penson, 2007; American Psychological Association, 2002). Further, young people between these ages experience changes in values and ethical behaviour, develop a clearer personal and sexual identity, place an increased importance on appearance and fitting in, learn to cope with stress and manage emotions, and develop abilities to manage adult relationships and associated roles (Abrams et al., 2007; American Psychological Association, 2002). Moreover, adolescence is a time of psychological vulnerability. The onset of several mental health problems peak during adolescence (Kessler, Chiu, Demler, Merikangas, & Walters, 2005). Further, stressful life events and daily stressors are associated with increases in internalizing symptoms such as anxiety and depression in adolescents (Low et al., 2012; McLaughlin & Hatzenbuehler, 2009). One such stressful life event is a serious health condition.

Indeed, cancer and its treatment are associated with numerous stressful events (e.g., receiving the diagnosis, acute medical events) and resultant stressors (e.g., disrupted schooling, treatment side effects), often experienced over an extended time. These cancer-related stressors add to and complicate existing adolescent developmental challenges, for example, restrictions in activity, increased dependency on caregivers, changes in physical appearance, and physical complications such as pain and fatigue (Epelman, 2013). Indeed, research on adolescents living with different types of chronic illness has shown that chronic illness can complicate the development and maintenance of friendships, the strive for normalcy, relationships with parents, and planning for the future (Taylor, Gibson, & Franck, 2008). The phase of the cancer-experience also impacts on development and in the case of cancer, related stressful events and daily stressors are not limited to the time during
treatment. Post cancer treatment completion, new challenges occur, including the emergence of late effects, reintegration to school and social life, and the risk of recurrence (Lehmann et al., 2014; Vetsch, 2017). Moreover, cancer-related consequences are influenced by current life stage, for example, as adolescents enter emerging adulthood (Arnett, 2000), new age-specific stressors occur, such as fertility concerns (Lehmann et al., 2014; Nilsson et al., 2014).

For adolescents diagnosed with cancer, numerous cancer-related challenges and stressors occur during a period already characterised by great change and psychological vulnerability. As such, it has been hypothesised that persons diagnosed with cancer during adolescence may experience psychological consequences, including psychological distress and reduced health-related quality of life (HRQOL).

The studies included in the current thesis focus primarily on adolescents and young adults (AYAs) diagnosed with cancer during adolescence (13-19 years) who have completed cancer treatment, often referred to as ‘survivors’. Whilst different definitions of the term ‘survivor’ exist, for the purposes of the present thesis, a survivor is defined as a person with a history of cancer from the time of diagnosis (Denlinger et al., 2014).

Psychological distress and HRQOL

Psychological distress refers to symptoms of anxiety, depression, and somatic anxiety and sometimes include posttraumatic stress symptoms (PTSS) (i.e. avoidance, intrusive thoughts, and arousal) (American Psychiatric Association, 1994; Drapeau, Marchand, & Beaulieu-Prévost, 2012). Clinical levels of psychological distress lead to severe consequences for both the individual and wider society, with mental disorders contributing significantly to the disease burden in AYAs (Patel, Flisher, Hetrick, & McGorry, 2007). Indeed, in addition to reduced quality of life, functional impairment and suffering, poor mental health in young people is associated with low educational achievements, poor sexual and reproductive health, substance abuse, and premature death (Patel et al., 2007). In AYA cancer survivors, psychological distress is related to e.g. low adherence to medical treatment which in turn is related to morbidity, mortality, and healthcare costs (Kaul et al., 2017). As such, adequate assessment and provision of interventions to prevent and reduce distress in AYA cancer survivors is anticipated to benefit both the individual and wider society.

Although the specific illness context surrounding a cancer diagnosis during adolescence, alongside the potential risk of psychological morbidity have been recognised, there is a dearth of studies examining the prevalence of psychological distress in this population specifically. Further, findings from the few existing studies are inconsistent.
Two studies examining psychological distress, including symptoms of anxiety and depression, among adolescents with cancer shortly after diagnosis found no increased risk for psychological distress (Allen, Newman, & Souhami, 1997; Neville, 1996). Indeed, some research has found adolescents report lower levels of depression compared to healthy controls within the first two years after diagnosis (Canning, Canning, & Boyce, 1992). However, a longitudinal study found that AYA cancer survivors reported higher levels of distress compared to population norms at the time of diagnosis and one year later (Kwak et al., 2013b). Findings from the same cohort demonstrated that 44% reported moderate to severe levels of PTSS (Kwak et al., 2013a). In addition, our research group found that adolescents diagnosed with cancer reported higher levels of depression than an age-matched reference group during the first six months following diagnosis. However, from 18 months up to four years after diagnosis, the cancer group reported lower levels of anxiety and depression than the reference group (Larsson, Mattsson, & von Essen, 2010).

Studies examining long-term distress among survivors of cancer during adolescence have found an elevated risk of PTSD and anxiety- and depressive disorders more than five years after diagnosis compared with age-matched controls without a history of cancer and population norms (Seitz et al., 2010). Further, elevated symptoms of anxiety, depression and PTSS have been found compared to controls and population norms (Seitz et al., 2010), siblings (Prasad et al., 2015), and persons diagnosed at a younger age (Kazak et al., 2010; Schwartz & Drotar, 2006). However, other studies have not demonstrated such differences (Pemberger et al., 2005; Zebrack et al., 2004; Zebrack et al., 2004; Zeltzer et al., 2008). Potential explanations for the inconsistent results may be significant between-study heterogeneity, for example, the adoption of different outcome measurements and clinical cut-points to detect persons with subclinical/clinical levels of distress, alongside variations in definitions of psychological distress. Further sources of clinical heterogeneity, and potential explanations for variation in findings, may be time since diagnosis, type of diagnosis, treatment and current age, thereby hampering comparison and precluding conclusions regarding prevalence of distress in the population (Abbey, Thompson, Hickish, & Heathcote, 2015; Eiser, Hill & Vance, 2000).

Another important outcome, both during and after cancer treatment, is HRQOL. HRQOL is a multidimensional concept which has been defined in several ways (Karimi & Brazier, 2016). Hays & Reeve ("Measurement and Modeling of Health-Related Quality of Life," 2008) have described HRQOL as “how well a person functions in their life and his or her perceived well-being in physical, mental, and social domains” (as cited in Karimi & Brazier, 2016, p. 646). A longitudinal study examining HRQOL among AYAs during the first two years after diagnosis, using the Short Form-36 (SF-36; Ware & Sherbourne, 1992), found lower levels of HRQOL on all dimensions when
compared with age-matched population norms within the first months after diagnosis (Husson et al., 2017b). Further, although HRQOL improved over time, physical and social function was compromised two years post-diagnosis. Our research group found that persons diagnosed with cancer during adolescence reported lower levels of HRQOL on mental health and vitality domains compared to an age-matched reference group during the first six months following diagnosis. However, four years after diagnosis, the cancer group reported higher vitality than the reference group (Larsson et al., 2010). Conversely, a cross-sectional study specifically examining survivors of cancer during adolescence, at least five years post diagnosis, found lower levels of life satisfaction among survivors compared to matched controls (Seitz et al., 2011). Moreover, older age at diagnosis is associated with poor HRQOL in some studies with persons diagnosed in childhood and adolescence (Felder-Puig et al., 1998; Stam, Grootenhuis, Caron, & Last, 2006). However, other research has not found age at diagnosis to predict HRQOL (Blaauwbroek et al., 2007; Nayiager, Anderson, Cranston, Athale, & Barr, 2017; Pemberger et al., 2005).

Similar to research regarding psychological distress, research regarding HRQOL in survivors of cancer during adolescence is inconclusive. Again, an aggregation of findings is hampered by high between-study heterogeneity, with differences in comparison groups, outcome measurements, type of cancer diagnosis, time since diagnosis, and treatments received (Eiser et al., 2000; Lund, Schmiegelow, Rechnitzer, & Johansen, 2011). Further, existing research tends not to differentiate between children, adolescents, and young adults (Eiser et al., 2000). Of additional importance is the current paucity of longitudinal studies investigating the development of HRQOL and psychological distress among survivors of cancer during adolescence.

Despite considerable uncertainty regarding the prevalence of psychological distress and HRQOL, current research indicates the majority of persons diagnosed with cancer during adolescence adjust well. However, research also suggests that a subgroup of the population report clinically relevant levels of psychological distress. The nature and development of this distress is poorly understood.

Cancer-related experiences

In addition to quantitative investigations of the presence of cancer-related stressors, sources of distress, and associated symptoms, qualitative research has explored the experiences of AYAs diagnosed with cancer during adolescence. These explorations have for example revealed challenges with body image (Larouche & Chin-Peuckert, 2006) and appearance (Williamson, Harcourt, Halliwell, Frith, & Wallace, 2010) among adolescents on cancer treatment. Other studies have focused primarily on AYAs’ experiences after
treatment completion, and explored loss of control and benefit finding (Wicks & Mitchell, 2010), unmet needs (Palmer, Mitchell, Thompson, & Sexton, 2007), cancer-related fertility matters (Crawshaw & Sloper, 2010), the impact of cancer on relationships (Lewis, Jordens, Mooney-Somers, Smith, & Kerridge, 2013). Positive and negative consequences have been reported (Lehmann et al., 2014). Whilst emotional difficulties have been identified (Fern et al., 2013; Grinyer, 2007; Lehmann et al., 2014; Palmer et al., 2007), studies exploring these difficulties in-depth are lacking. Such knowledge is crucial to inform the development of psychological interventions for the population.

Need for psychological support

Further to studies examining the prevalence of psychological distress, research has examined the psychological needs reported by persons diagnosed with cancer during adolescence and young adulthood. This research has demonstrated that subgroups report needs of mental health service and social support during and after treatment (Decker, Phillips, & Haase, 2004; Galan, de la Vega, & Miro, 2016; Keegan et al., 2012; Smith et al., 2013; Tsangaris et al., 2014; Zebrack, 2009), with subgroups reporting unmet needs (Keegan et al., 2012; Smith et al., 2013; Zebrack, 2009). Indeed, a recent (2016) Swedish study using a mixed-method approach revealed the majority of AYA survivors of childhood cancer reported insufficient support from healthcare to manage the social and psychological challenges associated with transition to adulthood (Svedberg et al., 2016). A study conducted in Germany found that only 12% of persons diagnosed with cancer during adolescence, who had completed treatment and reported clinical levels of symptoms of anxiety, depression, and/or PTSS, had received psychosocial care (Dieluweit et al., 2011).

Globally, there is a significant treatment gap regarding the provision of mental health support to young persons, with lack of resources e.g., poor funding and a dearth of appropriately trained mental health professionals being a key contributing factor (Belfer, 2008; Kieling et al., 2011). Additional barriers to accessing psychological support have been identified for AYA survivors of childhood cancer (Gardner et al., 2014). These include difficulties scheduling access to support services around work/school, financial limitations, lack of knowledge about available resources, and long distances to support services, with longer time since cancer treatment completion associated with more barriers. As such, for AYA survivors of childhood and adolescent cancer, there is a clear need to reduce the mental health treatment gap through the provision of empirically supported psychological interventions that overcome some of the unique barriers experienced by the population.
Psychological interventions

To the best of our knowledge, only two studies to date have evaluated the effectiveness of psychological treatments aimed to reduce psychological distress among persons diagnosed with cancer during adolescence specifically. First, a randomised controlled trial (RCT) evaluating a 40-minute meta-cognitive education intervention for newly diagnosed adolescents (Hinds et al., 2000) and second, a non-randomised controlled study of a six-session therapist-facilitated peer support group for adolescents on and off treatment (Heiney, Ruffin, Ettinger, & Ettinger, 1988). Neither of these studies demonstrated effects on psychological distress. Further, an RCT examining the effect of a music video intervention to promote resilience among AYA survivors, diagnosed in either adolescence or young adulthood, undergoing hematopoietic stem cell transplant, did not demonstrate an effect on psychological distress (Robb et al., 2014).

