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Pain Education for Adolescents and Young Adults Living Beyond Cancer: An Interdisciplinary Meeting Report

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1. Introduction

Over the past five decades, treatment advances have resulted in significant increases in cancer survival rates across the lifespan (1–4). Yet, the cost of cure is high. Many people living beyond cancer experience short- and long-term physical and/or psychological sequelae, including persistent pain. Most cancer treatment modalities can lead to pain (5), and many survivors report experiencing pain that persists beyond treatment and reduces quality of life (6,7). Yet, pain is both an understudied and undertreated consequence of cancer. Current approaches to managing pain after cancer can be similar to those for managing treatment-related pain, with pharmacotherapy as a principal treatment modality (5). Yet, pain after cancer has unique challenges, which requires unique solutions.

For persistent non-cancer pain, pain education is a recommended treatment approach (8). The aim of modern pain education is to change someone's understanding of the biological processes underpinning pain - what pain is, why it exists, and how it works (8). There is level 1a evidence that teaching people about the biology of pain improves pain, lessens pain-related fear, and reduces the impact that pain has on their life (8–10). Yet, there have been few attempts to provide or adapt pain education for individuals living with persistent pain after cancer (although see (11,12)), and none specifically for adolescent and young adult (AYA) populations, defined here as individuals aged 15-39 years (13).

In March 2018, an interdisciplinary meeting was held in Adelaide, South Australia to set a research agenda for pain education in AYA cancer survivors. While the term 'cancer survivor' can be used to reflect an individual from the time of diagnosis until the end of life (14), we use the term here to refer specifically to those individuals in the post-primary treatment (excluding

adjuvant therapy), disease-free phase. The primary objectives of the meeting were to: 1) consider whether there is a clinical need for pain education in AYAs living beyond cancer; 2) identify unique challenges to delivering pain education within the context of AYA cancer survival; and 3) establish key research questions. The committee comprised ten professionals with research and/or clinical expertise in pain education or psycho-oncology. There was representation from medical oncology, systems neuroscience, clinical psychology, physiotherapy, and occupational therapy, and from both public and private practice settings. Also in attendance was one individual with corporate stakeholder investment (a representative from a life insurance company) and those with a personal experience of AYA cancer. We provide here a summary of the meeting and the identified research goals.

2. Pain is common and challenging after AYA cancer

Pain has been identified as a common consequence of cancer and its treatment in adults (5). More recently, pain has also been identified as an issue in AYA survivors. Studies demonstrate that up to 58.7% of young adult (YA) survivors of childhood cancer report pain (15) and they are four times more likely than their siblings to experience pain (16). Recent estimates suggest that one third to half of YA survivors of childhood cancer also report at least mild pain-related impairment (17). Those who report persisting pain after cancer are at greater risk of high distress and suicidal ideation (18). Although studies with younger adolescent survivors (aged 15-18 years) are rare, pain is also reported in this age group, especially in survivors of central nervous system and bone tumors (19,20).

Pain can also trigger distress and fear of cancer recurrence. A recent narrative review noted an important interplay between distress and pain in AYA survivors of childhood cancer (7). YA survivors of childhood and adolescent cancer who report limb pain also report greater illness-related uncertainty (20). Although active malignancy can be established prior to the onset of pain, pain often becomes a primary symptom that informs diagnosis. Thus it is reasonable that pain may be viewed as a possible sign of recurrence, leading to worry and distress that persists long after primary treatment ends (21). It is also reasonable to suggest that remaining vigilant to potential symptoms of recurrent and new cancer serves a useful protective purpose (22). Yet, pain is also part of living a normal, active lifestyle, especially after intense cancer treatment. Knowing how to appraise and cope with pain is a salient challenge in AYA cancer survivorship (23).

Overall, we identified both the experiences of pain and pain-related fear as important targets in the clinical care of AYAs living beyond cancer. Following from this, we identified that both AYAs with persistent pain as well as those with heightened pain-related fear and distress (even without severe or interfering pain) have the potential to benefit from pain education. Finally, we identified a need for accessible, evidence-based interventions to help young people cope with post-cancer pain and its emotional consequences.