In relation to survivors who have completed treatment, psychological intervention studies have targeted AYAs diagnosed during childhood and adolescence, or during adolescence and young adulthood. An RCT examining the effectiveness of a one-day intervention based on cognitive behavioural therapy (CBT) and family therapy to reduce PTSS among adolescents (11-19 years) diagnosed with cancer during childhood or adolescence, found significant reductions in arousal, in comparison with a wait-list control (Kazak et al., 2004). Further, an initial investigation of the feasibility and acceptability of an Internet-administered CBT based intervention, plus structured writing sessions, for AYAs (20-36 years) diagnosed with cancer during childhood or adolescence, demonstrated moderate effectiveness on symptoms of anxiety and PTSS (Seitz, Knaevelsrud, Duran, Waadt, Loos, & Goldbeck, 2014; Seitz, Knaevelsrud, Duran, Waadt, & Goldbeck, 2014). Further, a nonrandomized open trial examined the preliminary efficacy of face-to-face meta-cognitive therapy on symptoms of anxiety, depression, and PTSS among persons aged 18-23 years diagnosed with cancer during childhood or adolescence (Fisher, McNicol, Young, Smith, & Salmon, 2015). Findings demonstrated large effect sizes for symptoms of anxiety, depression, and PTSS at post-treatment, with gains sustained at six months follow-up. Moreover, a single-arm study examining the potential efficacy of a mindfulness-based intervention for AYAs (14-24 years) diagnosed with cancer in childhood, adolescence or young adulthood found a large effect for emotional distress at three month follow-up (van der Gucht et al., 2017). Finally, a one-arm feasibility study, examining a mindful self-compassion intervention for young adults diagnosed with cancer in adolescence or young adulthood was found to be feasible and acceptable (Campo et al., 2017). Analysis of trends in clinical outcome improvements demonstrated large effect sizes for symptoms of anxiety, depression, and self-compassion.
Taken together, initial research indicates that psychological interventions falling under the CBT umbrella show promise in reducing psychological distress experienced by young persons who have survived cancer. These results are consistent with a review (Sansom-Daly, Peate, Wakefield, Bryant, & Cohn, 2012) of psychological interventions for AYAs with chronic illness that concluded skill-based interventions delivered over multiple sessions have potential to yield positive results with regard to psychological adjustment.

Despite the promise of CBT based treatments, access to evidence based psychological treatments for young people is limited (Belfer, 2008; Kieling et al., 2011). This gap is in part due to lack of resources (e.g., appropriately trained healthcare professionals) (Patel et al., 2007). In order to address the mental health treatment gap and provide access to clinically and cost-effective interventions, extensive developments have been made globally to implement the delivery of CBT based interventions in a self-help format (Rebello, Marques, Gureje, & Pike, 2014). These interventions are characterised by the communication of CBT specific principles primarily through self-help material, for example, via written paper-based materials or via the Internet (Bennett-Levy, 2010; Ridgway & Williams, 2011) as opposed to communicating by a CBT therapist. However, research suggests support, provided either face-to-face, via telephone or email, improves effectiveness (Farrand & Woodford, 2013; Gellaty et al., 2007). Indeed, supported CBT self-help is as effective as face-to-face CBT for common mental health difficulties such as symptoms of anxiety and depression (Cuijpers, Donker, van Straten, Li, & Andersson, 2010). Further, Internet-administered CBT self-help (ICBT) is a clinically and cost-effective treatment for symptoms of anxiety and depression in adults (Hedman, Ljótsson, & Lindefors, 2012) and young adults (Ebert et al., 2015) with equivalent effects as face-to-face CBT (Cuijpers, Donker, van Straten, Li, & Andersson, 2010; Hedman, Ljótsson, & Lindefors, 2012). Given the increased flexibility regarding delivery of CBT self-help interventions, this approach may overcome additional barriers AYA cancer survivors experience accessing support. Barriers include difficulties scheduling access to support services around work/school, financial limitations, lack of knowledge about available resources, and long distances to support services. Indeed Internet-administered interventions are proposed as solutions to overcome barriers for AYAs to access psychological support (Moody et al., 2015).

**Developing a psychological treatment**

Although empirically supported ICBT interventions exist for AYAs, increasing evidence suggests the importance of adapting and tailoring ICBT interventions for the specific target population to increase acceptability (Knowles et al., 2014). Further, attrition and adherence rates may improve if
the perspective of the target populations is included during development (Ferwerda et al., 2013). Moreover, reviews of self-help interventions for physical health populations have demonstrated smaller effect sizes than for general mental health populations (Farrand & Woodford, 2015; Matcham et al., 2014). As such, self-help interventions for youth general mental health populations may not be generalizable to the youth with physical health conditions, including AYA survivors of cancer during adolescence. Finally, in recent years there has been a growing recognition of the importance of considering the lived experience of target groups when developing psychological interventions (Vale, Thompson, Murphy, Forcat, & Hanley, 2012) for example by using qualitative methodologies (O’Cathain et al., 2015). Examples of research within psycho-oncology in which the target group has been included in the development of interventions are the FexCan intervention to reduce sexual problems and fertility distress among AYA survivors (Winterling et al., 2016) and a digital peer support service for childhood cancer survivors (Wärnestål, Svedberg, Lindberg, & Nygren, 2017). However, to the best of our knowledge, no research has been conducted to develop an ICBT intervention targeting psychological distress among AYAs diagnosed with cancer during adolescence.

There is a clear need to develop an ICBT intervention to reduce psychological distress for AYAs diagnosed with cancer during adolescence, and it is important to adopt a systematic approach to intervention development. In that complex interventions targeting behavioural change are often poorly designed, with lack of specificity regarding the underlying mechanisms proposed to produce change in outcomes, the Medical Research Council (MRC) in UK developed a pragmatic framework to guide the development, evaluation, and implementation of complex interventions (Craig et al., 2008). Whilst the initial MRC framework adopted a stepwise approach, akin to the development and evaluation of pharmaceuticals (Campbell et al., 2000), the revised framework recognised the development and evaluation of complex interventions as an iterative activity, including four phases: (a) development (Phase I); (b) feasibility and piloting (Phase II); (c) evaluation (Phase III); and (d) implementation (Phase IV) (Craig et al., 2008). Figure 1 provides an illustration of the revised MRC framework phases.
According to the revised MRC framework, interventions should be developed and tested in a carefully phased manner. First, the framework stresses the importance of thorough development work (Phase I) to increase the likelihood that the intervention will be effective. The development phase includes identification of the existing evidence base, identification or development of theories underlying potential change processes, and description of the specific intervention components, outcomes, and the processes via which intervention components are expected to result in desired outcomes. Second, careful feasibility and piloting (Phase II) work to examine key methodological uncertainties are recommended prior to conducting a full evaluation. Specifically, feasibility and pilot studies should be designed to detect methodological, procedural, and clinical uncertainties (Abbott, 2014; Thabane et al., 2010) for example regarding, recruitment, attrition, adherence, intervention delivery, and data handling, all common problems in RCTs (Thabane et al., 2010). Thereafter, exploratory and definitive evaluations (Phase III) can be conducted followed by implementation (Phase IV), including the dissemination of results and conduct of further studies to monitor and assist implementation processes (Craig et al., 2008).

Given evidence suggesting the need to modify existing ICBT interventions to increase acceptability (Knowles et al., 2014), coupled with recommendations regarding intervention development methodology (Craig et al., 2008), there is a need to conduct comprehensive development work to gain an in-depth and precise understanding of cancer-related distress experienced
by AYA survivors of cancer during adolescence. Such findings can be used to develop a tailored ICBT intervention for AYA survivors of cancer.

Concluding remarks

Whilst the majority of AYA cancer survivors appear to adjust well, subgroups reporting a clinically relevant level of psychological distress and needs of psychological support years following completion of treatment exist. There is no empirically supported tailored psychological treatment addressing psychological distress experienced by young persons diagnosed with cancer during adolescence. ICBT interventions may represent a feasible, acceptable, and cost-effect approach to address this treatment gap and the barriers to accessing psychological support experienced by the AYA cancer survivor population.

Background to the current thesis

The studies included in the current thesis are part of two research projects:
1. Psychological and health economic consequences of cancer during adolescence (principal investigator Louise von Essen)

Project 2 commenced in 2010 as a continuation of Project 1 with the overall aim to develop and evaluate an Internet-administered self-help intervention to reduce psychological distress among young persons diagnosed with cancer during adolescence. A description of the research process is provided below.

The original plan for project 2 was to conduct a wait-list RCT of an ICBT self-help intervention. The intervention was developed to be delivered within a stepped care model (Bower & Gilbody, 2005). Within this model, participants start with a lower-intensity intervention (Step 1) with progress monitored and those who do not respond ‘step up’ to a higher intensity treatment (Step 2) (van Straten, Hill, Richards, & Cuijpers, 2015). Version 1 of the intervention consisted of interactive support (including access to information, psychoeducation, and possibility to communicate with other survivors and experts) (Step 1) and ICBT (Step 2) to reduce symptoms of anxiety and depression. The rationale was: (a) a subgroup of adolescents diagnosed with cancer report increased levels of psychological distress and reduced HRQOL during the first year after diagnosis (Jörngården et al., 2007); (b) empirically supported psychological interventions developed for persons diagnosed with
cancer during adolescence are lacking (Seitz, Besier, & Goldbeck, 2009); (c) preventative mental health interventions for childhood and adolescent cancer survivors have been called for (Kazak, 2006); (d) adolescents diagnosed with cancer request peer support and information (Decker et al., 2004; Zebrack, 2009); (e) adolescents diagnosed with cancer in Sweden is a geographically dispersed group, with cancer treatment often demanding and unpredictable, and as such a flexible treatment approach for mental health is required; and (f) ICBT is effective for a range of mental disorders in adults and adolescents and can fit the population’s needs of flexibility.

According to the original plan, participants would be offered interactive support (Step 1) during the first six months post diagnosis. As per the Pediatric Psychosocial Preventative Health Model (PPPHM) (Kazak, 2006) Step 1 was conceptualised as a universal intervention, meaning it would be provided to all newly diagnosed adolescents. After six months access to Step 1, participants would be offered therapist-guided ICBT (Step 2), in addition to continued access to interactive support. The ICBT part of the intervention was conceptualised as targeted/clinical intervention according to PPPHM, and aimed to target subclinical and clinical levels of anxiety and depression. Participants who reported persistent problems after completing the ICBT part of the intervention would be guided to more appropriate healthcare.

Development of Version 1 of the intervention started in 2011. The following activities were undertaken: (a) literature reviews examining cancer-related psychological consequences, and the effectiveness of ICBT and psychoeducational interventions for adolescents with chronic illness and mental health difficulties to identify available evidence and theory; (b) interviews with persons with lived experience of cancer during adolescence, paediatric oncology nurses, and mental health staff at Uppsala Children’s Hospital, and patient organisations to explore needs and preferences regarding aspects of the intervention and study procedures for a controlled study evaluating the intervention; and (c) consultations with experts in clinical intervention development and evaluation; CBT and ICBT for mental health populations and people with chronic illness; adolescent psychiatry; health economics, and counselling regarding aspects of the intervention and proposed study procedures.

Subsequently, text- and video material were developed and persons with extensive experience in developing educational materials for young people reviewed portions of the material with respect to readability and comprehensibility. Furthermore, the U-CARE-portal (the Portal), via which the intervention would be administered, was developed in collaboration with researchers from the Department of Informatics and Media, Uppsala University (Grönnqvist et al., 2017).

In May 2012, a study testing the planned study procedures and delivery and acceptability of the intervention started with participants from the paediatric oncology centre at Uppsala University Children’s Hospital. Thirty adolescents
diagnosed with cancer (within the previous 4-120 weeks) were to be included. If the intervention and procedures were found acceptable and feasible, the plan was to commence the RCT. However, 10 months after study-start, only eleven of 33 potential participants had agreed to participate, with only six logging in to the Portal to test Step 1 of the intervention. Of these, three agreed to test the ICBT intervention (Step 2), with one completing it. Five participants were interviewed about their experiences of the intervention and Portal one month after their first login. Interviews e.g. revealed participants had experienced technical difficulties with logins and requested an increase in activity in the interactive functions.

In response to the difficulties encountered and following recommendations from the U-CARE Scientific Advisory Board, a panel of ten adolescents (with and without lived experience of cancer during adolescence) was formed to inform revisions and further intervention development according to a patient and public involvement (PPI) approach (INVOLVE, n.d.). Five meetings were held over five months. A consultation model of PPI (INVOLVE, 2012) was adopted, with the panel providing comments and suggestions for improvements regarding the layout and usability of the Portal, the acceptability and usability of the functions in the intervention, the readability, comprehensibility and acceptability of selected text and video-material, the feasibility and acceptability of questionnaires, invitation letters, and recruitment procedures. These consultations guided the development of a new interface in the Portal, revisions in the interactive functions and library texts, amendments to the study invitation letters and overall recruitment procedures, and selection of outcome measurements. However, it is important to emphasise that given a consultation model of PPI was adopted (Oliver et al., 2008), the research team made final decisions concerning changes to the intervention and planned study procedures. Furthermore, the panel was consulted regarding selected aspects of study procedures and intervention and further revisions were made after the panel was dissolved. Individual consultations with members of the panel and other young people were conducted before, during, and after the panel was dissolved.

Subsequently, the study team decided to revise the intervention by integrating the two steps and directing the intervention towards individuals experiencing psychological distress after end of cancer treatment. There were two main reasons for these decisions. First, recruitment difficulties and low activity and retention were found in the study testing study procedures and the intervention. Indeed, several barriers to recruitment and engagement with preventative interventions for at-risk youth populations have been identified by others, including not seeing the relevance of participating (Redmond, Spoth, Shin, & Hill, 2004) and perceiving the intervention as too demanding (Hooven, Walsh, Willgerodt, & Salazar, 2011). These barriers may be especially salient for adolescents undergoing cancer treatment given the often significant impact of treatment side-effects such as pain, nausea, and fatigue.
In addition, recruitment difficulties were identified in other ongoing trials conducted within the U-CARE research program e.g. targeting distress shortly after diagnosis among parents of children with cancer (Cernvall, Carlbring, Ljungman, Ljungman, & von Essen, 2015) and persons with recent myocardial infarction (Norlund, Olsson, Burell, Wallin, & Held, 2015). Second, the period after treatment completion has been suggested to be especially challenging for AYAs with simultaneous decreases in support from healthcare (Kwak et al., 2013b; Olsson, Jarfelt, Pergert, & Enskär, 2015). Therefore, AYAs were hypothesised to be more open to accept psychological interventions after cancer treatment completion than earlier during the disease trajectory. This hypothesis was partially supported by experiences from the research group’s research on parents of children diagnosed with cancer indicating a greater willingness among parents of children diagnosed with cancer to participate in intervention research after end of the child’s treatment than shortly after diagnosis (Cernvall et al., 2015; Ljungman et al., 2017). In sum, after the research group had been introduced to the MRC guidelines by the U-CARE Scientific Advisory Board Studies II-IV were planned.

Further development and testing of the YoungCan intervention

According to the MRC framework, an important part of the development of a complex intervention is to identify and/or develop theory. To the best of our knowledge, two theoretical frameworks have been developed to guide the development of psychosocial interventions for adolescents with cancer. One is the Adolescence Resilience Model (Haase et al., 2016) which is based upon meaning-based and life-span development perspectives and is focused on improving resilience and quality of life by targeting positive health concepts. The model specifies risk and protective factors that can be targeted to promote adaption. Another is the Pediatric Medical Traumatic Stress (PMTS) model (Kazak, 2005) which is based on a posttraumatic stress framework and family systems approach. The model aims to conceptualise the psychological reactions of families within the paediatric healthcare setting and describes three developmental phases of PMTS to which interventions can be tailored along with intervention goals. These models do not specify the development and maintenance of cancer-related psychological distress. Moreover, controlled trials of treatments based on the models have not demonstrated convincing effects in terms of cancer-related distress (Kazak et al., 2004; Robb et al., 2014). Indeed, the use of a PTSS framework to understand common cancer-related distress symptoms has been questioned (Kangas, 2013) due to: (a) ambiguities regarding what constitutes the precipitating stressor, given cancer-related intrusions often are future-oriented instead of past-oriented; and (b) overlap between PTSS and treatment-related symptoms (Kangas, 2013; Kangas, Henry, & Bryant, 2002). This criticism has been actualized with the publication of the DSM-5 (American Psychiatric
Association, 2013). In contrast to the DSM-IV (American Psychiatric Association, 1994), in the DSM-5, a life threatening illness such as cancer only qualifies as traumatic event if it involves sudden and catastrophic events (American Psychiatric Association, 2013, p. 274). The amendments to the diagnostic criteria in DSM-5 aim to differentiate stress reactions reflecting PTSD from those better represented by other stress-, anxiety, and mood disorders (Kangas, 2013). This differentiation has important implications for development of psychological treatments. Exploring and conceptualising the cancer-related distress that persons diagnosed with cancer during adolescence experience is essential to inform development of psychological treatment for this distress. For this reason, Study II and III within the current thesis were conducted.

*Epistemological approach underpinning the current thesis*

The epistemological position underpinning the studies included within this thesis is pragmatism (Morgan, 2007, 2014). Pragmatism is a suitable paradigm for research utilising both qualitative and quantitative approaches (Morgan, 2007). A pragmatic approach includes: (a) adoption of research methods that are best suited to answer the research question; (b) the end result of research has the overall goal to improve human welfare; (c) findings yielded through qualitative approaches can be used to form theories which in turn can be investigated via quantitative approaches, and vice versa (mixed methods); (d) inter-subjectivity, meaning that although a single reality exists, individuals make their own interpretations of it; and (e) transferability, with findings considered transferable to other settings however to different degrees, as opposed to being either completely context-dependent or generalisable. Of additional importance, as the interventions included in this thesis are based on CBT, functional contextualism, which underpin several third-wave cognitive behaviour therapies, is rooted in pragmatism (Biglan & Hayes, 1996). In the present thesis the pragmatic approach is manifested in the integration of both qualitative and quantitative methods and inductive and deductive approaches to advance the understanding of cancer-related psychological distress and the acceptability and feasibility of CBT for the target population.

**Overall aim**

The overall aim of the present thesis was to investigate and explore psychological distress following cancer during adolescence and to develop a tailored psychological intervention to reduce cancer-related distress experienced by young people diagnosed with cancer during adolescence.
Specific aims

Study I
To investigate development of HRQOL and symptoms of anxiety and depression among persons diagnosed with cancer during adolescence from shortly after up to 10 years after diagnosis. A secondary aim was to examine the proportion reporting subclinical levels of anxiety and depression from shortly after up to 10 years after diagnosis.

Study II
To explore cancer-related psychological distress experienced by young survivors of cancer during adolescence.

Study III
To preliminary investigate individualised CBT for young survivors of cancer during adolescence; and to conceptualise cancer-related psychological concerns experienced by the survivors using cognitive-behavioural theory.

Study IV (study protocol presented in thesis)
To investigate the feasibility of the Internet-based self-help intervention YoungCan (Appendix 1) to reduce symptoms of anxiety and depression among young survivors of cancer during adolescence and the planned study procedures for a controlled trial evaluating the intervention’s clinical efficacy and cost-effectiveness.
Methods

Design

An overview of the characteristics of Study I-III is provided in Table 1.

In Study I, data was collected within a study with a longitudinal design, with the overall aim to investigate psychosocial and health economic consequences of cancer during adolescence. Adolescents diagnosed with cancer completed questionnaires measuring HRQOL (SF-36) (Ware & Sherbourne, 1992) and symptoms of anxiety and depression (HADS) (Svanborg & Åsberg, 1994): shortly after diagnosis (T1), six (T2), 12 (T3), and 18 (T4) months after diagnosis, and two (T5), three (T6), four (T7), and 10 (T8) years after diagnosis. Data collected at T1-T7 has been reported (Jörngården, Mattsson, & von Essen, 2007; Larsson, Mattsson, & von Essen, 2010). In Study I data collected from T1 up to T8 was used to examine the development of HRQOL and symptoms of anxiety and depression over time.

Study II and Study III were part of a project aiming to explore cancer-related distress and preliminary examine individualised face-to-face CBT using an uncontrolled, within-group design. Clinical outcomes were assessed at baseline, post-treatment, and three months follow-up. Potential participants were identified via the Swedish Childhood Cancer Registry (National Quality Registry initiated in 1982). All participants were offered up to 15 sessions of individualised face-to-face CBT. Before starting CBT, two unstructured interviews were conducted with each participant to explore experiences of cancer-related distress. In Study II, data from the unstructured interviews was used, and in Study III data from both the unstructured interviews and behavioural case formulations, conducted as a part of the CBT treatment, were used. Further, descriptive data regarding recruitment and eligibility, data collection, and treatment delivery, and individual clinical outcomes collected at pre-, post-, and follow-up assessments was collected and reported.

In Study IV, preliminary data was collected from a feasibility study of an Internet-administered self-help intervention, YoungCan (see Appendix 1), aimed to reduce symptoms of anxiety and depression among AYAs diagnosed with cancer during adolescence. The study adopted an uncontrolled, within-group design with assessments at baseline, post-treatment, and three months follow-up with an embedded mixed-methods process evaluation. All participants were offered the intervention during 12 weeks. Descriptive data regarding recruitment, eligibility, and attrition is presented within this thesis.
<table>
<thead>
<tr>
<th>Design</th>
<th>Participants</th>
<th>Time of data collection</th>
<th>Type of data collection</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Longitudinal</td>
<td>T1: N=61; T8: n=28 persons diagnosed with cancer during adolescence aged 13-19 years at T1</td>
<td>Shortly after diagnosis (T1); 6 (T2); 12 (T3); and 18 (T4) months after diagnosis; 2 (T5); 3 (T6); 4 (T7); and 10 (T8) years after diagnosis</td>
<td>Self-report questionnaires via telephone</td>
</tr>
<tr>
<td>II. Explorative, qualitative</td>
<td>N=10 persons diagnosed with cancer during adolescence aged 17-25 years</td>
<td>1 to 8 years after diagnosis</td>
<td>Registry data; self-report questionnaires via paper and pencil; unstructured face-to-face interviews</td>
</tr>
<tr>
<td>III. Uncontrolled-, within-group; pre, post, and follow-up</td>
<td>N=10 persons diagnosed with cancer during adolescence aged 17-25 years</td>
<td>1 to 8 years after diagnosis at baseline</td>
<td>Registry data; self-report questionnaires via paper and pencil; unstructured face-to-face interviews; behavioural case formulations; structured face-to-face clinical interviews; descriptive data regarding recruitment and eligibility, data collection and treatment delivery</td>
</tr>
<tr>
<td>IV. Uncontrolled-, within-group; pre, post, and follow-up</td>
<td>N=6 persons diagnosed with cancer during adolescence aged 17-22 years</td>
<td>Data not yet available</td>
<td>Descriptive data regarding recruitment and eligibility, data collection, attrition, resources needed to complete the study and programme, safety procedures, activity in the intervention; self-report questionnaires via Internet; structured clinical interviews via telephone; semi-structured interviews via telephone</td>
</tr>
</tbody>
</table>

Table 1. Design, participants, time and type of data collection in Study I-IV.
Procedure and participants

Study I

Participants were consecutively included from 1999 to 2003 at three of the six Swedish paediatric oncology centres (Lund, Umeå, and Uppsala). Participants eligible for inclusion were: (a) aged 13-19; (b) Swedish-speaking; (c) diagnosed with a malignancy or a recurrence (and in that case having been disease-free and off cancer treatment for ≥ one year); (d) had received chemotherapy; and; (e) assessed as being emotionally, cognitively, and physically able to participate. Assessments of eligibility was conducted by a nurse at each centre approximately three weeks after diagnosis. Eligible potential participants were provided study information and asked for informed consent. In addition, parental consent was collected for potential participants aged 13–17 years. During the inclusion period, 100 potential participants diagnosed with cancer (10 with a recurrence) were identified and 89 were invited to participate, with N=61 of these included (five with a recurrence) (participation rate=69%). Figure 2 presents the number completing each assessment along with reasons for attrition.

Figure 2. Number of participants completing each assessment along with reasons for attrition at T2-T8.

In total, n=19 (31%) individuals participated at all assessments. At the last assessment (T8), 28 (46%) persons participated, all off cancer treatment. All self-report data was collected via telephone and participants completed the HADS at each assessment, the SF-36 subscales Vitality (VT) and Mental Health (MH) at T1-T4 and the full SF-36 at T5-T8. Background data was primarily collected at T1. At T1-T7 participants were asked for consent to be contacted again. Before each data collection, the paediatric oncology centre where the respective person had been treated was contacted to ensure
participants were cognitively, emotionally, and physically able to participate. An overview of clinical and demographic characteristics for participants in Study I and II-III is presented in Table 2.

The procedure was approved by the local Ethics Committee at the Faculty of Medicine at the universities of Lund, Umeå and Uppsala in 1998 (DNR: 98/506) and the Regional Ethical Review Board in Uppsala in 2009 (DNR: 2009/409).

Table 2. Clinical and demographic characteristics of participants in Study I and II-III.

<table>
<thead>
<tr>
<th></th>
<th>Study I (N=61)</th>
<th>Study II-III (N=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age at diagnosis (SD)</td>
<td>15.5 (1.7)</td>
<td>15.9 (1.4)</td>
</tr>
<tr>
<td>Mean age at study entry (SD)</td>
<td>15.5 (1.7)</td>
<td>21.0 (2.8)</td>
</tr>
<tr>
<td>Female/Male n</td>
<td>24/37</td>
<td>4/6</td>
</tr>
<tr>
<td>Recurrence yes/no</td>
<td>5/56</td>
<td>1/9</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukemia</td>
<td>21</td>
<td>4</td>
</tr>
<tr>
<td>CNS tumour</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>Other malignancy</td>
<td>5</td>
<td>1</td>
</tr>
</tbody>
</table>

Study II-III

The same individuals participated in Study II and III. Eligible participants: (a) were aged 15-25; (b) had completed treatment for cancer diagnosed during adolescence; (c) had been treated in the paediatric oncology centre in Uppsala or Stockholm; (d) reported a need for psychological support; (e) was not currently participating in psychological treatment; and (f) was able to attend weekly CBT sessions in Uppsala or Stockholm for up to 15 weeks. The Swedish Childhood Cancer Registry was used to identify potential participants. These were invited via telephone or letter by the researchers. Those displaying severe psychiatric difficulties requiring immediate treatment were excluded and guided to appropriate care. Participation was offered to individuals meeting eligibility criteria and informed consent was obtained. After inclusion, participants completed the baseline assessment and two unstructured interviews were conducted before commencement of the CBT treatment. The study procedures were approved by the Regional Ethical Review Board in Uppsala (DNR: 2014/443).
Study IV

Individuals eligible for inclusion: (a) were aged 15-25; (b) had completed treatment for cancer diagnosed during adolescence; (c) had access to the Internet, an e-mail address, and a mobile telephone; (d) were able to read and write in Swedish; and (e) reported a need for psychological support. Those who currently received psychotherapy or endorsed symptoms of severe mental health problems in immediate need of treatment were excluded and guided to appropriate healthcare services.

Potential participants were identified via the Swedish Childhood Cancer Registry and invited via telephone or postal letter by the research team. Potential participants registered their contact details and provided informed consent via a secure website (U-CARE-portal) (Portal). Individuals with severe mental health problems in need of immediate care were excluded and guided to appropriate healthcare. Data was collected via telephone and the Portal. Ethical approval for study procedures were obtained from the Regional Ethical Review Board in Uppsala (DNR: 2016/210).

Data collection and measures

Table 3 provides an overview of the constructs investigated and corresponding measures used in Study I, III, and IV.

Sociodemographic and clinical cancer characteristics (Study I-IV)

In Study I, sociodemographic and clinical data was primarily collected at T1, in addition coordinating nurses retrieved clinical data from the medical journals during the study.

In Study II-IV, data regarding age, date of diagnosis, and cancer type was retrieved from the Swedish Childhood Cancer Registry. Self-reported data regarding demographics, clinical variables, and previous participation in counselling or psychotherapy was collected at the baseline assessments (via paper and pencil in Study II-III, and via telephone and the Portal in Study IV).

Feasibility and process outcome measurements (Study III-IV)

In Study III, data was collected regarding recruitment, data collection, and treatment delivery. In Study IV, data regarding the feasibility of recruitment, eligibility criteria, attrition, safety procedures, data collection, and resources needed to conduct the study and deliver the intervention was collected. In addition, data regarding therapist and participant adherence to the ICBT and feasibility and acceptability of support functions was collected via continuous
logging of all activity in the Portal in Study IV. In Study IV, progression criteria (Thabane et al., 2010) were set for some outcomes to decide if revisions should be made before continuing with a controlled trial.

Table 3. Overview of constructs and measures in Study I, III, and IV.

<table>
<thead>
<tr>
<th>Construct</th>
<th>Measure</th>
<th>Study I</th>
<th>Study III</th>
<th>Study IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>BAI</td>
<td>X</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GAD-7</td>
<td>-</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HADS</td>
<td>X</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Body image dissatisfaction</td>
<td>BIS</td>
<td>-</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Costs</td>
<td>TIC-P</td>
<td>-</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td>Depression</td>
<td>HADS</td>
<td>X</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>MADRS-S</td>
<td>-</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>PHQ-9</td>
<td>-</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td>Experiential avoidance</td>
<td>AAQ-II</td>
<td>-</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Health anxiety</td>
<td>SHAI</td>
<td>X</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>HRQOL</td>
<td>EQ-5D</td>
<td>-</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>SF-36</td>
<td>X</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>FAS</td>
<td>-</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Functional impairment</td>
<td>SDS</td>
<td>-</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>PTSS</td>
<td>PCL-C</td>
<td>-</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Rumination</td>
<td>R-RSQ</td>
<td>-</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Social anxiety</td>
<td>SIAS</td>
<td>-</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td>Somatic symptoms</td>
<td>PHQ-15</td>
<td>-</td>
<td>X</td>
<td>-</td>
</tr>
<tr>
<td>Worry</td>
<td>PSWQ</td>
<td>-</td>
<td>X</td>
<td>-</td>
</tr>
</tbody>
</table>

*Note. AAQ-II = Acceptance and Action Questionnaire-II; BAI = Beck Anxiety Scale; BIS = Body Image Scale; GAD-7 = Generalized Anxiety Disorder-7; FAS = Fatigue Assessment Scale; HADS = Hospital Anxiety and Depression Scale; MADRS-S = Montgomery Åsberg Depression Rating Scale-Self Assessment; PHQ-9 = Patient Health Questionnaire-9; PHQ-15 = Patient Health Questionnaire-15; PCL-C = PTSD Checklist-Civilian version; PSWQ = Penn State Worry Questionnaire; R-RSQ = Rumination Scale of the Response Style Questionnaire; SDS = Sheehan Disability Scale; SF-36; Short Form-36; SHAI = Short Health Anxiety Inventory; SIAS = Social Interaction Scale; TIC-P = Trimbos and Institute of Medical Technology Assessment Cost Questionnaire for Psychiatry.*

Psychological outcome measurements (Study I, III, and IV)

**Study I**

The selection of questionnaires was guided by the circumstance that participants would be followed for 10 years, starting in early adolescence, and comparisons with a matched control group would be made. As such, generic instruments, adequate for use with both adolescents and adults were used.

The HADS questionnaire (Zigmond & Snaith, 1983), developed to measure symptoms of anxiety and depression in medical populations, was used. It does not include items measuring somatic symptoms, as such the potential influence of symptoms associated with both physical illness and anxiety and depression is hypothesised to be lessened. The HADS consists of two 7-item subscales, one measuring anxiety and the other depression. Items are rated
from 0 to 3 yielding a maximum score of 21 (maximum distress) on each subscale. Scores can be interpreted either by a comparison with norm-data or values for a reference-group or by applying a cut-point to identify possible clinical cases. A cut-point of 8 has been suggested to identifying doubtful/possible cases of anxiety and depression among adults (Zigmond & Snaith, 1983), whereas a cut-point of 7 for depression and 9 for anxiety have been suggested for adolescents (White, Leach, Sims, Atkinson, & Cottrell, 1999). The HADS has demonstrated adequate internal consistency and sensitivity to change (Kugaya, Akechi, Okuyama, Okamura, & Uchitomi, 1998) and at least moderate discriminant validity in adult cancer populations (Vodermaier & Millman, 2011). Research indicates good internal consistency for the Swedish version used with adults (Lisspers, Nygren, & Söderman, 1997). However, low internal consistency has been found for the depression subscale with Swedish AYAs 13-23 years (Jörngarden, Wettergen, & von Essen, 2006).

The SF-36 (version 1.0) was used to measure HRQOL. It consists of 36 items and eight subscales: Bodily Pain (BP); General Health (GH); Mental Health (MH); Physical Functioning (PF); Role Emotional (RE); Role Physical (RP); Social Functioning (SF); and Vitality (VT) (Ware & Sherbourne, 1992). Two overarching summary scales can be derived from the subscales: The Physical Component Summary (PCS), measuring physical health with the subscales: PF, RP, BP, and GH; and the Mental Component Summary (MCS), measuring mental health based on the subscales: VT, SF, RE, and MH. Summary scales are standardised with a mean of 50 and a standard deviation of 10 (Sullivan, Karlsson, & Ware, 1994). The SF-36 has demonstrated adequate discriminant validity, acceptable item-internal consistency, and good internal consistency among childhood cancer survivors from age 16 (Reulen et al., 2006). The subscales VT and MH has good internal consistency in the Swedish general population ages 13-23 (Jörngarden et al., 2006).

**Study III**

Due to the exploratory nature of Study III, no primary or secondary outcomes were stated. Outcomes were chosen guided by previous research examining distress among adult and childhood cancer survivors, youth with other long-term health conditions, and qualitative explorations of negative experiences in the target population. The aim was to capture diverse manifestations of distress, consequences of these, and potential processes involved in their maintenance.

The 21-item BAI was used to measure symptoms of anxiety (Beck, Epstein, Brown, & Steer, 1988). Body dissatisfaction was assessed with the 10-item BIS (Hopwood, Fletcher, Lee, & Al Ghazal, 2001). Symptoms of depression were measured with the 9-item MADRS-S (Svanborg & Åsberg, 1994). The 10-item AAQ-II was used to assess experiential avoidance (Bond et al., 2011). The 10-item FAS (Michielsen, de Vries, & van Heck, 2003) was used to assess
fatigue and functional impairment in work, social, and family life was
examined with the 3-item SDS (Sheehan, 1983). Health anxiety was measured
using the 18-item SHAI (Salkovskis, Rimes, Warwick, & Clark, 2002) and
PTSS with the 17-item PCL-C corresponding to the B (re-experiencing), C
(avoidance), and D (hyperactivity) criteria in DSM-IV (Weathers, Litz,
Herman, Huska, & Keane, 1993.). Items were cued to the cancer experience.
The 22-item R-RSQ was used to assess rumination (Nolen-Hoeksema, 1991)
and somatic symptoms were measured with the PHQ-15 (Kurt Kroenke,
Spitzer, & Williams, 2002). Worry was assessed with the 16-item PSWQ
(Meyer, Miller, Metzger, & Borkovec, 1990).

Study IV
In Study IV, the feasibility and acceptability of the instruments to collect data
was investigated, and the intention was to use short, well-established, open
access, measures. Moreover, the number of measures was restricted.
Symptoms of depression was measured with the PHQ-9 (Kroenke, Spitzer,
& Williams, 2001) and the GAD-7 (Spitzer, Kroenke, Williams, & Löwe,
2006) was used to measure symptoms of anxiety. Body dissatisfaction was
measured with the BIS and PTSS with the PCL-C. SIAS (Mattick & Clarke,
1998) was used to examine reactions to social interactions and the EQ-5D
(EuroQol Group, 1990) to calculate quality-adjusted life years. A modified
short version of TiC-P (Bouwmans et al., 2013) was used to assess direct and
indirect medical costs and indirect non-medical costs.

Diagnostic interviews (Study III-IV)
The M.I.N.I. International Neuropsychiatric Interview for DSM-IV and ICD-
10 (Sheehan et al., 1998), a well-validated structured diagnostic interview was
used to assess psychiatric disorders and identify participants reporting severe
mental health problems in need of immediate treatment in Study III and IV.
Interviews were conducted face-to-face in Study III and via telephone in Study
IV.

Interviews (Study II-IV)
In Study II-III two individual unstructured interviews were conducted with
each participant within a two-week interval. These were conducted at the
paediatric oncology unit in Uppsala or at a private psychology practice in
Stockholm, and lasted between 33 and 104 minutes. Two female and one male
clinical psychologist with experience of qualitative research performed the
interviews. All interviews commenced with the question: “Please tell me how
you think and feel about having had cancer”. Probes were used for
clarification, and to encourage elaboration and reflection. A senior researcher
with extensive experience of qualitative research reviewed at least one
interview from each psychologist and provided feedback to improve quality. Before the second interview with the same participants, the first interview was listened to by at least one psychologist to identify areas in need of exploration and/or clarification.

In Study IV, semi-structured interviews via telephone were planned to be conducted with all participants at baseline and at three months follow-up and at study exit with participants who chose to exit the study. The intent was to explore acceptability of the intervention and study procedures. At baseline, participants were to answer questions regarding current problems and their development and maintenance, treatment expectations, and previous experiences of psychological treatment. At three months follow-up participants were to answer questions about experiences of the intervention and study procedures and reasons for potential non-adherence. Participants exiting the study were planned to be asked about reasons for exiting and suggestions for improvements with regard to intervention and study procedures.

Behavioural case formulations (Study III)
In Study III, behavioural case formulations (Sturmey, 2008), to guide tailoring of treatments, were developed by the CBT therapists providing treatment. Formulations described participants’ current and previous problems, precipitating events, and specification of topography and prioritization of concerns (Dougher, 2000; Persons, 2008). Further, functional analyses to generate hypotheses regarding mechanisms causing and maintaining participants’ problems guided selection of CBT treatment-components. The analyses were informed by learning theory with the concept of experiential avoidance suggested as a trans-diagnostic core pathological process (Hayes, Wilson, Gifford, Follette, & Strosahl, 1996).

Interventions
Study III
In Study III, participants were offered up to 15 sessions of individualised face-to-face CBT. Given the explorative aims of the study and the fact that the unique needs of the target population are not specifically addressed in existing CBT protocols, treatment was not manualised but based on a behavioural case formulation-driven approach (as described above) (Dougher, 2000; Persons, 2008; Sturmey, 2008). Typically, a working case formulation was developed during the first two or three treatment sessions, thereafter continuously assessed and revised if needed. Empirically supported treatment components addressing the mechanisms hypothesised to cause and maintain problems
were included in treatment. General CBT components directed towards promoting change and building alliance including collaborative goal setting, psychoeducation (Dobson & Dobson, 2017), and conducting joint functional analyses were applied in all treatments. An overview of the used treatment components is provided in Table 4. Sessions were typically structured in typical CBT format including a general mood/distress check-in and follow-up from last session, agenda setting, homework review, in-session activity including e.g. introduction and/or practice of behavioural treatment component, summary, session feedback, and formulation and planning of homework (Dobson & Dobson, 2017).

Table 4. Components included in the treatments in Study III and the number of treatments in which the components were included.

<table>
<thead>
<tr>
<th>Component</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional analysis</td>
<td>10</td>
</tr>
<tr>
<td>Goal setting</td>
<td>10</td>
</tr>
<tr>
<td>Psychoeducation including experiential exercises</td>
<td>10</td>
</tr>
<tr>
<td>Setting a maintenance plan</td>
<td>9</td>
</tr>
<tr>
<td>Exploring values</td>
<td>8</td>
</tr>
<tr>
<td>Self-monitoring</td>
<td>8</td>
</tr>
<tr>
<td>Mindfulness-based exercises</td>
<td>7</td>
</tr>
<tr>
<td>Value-guided behaviour change relating to social avoidance and fear of failure</td>
<td>6</td>
</tr>
<tr>
<td>Worry-time, worry exposure, problem solving</td>
<td>5</td>
</tr>
<tr>
<td>Behavioural activation</td>
<td>3</td>
</tr>
<tr>
<td>General affect exposure</td>
<td>3</td>
</tr>
<tr>
<td>Stress management techniques</td>
<td>3</td>
</tr>
<tr>
<td>Emotion regulation/distress tolerance training</td>
<td>2</td>
</tr>
<tr>
<td>Exposure (interoceptive exposure and exposure and response prevention)</td>
<td>2</td>
</tr>
<tr>
<td>Interpersonal effectiveness skills training</td>
<td>2</td>
</tr>
<tr>
<td>Relaxation exercises</td>
<td>1</td>
</tr>
</tbody>
</table>

**Study IV**

The YoungCan intervention, see Appendix 1 was provided via the Portal, a secure Internet portal supporting delivery of complex interventions. YoungCan consists of ICBT, psychoeducation, and interactive peer support. Participants worked independently with the intervention during 12 weeks with guidance from a therapist. Therapist guidance followed a standardised treatment manual developed for the study. Guidance included an initial telephone support session, aimed to support individual tailoring of the treatment through formulation of idiographic goals and individual problem analyses. In addition, therapists provided weekly, and at need feedback on homework, encouragement, support to troubleshoot difficulties and guidance regarding continued work provided via the Portal or via telephone (based on
participant preference). Participants who did not log in or make progress were contacted via messages from the Portal, text messages, and/or telephone.

The ICBT was organised in six chapters, the first and last mandatory and offered at the beginning and end of the 12-week period, respectively. The remaining chapters were assigned to participants according to need as defined in a clinical assessment, informed by the Five Areas Assessment Model (Williams & Garland, 2002) conducted during the initial support session.

In addition to the ICBT, participants had access to support functions such as a library, possibility to interact with other participants, and a Questions and Answers (Q&A) function.

**Therapist training and adherence**

A full-day workshop, delivered over two days, was provided to therapists working with the intervention before study-start. The workshop was held by the author of this thesis who developed the intervention in collaboration with members in the research group. The workshop included: (a) introduction to the target population and review of research concerning cancer-related distress experienced by the population; (b) background and rationale for the study; (c) description of the development of the intervention; (d) description of the ICBT chapters including underlying theory, rationale for treatment components, and suggestions for further reading; (e) introduction to ICBT and provision of support via the Internet; (f) ICBT therapist skills training; and (g) presentation of the treatment manual including the Five Areas Assessment Model (Williams & Garland, 2002), idiographic goal setting, and problem analyses.

**Data analyses**

**Study I**

Initial status and development over time for the SF-36 and HADS subscales was examined using mixed models with intercepts and slopes included as random effects. Development was investigated using polynomial change trajectories and model fit was the base for choice of model (Singer & Willett, 2003). Unconditional models were tested and potential predictors including gender, age, and leukemia vs not-leukemia were subsequently added. The proportion reporting possible anxiety and depression was calculated with descriptive statistics. Independent two-tailed t-tests were used to examine potential differences between responders and non-responders at T8 for the SF-36 and the HADS subscales at T1 and T7. \( \alpha < .05 \) was used as an indicator of a significant difference. All analyses were performed in IBM SPSS Statistics 20.
Study II

An inductive qualitative manifest content analysis (Graneheim & Lundman, 2004) was used to analyse data. Interviews were audio-recorded and a transcription agency transcribed the interviews verbatim. Following transcription, the author of this thesis (MA) listened to all interviews to detect potential errors in the transcriptions and gain an overview of the dataset. MA identified and condensed meaning units relating to psychological stress. Next, another licensed psychologist and PhD student in medical sciences (JTC) listened to all interviews and read all transcripts, reviewed meaning units and made independent condensations of them which were discussed and revised with MA. Thereafter, MA and JTC independently coded, compared, and discussed all condensed meaning units. When needed, codes were revised, codes were thereafter compared and sorted into subcategories and categories based on similarities and differences by MA and JTC independently, followed by joint review, revision, and further elaboration. Next, MA, JTC and a researcher and PhD in behavioural sciences (EH) individually reviewed whether meaning units, codes, and categories were grounded in data, whether there was congruence and coherence in abstraction levels, and if the categories and labels attached to them covered data and reflected psychological distress. Last, individual reviews including identified ambiguities, incongruences, and disagreements were discussed by MA, JTC, and EH and codes, subcategories, and categories were refined with respect to grouping and labelling until categories were considered to accurately cover and reflect data.

Study III

Participant flow through the study was followed using relevant parts of the Consolidated Standards of Reporting Trials (CONSORT) diagram for parallel randomised trials (Moher et al., 2010). Clinical outcomes at baseline, post treatment, and three months follow up were reported with descriptive statistics. The Jacobson-Truax Index (Jacobson & Truax, 1991) was used to calculate reliable change scores on the MADRS-S, BAI, and PCL-C.

Qualitative framework analysis (Ritchie & Spencer, 1994) and theoretical thematic analysis (Braun & Clarke, 2006) guided the analysis to identify and conceptualise cancer-related concerns. As an initial step, all behavioural case formulations, interview transcripts, and clinical notes were read carefully by the author of this thesis (MA) to gain an overview of and familiarise with the data as a whole. A framework to organise and manage data was developed according to the categories ‘cancer-related concerns’ and ‘non-cancer-related concerns’. Thereafter, MA read the behavioural case formulations and identified concerns which were sorted into ‘cancer-related’ and ‘non-cancer-related’ concerns respectively. The concerns included in the category ‘cancer-related concerns’ were thereafter collated into themes and defining key
characteristics. The process was informed by cognitive-behavioural theory (Barlow, 2014; Blackledge, Ciarrochi, & Deane, 2009). Subsequently, MA read all interview transcripts and identified cancer-related experiences relating to each of the themes generated under the category ‘cancer-related concerns’ which were collated into themes of cancer-related experiences. A psychologist and PhD in medical sciences (MC) reviewed the themes of cancer-related concerns and experiences with respect to coherence, congruence, and distinctiveness (Braun & Clarke, 2006) and themes were subsequently elaborated and refined.

**Study IV**

Preliminary findings regarding recruitment and flow of participants through the study was illustrated using relevant parts of the Consolidated Standards of Reporting Trials (CONSORT) diagram for parallel randomised trials (Moher et al., 2010).
Results

Study I

The development over time for HRQOL, and symptoms of anxiety and depression is depicted in Figure 3. Table 5 presents final models of initial status and change over time for the study variables. A cubic model provided the best fit to the data regarding MH and VT suggesting an initial increase which diminished over time into a decrease which diminished over time. A cubic model also provided the best fit for HADS-Depression suggesting an initial decrease abating over time into an increase which then abated over time. The initial decline, following increase and final decrease was more pronounced for girls. For PCS and HADS-Anxiety quadratic models showed best fit to data suggesting an increase in PCS (from T5) that declined over time, and an initial decline in HADS-Anxiety that diminished over time into an increase. An unconditional model provided best fit to the data regarding MCS.

*Figure 3. Observed means and 95% confidence intervals for the study variables from shortly after diagnosis up to 10 years after diagnosis in Study 1.*
Table 5. *Final models of initial status and change over time for Study I variables*

<table>
<thead>
<tr>
<th>Shape</th>
<th>Initial status</th>
<th>Linear term</th>
<th>Quadratic term</th>
<th>Cubic term</th>
<th>Predictors of initial status</th>
<th>Predictors of change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(intercept)</td>
<td>(slope)</td>
<td>(slope)</td>
<td>(slope)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SF-36 MH</td>
<td>Cubic</td>
<td>64.87***</td>
<td>13.29***</td>
<td>-2.73***</td>
<td>0.14***</td>
<td>-</td>
</tr>
<tr>
<td>SF-36 VT</td>
<td>Cubic</td>
<td>47.80***</td>
<td>19.90***</td>
<td>-4.20***</td>
<td>0.22***</td>
<td>-</td>
</tr>
<tr>
<td>SF-36 MCS</td>
<td>No change</td>
<td>50.24***</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>SF-36 PCS</td>
<td>Quadratic</td>
<td>48.90***</td>
<td>1.81**</td>
<td>-0.15**</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HADS-A</td>
<td>Quadratic</td>
<td>4.13***</td>
<td>-0.54***</td>
<td>0.05***</td>
<td>Girl (Est. = 1.39, p=.06)</td>
<td>-</td>
</tr>
<tr>
<td>HADS-D</td>
<td>Cubic</td>
<td>4.22***</td>
<td>-1.64***</td>
<td>0.27**</td>
<td>0.10*</td>
<td>Girl× Linear term (Est. = -1.07*)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Girl× Quad term (Est. = -0.41**)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Girl× Cubic term (Est. = -0.3**)</td>
</tr>
</tbody>
</table>

*Note. SF-36, Short Form 36; MH, Mental Health subscale; VT, Vitality subscale; MCS, Mental Component Summary; PCS, Physical Component Summary; HADS-A, Hospital Anxiety and Depression Scale- Anxiety subscale; HADS-D, Hospital Anxiety and Depression Scale- Depression subscale; *p<0.05, **p<0.01, ***p<0.001.*

The proportion reporting possible clinically relevant symptoms of anxiety at T1 were 15% (n=7) and at T8 29% (n=8). Of the eight participants reporting anxiety over the cut-point at T8, four had reported elevated anxiety on at least one previous assessment. At T1 18% (n=11) reported possible depression and none at T8. Responders and non-responders at T8 did not differ significantly on any of the study variables at T1 and T7.
Study II

Data was sorted in distress experienced during vs after end of treatment. Five categories, of which one described distress during treatment, and 14 subcategories were formulated. Categories and subcategories are presented in Table 6.

Table 6. *Categories and subcategories of distress reported by young survivors of adolescent cancer.*

<table>
<thead>
<tr>
<th>Categories</th>
<th>Subcategories</th>
</tr>
</thead>
<tbody>
<tr>
<td>During treatment</td>
<td>A tough treatment</td>
</tr>
<tr>
<td></td>
<td>A mental challenge</td>
</tr>
<tr>
<td></td>
<td>Particularly stressful events</td>
</tr>
<tr>
<td></td>
<td>Loss of control over one’s life and body</td>
</tr>
<tr>
<td></td>
<td>Lonely and disconnected</td>
</tr>
<tr>
<td>After end of treatment</td>
<td>Marked and hindered</td>
</tr>
<tr>
<td></td>
<td>Cancer free but not free</td>
</tr>
<tr>
<td></td>
<td>Being the one with cancer</td>
</tr>
<tr>
<td></td>
<td>Not feeling good enough</td>
</tr>
<tr>
<td></td>
<td>Not being in the right place in life</td>
</tr>
<tr>
<td></td>
<td>Insecure and left out</td>
</tr>
<tr>
<td>Struggling with the fragility of life</td>
<td>Affect ed by people’s withdrawal</td>
</tr>
<tr>
<td></td>
<td>Everything may soon be gone</td>
</tr>
<tr>
<td></td>
<td>Lost time and lost hope</td>
</tr>
<tr>
<td>An ongoing battle with emotions</td>
<td>Not understanding own feelings</td>
</tr>
<tr>
<td></td>
<td>Drained by feelings</td>
</tr>
<tr>
<td></td>
<td>Fighting one’s feelings</td>
</tr>
</tbody>
</table>

Participants described the treatment as a mental challenge that they had just wanted to get through. Whilst they reported difficulties in remembering how and what they had felt and thought during treatment, they reported emotional and cognitive reactions to events perceived as particularly stressful. Such reactions included fear of dying, along with passive and active strategies used to handle painful experiences. Moreover, loss of control, powerlessness and dependency on others, and efforts to regain control, along with feeling lonely, abandoned, and disconnected was experienced during treatment.

Participants described feeling marked and hindered by the cancer experience after treatment completion. Experiences included feeling negatively affected by cancer-related health problems, fear of recurrence, and being differently treated and pitied by others. Moreover, feelings of not being good enough, self-reproaches, feelings of failure and worthlessness with regard to accomplishments, feelings of lagging behind, social insecurity, and a sense of being different and not seen or liked were described. Furthermore, participants described struggling with fragility of life including cancer-related sudden losses and feelings of being let down by friends, changed life conditions and future prospects due to the cancer. An ongoing battle with emotions and difficulties understanding and allowing feelings, feeling drained and overwhelmed by feelings, including anxiety and worry, anger, feelings of
injustice, depression, and numbness was described. Participants also described having tried to fight their feelings for a long time by using strategies including shutting off inner experiences, distracting themselves, and avoiding distressing triggers, however expressed a need to face and talk about painful experiences.

Study III
The flow of participants and reasons for non-participation is shown in Figure 4. The Swedish Childhood Cancer Registry was used to identify 234 potential participants, 201 of these (86%) were informed about the study, with a total of 13 (6%) expressing interest in participating and being scheduled for an eligibility interview. Following the eligibility interview, ten participants were included (5% participation rate). The baseline-assessment was completed by nine participants, the post-assessment by seven participants, and the follow-up assessment by eight participants. Six items were missing in the self-report questionnaires.

Nine participants completed the CBT with a mean of 12.6 sessions (range=7-15), a mean total treatment length of 25 weeks (range=18-36) and a mean of 3.4 cancelled sessions (range=0-11). Behavioural case formulations guided selection of treatment components.

Six participants fulfilled criteria for a psychiatric disorder according to the M.I.N.I. at baseline, two at post-assessment (n=7), and four at follow-up (n=8). Three met criteria for reliable change in at least one measure at post-assessment (n=7), and five at follow-up (n=8). Self-report data at baseline-, post-, and follow-up assessment is presented in Table 7.
Figure 4. Flow of participants through Study III.

The majority (n=62; 71%) of the identified concerns (N=87) were related to cancer. These were according to cognitive behavioural theory categorised as: social avoidance, fear and avoidance of emotions and bodily symptoms, imbalance in activity, and worry and rumination. The theme social avoidance was characterised by fear of being rejected and excluded, fear of causing discomfort and being a burden, difficulties expressing own experiences and needs, loneliness, body dissatisfaction, not feeling liked or accepted, post-mortem rumination, withdrawal and not taking social initiatives, overworking to perform well in social situations, and cautious distance and passive aggressive behaviours. Key defining characteristics of the theme fear and avoidance of emotions and bodily symptoms included fear and avoidance of symptoms associated with illness, fear and avoidance of anxiety symptoms, fear and avoidance of being alone and of cancer-related reminders, and
obsessions and compulsions. The theme imbalance in activity was characterised by low contact with positively reinforcing activities, stress sensitivity and fear of failure, maladaptive stress behaviours and procrastination, emotional numbness and dejection, low motivation, lack of routines and identity difficulties. Worry and rumination was characterised by worry about the future, decisional anxiety, and depressive and existential rumination.

Table 7. Means, standard deviations, and ranges for self-reports at baseline-, post-, and follow-up assessments in Study III.

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n=9)</th>
<th>Post (n=7)</th>
<th>Follow-up (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD (range)</td>
<td>Mean</td>
</tr>
<tr>
<td>AAQ-II</td>
<td>36.3</td>
<td>10.6 (23-55)</td>
<td>32.4</td>
</tr>
<tr>
<td>BAI</td>
<td>14.6</td>
<td>16.5 (1-56)</td>
<td>7.9*</td>
</tr>
<tr>
<td>BIS</td>
<td>12.6</td>
<td>7.2 (5-26)</td>
<td>8.1</td>
</tr>
<tr>
<td>FAS</td>
<td>26.8</td>
<td>5.6 (20-36)</td>
<td>22.3</td>
</tr>
<tr>
<td>MADRS-S</td>
<td>17.0</td>
<td>6.2 (8-27)</td>
<td>10.9*</td>
</tr>
<tr>
<td>PCL-C</td>
<td>37.0</td>
<td>14.2 (20-70)</td>
<td>27.1*</td>
</tr>
<tr>
<td>PHQ-15</td>
<td>10.2</td>
<td>6.8 (2-23)</td>
<td>6.4</td>
</tr>
<tr>
<td>PSWQ</td>
<td>48.9</td>
<td>11.5 (32-63)</td>
<td>40.9*</td>
</tr>
<tr>
<td>R-RSQ</td>
<td>53.1</td>
<td>13.9 (31-72)</td>
<td>47.8*</td>
</tr>
<tr>
<td>SDS</td>
<td>12.9</td>
<td>5.9 (4-21)</td>
<td>7.5*</td>
</tr>
<tr>
<td>SHAI</td>
<td>14.9</td>
<td>4.4 (8-20)</td>
<td>12.0</td>
</tr>
</tbody>
</table>

*a(n=8) Note. AAQ-II = Acceptance and Action Questionnaire-II; BAI = Beck Anxiety Inventory; BIS = Body Image Scale; FAS = Fatigue Assessment Scale; MADRS-S = Montgomery Åsberg Depression Rating Scale-Self Assessment; PCL-C = The PTSD Checklist-Civilian Version; PHQ-15 = Public Health Questionnaire-15; PSWQ = Penn State Worry Questionnaire; R-RSQ = Rumination Scale of the Response Style Questionnaire; SDS = Sheehan Disability Scale; SHAI = The Short Health Anxiety Inventory

Study IV

See Figure 5 for the flow of participants and reasons for non-participation. The Swedish Childhood Cancer Registry was used to identify potential participants, 409 were identified and 320 (78%) of these were informed about the study by the research team, of which 13 (4%) registered at the website and provided informed consent. Following the eligibility interview, seven were included, rendering an overall participation rate of 2%. The complete baseline assessment (semi-structured interview and online self-report questionnaires) was completed by six participants. One completed the online self-report questionnaires at the post assessment whereas none completed the semi-structured interview at the post assessment. The study was closed in advance and the follow-up assessment was not administered.
Figure 5. Flow of participants and reasons for non-participation in Study IV.

Note. Minor amendments to the original diagram published in the study protocol for Study IV has been done due to unforeseen events during the recruitment process.
Discussion

Main findings

Development of HRQOL and symptoms of anxiety and depression

One aim of the present thesis was to investigate the development of HRQOL and symptoms of anxiety and depression from shortly after diagnosis up to 10 years after diagnosis among persons diagnosed with cancer during adolescence. Shortly after diagnosis 15% reported a subclinical level of symptoms of anxiety, compared with 29% 10 years after diagnosis. With regard to symptoms of depression, 18% reported a subclinical level shortly after diagnosis, and none 10 years after diagnosis. Whilst the findings must be interpreted with caution due to the small sample size (n=28 at T8) they suggest HRQOL and psychological distress do not simply steadily decrease from diagnosis until they reach an asymptomatic and stable level. Rather, the development of psychological distress appears to be more complex, making it difficult to predict who will report elevated distress and when. Longitudinal research by others has identified differing trajectories relating to anxiety, depression, somatization, and potential risk factors in AYA cancer survivors who have entered adulthood (Brinkman et al., 2013). Perceived worsening of health, cancer-related pain, and changes in employment and relationship status has been found to predict persistent and increasing levels of psychological distress. Ten years after diagnosis the participants had entered adulthood and as such elevated anxiety symptoms may be related to the transition from adolescence to young adulthood. Indeed, 10 years after diagnosis participants reported negative cancer-related consequences such as health worries, frustration about healthcare, and fertility concerns not reported previously (Lehmann et al., 2014). Research by others has shown higher levels of distress among survivors 25-29 years compared to older survivors (Salsman et al., 2014). Future studies are needed to examine distress trajectories among AYA survivors of cancer during adolescence from the time of diagnosis and onwards, paying attention to subgroups reporting persistent or increasing distress to identify possible risk factors relating to different phases of survivorship and transitions into adulthood.

It is important to consider findings from Study I in the context of psychological distress trajectories for adolescents in the wider community.
Longitudinal studies examining symptoms of anxiety and depression from mid- to late adolescence (corresponding to the first four years in Study I) reveal a complex picture. Some research has demonstrated increases in psychological distress from mid to late adolescence (Hale, Raaijmakers, Muris, van Hoof, & Meeus, 2008; Oort, Greaves-Lord, Verhulst, Ormel, & Huizink, 2009) and declines in levels of symptoms of anxiety and depression during young adulthood (Ferro, Gorter, & Boyle, 2015; Galambos, Leadbeater, & Barker, 2004). Other studies have found increasing levels of symptoms of anxiety and depression from adolescence to young adulthood (Calling, Midlov, Johansson, Sundquist, & Sundquist, 2017; Copeland, Angold, Shanahan, & Costello, 2014; Leadbeater, Blatt, & Quinlan, 1995). As such, it is difficult to draw conclusions regarding whether the observed findings in Study I reflect normal development or are related to cancer survivorship.

Of further importance, are findings showing that adolescents with chronic health conditions report higher levels of symptoms of anxiety and depression in comparison with population norms (Jones et al., 2017; Pinquart & Shen, 2011a, 2011b). Indeed, the majority of participants in Study I did not report a high level of symptoms of anxiety and/or depression or low HRQOL, and from 18 months to four years post diagnosis, the reported level of depression was lower than for an age-matched reference group (Larsson et al., 2010). Our findings are consistent with results from systematic reviews examining distress among survivors of cancer in childhood and adolescence (Eiser et al., 2000; Lund et al., 2011).

A number of explanations for high levels of HRQOL and low levels of psychological distress in AYA cancer survivors have been proposed. First, response shift has been suggested for children with cancer (Brinksma et al., 2014) and adult cancer survivors (Jansen, Stiggelbout, Nooij, Noordijk, & Kievit, 2000). Response shift implies a change of internal standards, values or conceptualisation of HRQOL and mental health, resulting in a change in the self-evaluation of these constructs (Sprangers & Schwartz, 1999). Second, posttraumatic growth (PTG) has been proposed. PTG is conceptualised as an experience of positive psychological change including an increased appreciation of life, improved relations to others and the self, and new values and priorities as a result of a struggle with a trauma or stressful event (Tedeschi & Calhoun, 2004). PTG has been found to predict HRQOL and symptoms of anxiety and depression in AYAs with cancer (Husson et al., 2017a). However, other studies have not found a difference in PTG between AYA cancer survivors and controls (Greup et al., 2017). Given the inconsistent findings the concept’s usefulness is unclear. Third, an increased prevalence of a repressive adaptive style, characterized by high defensiveness and low distress, has been reported for children and adolescents diagnosed with cancer and other chronic illnesses (Erickson, Gerstle, & Montague, 2008; Phipps & Steele, 2002). However, there is discussion regarding whether it
should be considered a mechanism involved in resilience or not, and the validity of self-reported psychosocial function among repressors has been questioned (Erickson, Gerstle, & Montague, 2008). Additionally there is lack of consensus whether these constructs should be considered as an outcome, a trait, or a coping strategy and how they should be measured. Moreover, the processes via which they potentially develop are unclear (Meyerson, Grant, Carter, & Kilmer, 2011; Phipps, 2007).

The comparably low distress levels reported by adolescent cancer survivors compared to persons with other health conditions may be explained by the fact that the majority successfully complete their cancer treatment, in contrast to some other illnesses (e.g. diabetes, fibromyalgia, chronic fatigue syndrome). However, it is important to acknowledge that two thirds of childhood cancer survivors report at least one late effect of their cancer treatment, and nearly one half of young adult survivors of cancer have at least one major cancer-related adverse health outcome (Hudson et al., 2003) with most late effects increasing in incidence with age (Oeffinger et al., 2006). This implies that for many, the impact of cancer is not temporary.

Lastly, the findings from Study I should be viewed in light of research showing that survivors of cancer during childhood, adolescence, and emerging adulthood have an increased risk of hospital contacts for mental disorders (Lund et al., 2013) and being prescribed antidepressants compared to age-matched controls (Deyell et al., 2013; Johannsdottir et al., 2017; Lund et al., 2015), survivors treated more recently being at extra risk (Lund et al., 2015). Future longitudinal research should investigate the development of distress, response shift, PTG, and repressive adaptive style including social desirability among adolescents diagnosed with cancer compared with other long-term health conditions and combine use of self-reports of distress with more objective measures of distress to advance our understanding of the general and specific psychological adaptation among AYA cancer survivors.

Development and feasibility of ICBT

A further aim of the present thesis was to take the first steps towards developing a psychological treatment to reduce cancer-related distress among AYA survivors of cancer during adolescence. In Study II cancer-related psychological distress was explored to inform intervention development. In Study III a preliminary investigation of individualised CBT for young survivors of cancer during adolescence was conducted alongside conceptualisation of cancer-related distress according to cognitive behavioural theory. In Study IV the acceptability and feasibility of the YoungCan intervention was tested in a study for which the protocol is presented herein. A major finding from Study II-IV concern significant difficulties with recruitment.
Recruitment

Significant difficulties with recruitment were identified in Study II-IV. In Study II-III, only 5% of invited potential participants were included, and in Study IV only 2% of invited were included. Difficulties recruiting AYA and adult cancer survivors to psychological intervention studies have been reported (Cantrell et al., 2012; Richter et al., 2015; van Scheppingen et al., 2011). However, a significant number of trials do not adequately report the recruitment rates as recommended by CONSORT (Moher et al., Walters et al., 2017; van Scheppingen et al., 2011). As such, challenges with recruiting the AYA cancer population may have been underreported within the literature. Given the consistent recruitment difficulties experienced across Studies II-IV, it is important to explore factors that may explain poor recruitment warranting further investigation. The following factors will be briefly discussed below: practical barriers to help-seeking; prevalence of psychological distress; mental health literacy; and stigma.

First, reported barriers to participation in Study II-III included lack of time and travel distance, reported in other psychological intervention trials with the population (Barnett et al., 2016; Kazak et al., 2004). Further, difficulties scheduling sessions once a week resulted in significant extension to planned treatment times in Study III. Although ICBT was hypothesised to potentially overcome barriers relating to scheduling and travel distance, recruitment rates were still poor in Study IV. However, other practical barriers reported in the literature include transitions in employment and housing with associated changes in contact details (Barnett et al., 2016). As such, whilst ICBT may overcome barriers regarding travel and provide more flexibility regarding scheduling with school and work, it does not overcome the practical barriers to recruitment reported by AYAs in the literature, like lack of time, changes in housing, and methods of contact.

Second, a prevalence based recruitment strategy was used in Study II-IV. Given the variations in prevalence of distress found in research with AYA survivors of cancer diagnosed in adolescence (e.g. Canning et al., 1993; Kwak et al., 2013a, 2013b; Larsson et al., 2010; Neville, 1996; Pemberger et al., 2005; Seitz et al., 2010), the reliance on this strategy may be problematic. Indeed, over-estimation of the number of eligible participants and under-estimation of the length of the recruitment period is common in clinical research (Elliott, Husbands, Hamdy, Holmberg, & Donovan, 2017). Further, the self-reported need for psychological support in adult cancer populations has been found to be lower than anticipated on the basis of prevalence rates of psychological distress (van Scheppingen et al., 2011). To the best of our knowledge no research has examined needs of psychological support among survivors of cancer during adolescence specifically. As such, examination of the need for psychological support in AYA survivors of cancer during adolescence and its correspondence with cancer-related distress is warranted.
Third, not recognising distress symptoms (Jorm, 2000) or normalising and underrating distress symptoms (Paulus, Wadsworth, & Hayes-Skelton, 2015), believing that receiving support can make problems worse or that needing support is a sign of weakness (Salaheddin & Mason, 2016) are other possible barriers to help-seeking. The latter can be viewed as a form of mental health stigma (Jennings et al., 2015). Indeed, in Study II, being pitied and feeling different and excluded due to the cancer was identified as an aspect of cancer-related distress. As such, survivors may not express concerns or accept support as they do not want to identify themselves with having mental health problems associated with being stigmatised.

Treatment delivery
While the small sample size in Study III precluded analysis of treatment effect, analysis of individual outcomes showed that a number of participants experienced significant difficulties after end of treatment, suggesting that the individualised CBT did not meet their needs. Preliminary findings from Study IV show that four out of six participants were “non-attendees” or poor attendees” i.e. did not complete more than the first part of the assigned ICBT chapter. Exploration of acceptability of intervention and study procedures was planned to be conducted via semi-structured telephone interviews in Study IV for participants at the post-up assessment and shortly after study-exit for participants who decided to withdraw from treatment. However, none of the participants in Study IV was reached for an interview. The low recruitment rates combined with low activity in the intervention and significant attrition suggest that the intervention and study procedures in Study IV were neither feasible nor acceptable. This may be explained by the fact that a consultative, rather than a collaborative, approach to involvement of end-users was used in intervention development. People with lived experience were consulted regarding selected parts of the intervention and procedures but were not involved in the entire process. Involving people with lived experience of the phenomena at hand following established frameworks (Bagley et al., 2016) may be associated with improvements in quality and relevance. Indeed, the adoption of a collaborative approach with in-depth collaboration from the planning and throughout the study may have resulted in more feasible and accepted procedures and a more relevant intervention.

Exploration and conceptualisation of cancer-related distress
Further aims of the current thesis were to explore (Study II) and conceptualise (Study III) cancer-related psychological distress reported by AYA survivors of cancer during adolescence. Findings from Study II showed that AYA survivors had perceived the treatment period as mentally challenging, with loss of control, loneliness and not feeling connected with friends being salient features of distress. After end of treatment, survivors described feeling marked and hindered by the cancer experience, struggling with feelings of inadequacy
and insecurity, existential issues, and experiencing difficulties understanding, accepting, and handling emotions. In Study III, descriptions of cancer-related distress were conceptualised as social avoidance, fear and avoidance of emotions and bodily symptoms, imbalance in activity, and worry and rumination according to cognitive behavioural theory. Findings are consistent with and complement prior research investigating distress as well as models to guide interventions by providing a comprehensive understanding of cancer-related concerns.

Cancer-related loneliness and anxiety in social interactions was reported in Study III. Findings suggest that experiences of stigmatisation, a drop in social status, social exclusion, and lack of belongingness had an impact on these difficulties. The results agree with findings by others showing relationship difficulties among AYA cancer survivors (Warner et al., 2016) and that social anxiety disorder is the most common anxiety disorder in late adolescence and young adulthood (Ollendick & Hirshfeld-Becker, 2002). Moreover, social exclusion and rejection by friends is strongly associated with adolescent social anxiety (La Greca & Ranta, 2015). However, no existing psychological intervention for AYA cancer survivors addresses loneliness, social anxiety, and avoidance specifically.

Cancer-related fear and avoidance of bodily symptoms including physical symptoms and emotional arousal was reported in Study III. These findings are consistent with results showing that exposure to health-related stressful life events involving serious illness or death are associated with fear of physical symptoms (McLaughlin & Hatzenbuehler, 2009). Indeed, an increased level of panic disorder has been found among childhood cancer survivors (de Laage et al., 2016; Seitz et al., 2010) and fear of recurrence has been reported by AYA cancer survivors (Cho & Park, 2017). Despite reporting avoiding cancer-related reminders, none of the participants in Study III met the criteria for cancer-related PTSD. Indeed, PTSD symptoms was not identified as a prioritised concern in any of the behavioural case formulations conducted in Study III and was not a direct target in any of the treatments. This is interesting given the attention to PTSS in the literature on cancer survivorship, as well as in existing interventions (Kazak et al., 2004; Seitz et al., 2014).

Last, consistent with a recent pilot trial of meta-cognitive therapy for AYA cancer survivors (Fisher, McNicol, Young, Smith, & Salmon, 2015) worry and rumination were identified as significant potential treatment targets in Study III along with imbalance in activity characterised by engagement in few positively reinforcing activities, stress sensitivity, procrastination, and aversive control. These findings are in line with the wider chronic illness and depression literature suggesting cancer-related depression being caused by restricted activities and disrupted routines thereby interfering with valued activities (Williamson, 2000).
Methodological strengths and limitations

Study I

The main strengths of Study I are its longitudinal design, the long follow-up, the narrow age range of the sample and the consideration of time since diagnosis. Although the inclusion and retention rates were acceptable, the sample size was small with only 28 individuals participating at T8, the most common reason for attrition being death. Indeed given the small sample size the risk of biased estimates and type II-errors needs to be considered. Whilst there were no differences between included participants and eligible non-participants with respect to sex, age, time since diagnosis, and estimated prognosis at T1 (Hedström et al., 2005), it is important to consider the possibility that those who declined participation differ from participants on unknown parameters that may have impacted on findings. It is also important to consider the possible impact of the variation with regard to diagnoses and treatments, and an underrepresentation of individuals diagnosed with CNS-tumours. Last, the appropriateness of the HADS as a screener for anxiety and depression has been questioned due to uncertainties regarding its factor structure and recommended cut-points (Coyne & van Sonderen, 2012). Additionally a low alpha value for the HADS-Depression subscale (Hedström et al., 2005) implies a risk that the proportion of possible cases has been over- or underestimated. Indeed, in contrast to the findings from Study I indicating that depression is not a challenge for long-term survivors of adolescent cancer findings from Study III indicate that depression is a concern for some AYA cancer survivors.

Study II and III

The small sample and uncontrolled design hamper conclusions regarding acceptability and preliminary effect of the intervention provided in Study III. The number of participants was neither based on a power calculation nor on data saturation (Saunders et al., 2017) and the sample size was small, consequently, the investigated phenomena may not be described completely. In spite of efforts to strengthen credibility and dependability (Graneheim & Lundman, 2004) and to transparently describe the data collection and analysis process (Fossey, Harvey, McDermott, & Davidson, 2002; Malterud, Siersma, & Guassora, 2016), the researchers’ limited experience and training in qualitative analyses and its possible impact on the trustworthiness of findings should be considered. Moreover, the background, theoretical orientation, and clinical experience of the therapists who conducted the interviews and treatments should be considered. The power asymmetry with regard to the researcher/participant; therapist/patient; older/younger; and in some cases male/female relationships may have restricted what and how much was shared...
in interviews and treatments. However, the fact that interviewers had training in clinical psychology, including establishing rapport and using open questions, and interviewed each participant twice may have overcome some of these challenges and may have contributed to rich data.

In Study III, the treatment sessions were not video- or audio recorded, weekly person-specific assessments were not included, empirical evaluation of individual behavioural case formulations were not conducted, and the validity of formulations and therapist competence was not formally assessed. As such, while internal and external supervision potentially increased the validity of the formulations and tailoring of the treatment, the lack of formal quality assessments need to be kept in mind when interpreting the findings. The data analysis in Study III was primarily conducted by one person the author of this thesis with assistance of another person. Active involvement of several researchers in the analysis with continuous dialogue could have increased reflection and provided new perspectives on the data, thereby increasing trustworthiness. Last, although one strength of Study II-III was the attempt to identify experiences and concerns specifically related to cancer, it is impossible to conclude whether participants would have experienced these difficulties anyway.

Study IV

Major strengths of Study IV were the inclusion of feasibility and acceptability criteria; the exploration of possible mechanisms of impact; and the use of both self-reports and clinician-rated measures of psychological distress. However, the small sample size and high attrition limits conclusions regarding other aspects than the feasibility of the recruitment and eligibility criteria.

Ethical considerations

All participants in Study I-IV provided informed consent before study-start. In Study I, oral informed consent was collected, in Study II-III, written consent was collected, and in Study IV consent was provided via a study website. In Study I, oral informed consent was collected from caregivers to participants younger than 18 years at study-start. In Study II-IV, all caregivers to potential participants younger than 18 years that were scheduled for an eligibility interview (Study II and III) or who provided informed consent via the study website (Study IV) were provided oral information about the study via telephone (Study II and III) and/or letter (Study II-IV). During the eligibility interviews (Study II-IV), an assessment of the potential participant’s understanding of the study and the implications of participation was undertaken to determine the need for parental consent according to Swedish legislation.
Potential participants were invited to Study I approximately three weeks after diagnosis. The time was chosen based on a clinical impression that the potential acute shock associated with receiving the cancer diagnosis usually had lessened by this time, while the psychological impact of receiving a diagnosis still could be captured. Before each assessment in Study I, a coordinating nurse at the respective paediatric oncology centre was contacted to assess whether the respective participant was cognitively, emotionally, and physically able to participate. This procedure prevented that the research group set out to reach deceased participants. In Study II-IV, names and personal numbers were retrieved from the Swedish Childhood Cancer Registry, addresses were thereafter retrieved from Statens personadressregister (SPAR). In a third step telephone numbers were searched via Internet search engines. In one known case, a postal invitation was sent to a person who had died in the time between information was retrieved from the Registry and the invitation was sent. Subsequently, the status for all potential participants were double-checked with the Swedish Population Registry shortly before invitation. In a few cases, persons receiving study-information reported that they were not diagnosed with cancer. Subsequently, the diagnostic codes included in the data from the Swedish Childhood Cancer Registry were re-reviewed by a paediatric oncologist and all individuals with diagnostic codes for which there was a risk that the individuals had not perceived that they had been diagnosed with cancer were excluded. Mentioned challenges are potentially ethical concerns associated with using the Swedish Childhood Cancer Registry to recruit to studies requiring careful considerations. It can be expected that for some the recruitment procedure raised their awareness about being registered in the Registry which may have caused distress. This relates to the ongoing discussion regarding open science, for example with regard to privacy and handling of sensitive data. It also relates to discussions regarding with what intervals informed consent should be collected from people registered in registries to ensure that they still consent to be included in the registry.

Study III and IV were uncontrolled intervention studies allowing all participants access to a treatment which was not empirically supported. Although no empirically supported treatment exists for the target population this needs to be mentioned. A number of measures were undertaken throughout Study III and IV to assure patient safety e.g. treatments were tailored based on individual case formulations and needs; therapist supervision was provided; patient safety guidelines were developed and followed; and post- and follow-up assessments including guidance to appropriate healthcare if needed were conducted. Moreover, in Study IV, the Portal via which the intervention was administered, includes functions to alert responsible researchers and therapists in case participants report high distress scores or written communication indicating risk for harm to self or other is detected.
Concluding remarks and future research

This thesis contributes to the existing literature by further increasing our understanding of long-term psychological distress experienced by AYA survivors of cancer during adolescence.

In Study I the development of HRQOL and symptoms of anxiety and depression, from shortly after a cancer diagnosis during adolescence, up to 10 years post diagnosis was examined. Findings suggest development of HRQOL, anxiety and depression is non-linear, with the majority of AYA cancer survivors appearing to adjust well. However, a subgroup report elevated levels of distress even years after diagnosis. In Study II experiences of psychological cancer-related distress were explored. Five categories of distress were identified, one reflecting distress experienced during treatment, and four distress after end of treatment. In Study III individualised CBT was preliminary investigated and experiences of cancer-related distress were identified and conceptualised using cognitive-behavioural theory. Findings suggest participants’ cancer-related distress can be conceptualised as social avoidance, fear and avoidance of emotions and bodily symptoms, imbalance in activity, and worry and rumination. However, significant difficulties with recruitment were encountered, limiting conclusions regarding the promise of individualised CBT for the identified cancer-related concerns. The recruitment difficulties encountered in Study III were also evident in Study IV in which the feasibility of an Internet-administered self-help intervention aimed to reduce symptoms of anxiety and depression among young people diagnosed with cancer during adolescence was examined. In spite of limitations, findings from the studies presented in this thesis contribute to the existing literature by highlighting important considerations concerning our current understanding of cancer-related distress among survivors of adolescent cancer and the development of psychological support specifically tailored to their needs, alongside methods to evaluate such support. Findings have further yielded a number of hypotheses regarding possible future directions to explore.

First, future studies are needed to increase understanding regarding development of distress among young survivors of cancer during adolescence compared to healthy controls and AYAs with other chronic illnesses. Furthermore, processes underpinning differences in levels of distress and changes in distress over time within the AYA cancer population and compared to other chronic illness and healthy controls needs to be further explored.

Second, future research should further examine needs for psychological support, for example, the correspondence between perceived need and self-reported distress and what types of support may be acceptable and feasible for the population. Moreover, barriers to recruitment to psychological interventions, and the role of mental health literacy and stigma in help-seeking for distress, should be further investigated.
Third, future studies are needed to examine the clinical value of cancer-related social avoidance, fear and avoidance of emotions and bodily symptoms, imbalance in activity and worry and rumination among AYAs diagnosed with cancer during adolescence. Moreover, the mechanisms via which cancer-related concerns develop and are maintained should be further explored, including the identification of potential cancer-related precipitating factors and behaviours adopted during treatment that may maintain current difficulties. For example, findings from Study III have yielded hypotheses regarding the impact of being avoided and excluded by friends during cancer treatment on subsequent social avoidance that warrant further investigation. Furthermore, research should investigate whether survivors’ cancer-related concerns are best understood using a stress-, anxiety-, or depression framework as this has implications for the selection of treatment components.

Forth, given research highlighting difficulties with help seeking, poor mental health literacy and high levels of stigma from other AYA populations, combined with findings concerning defensiveness along with PTG among AYA survivors, a more positively framed approach to intervention may represent a more acceptable approach to increase acceptance of support. As such, future research may examine the acceptability and feasibility of interventions with focus on promoting well-being, in addition to reducing distress, to potentially increase acceptability and uptake. Last, active collaboration with individuals with lived experience of cancer during adolescence to inform future research and development of feasible and acceptable study procedures and interventions are strongly recommended.

Taken together the experiences from the studies presented in this thesis demonstrate a need to return to the development phase as described in the MRC framework and reconsider the development of a psychological intervention for the study population and intended study procedures for future feasibility and controlled studies. Further development should proceed with active collaboration with the target population, taking into account learnings from the studies included within this thesis.
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