3. Unique challenges of post-cancer pain

A crucial challenge of tailoring pain education for cancer survivors lies in (re)conceptualizing the link between pain and threat. Key concepts of modern pain education, developed within the context of non-cancer related persistent pain, include: pain is a protective sensation that is open

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3 to modulation by many things across biological, psychological, contextual, and social domains;
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6 pain is not a marker of tissue state (damage or disease), rather it is a marker of our perceived
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8 need to protect body tissue; and, our pain system becomes more protective as pain persists
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11 (8,24). A wealth of experimental and clinical evidence (e.g., (25–27)) supports these concepts and
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13 the notion that most persistent pains do not serve a useful protective function. In non-cancer
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15 related pain, clinicians and patients can draw confidence in this notion by understanding tissue
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17 resilience under load relative to the stage of tissue healing and adaptation- the true risk of tissue
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19 damage is very low, despite the level of pain (8). In cancer survival however, the notion that pain
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21 does not serve a protective function is no longer straightforward because the context is not one
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23 of injury, healing, and resilience under load. Instead, the context is often one in which pain once
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25 was and could again be tightly linked to bodily threat. One might even argue that an over-
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27 protective pain system actually holds some ecological value – it may increase the likelihood of
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29 detecting cancer recurrence earlier (although, of note, early detection of recurrent disease does
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31 not always correlate with improved outcomes (22)). Notwithstanding these complexities, we
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33 offer a potential narrative for pain education in AYA cancer survivors, based on addressing the
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35 link between pain and threat, in Box 1.
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42 Cancer survivorship is also a changing environment. Routine follow-up examinations can
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44 bring only temporary reassurance that pain does not indicate a recurrence or secondary cancer.
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47 New and persistent pains can indicate new or recurrent disease at any stage during AYA cancer
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49 survival, even many years after treatment and follow-up has ended. These realities reflect a
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51 significant challenge for the young patient building a new understanding of pain, for the scientist
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attempting to develop appropriate education content, and for the clinician delivering education in this uncertain environment.

An additional challenge is that post-cancer pain exists within a complex constellation of survivorship concerns and needs. Other needs may be prioritized above managing pain. These needs include returning to school or work, maintaining and rebuilding social relationships, seeking psychological support, and reducing or accommodating impairment caused by cancer treatment. Pain is also not the only disabling and distressing post-cancer symptom. Cancer survivorship is often accompanied by altered bodily sensation. For example, fatigue is prevalent and impairing after many cancers. Often pain and fatigue coexist in AYA survivors, with each potentially contributing to the other over time (28,29). This situation represents a significant challenge for researchers in developing educational content and delivery methods that might be integrated in wider survivorship management. A final consideration is that survivors may not prioritise their pain for various reasons, such as fear of appearing ungrateful to their clinical care team who saved their life, a coping style where survivors see physical symptoms as normal, and not wanting to be perceived as not coping. Such avoidance of pain reporting represents a challenge in identifying those survivors who may benefit from pain education the most.

4. Unique challenges of the AYA population

Treatment completion in AYAs co-occurs with normative developmental, physical, and social changes that pose unique issues in survivorship. For younger survivors, there can be a transition from pediatric to adult medical care. The responsibility for monitoring and reporting symptoms such as pain thus moves from the parent or caregiver to the young adult survivor, although some

teenagers will likely take on this responsibility sooner. The transition of care also brings a challenge for integrating education in a way that remains consistent across providers. The transition to survivorship can also coincide with the profound transition from adolescence to adulthood and to independence. Reconceptualizing pain may be the first step in promoting broader self-management of pain across all aspects of the survivors' life, a challenge that will be particularly resonant in those survivors still building a sense of independence and self-efficacy.

Interventions targeting pain must also be situated within the broader understanding of how late effects emerge across time. The prevalence of frailty and comorbidities is high among AYA cancer survivors, suggestive of accelerated aging (30). Pain may not occur immediately following treatment completion, but instead may emerge years later. This is in line with evidence that pain is more common in older than younger adult survivors of childhood cancer (16). Thus, there is a need to assess for pain problems at multiple points throughout the AYA survivorship trajectory. Moreover, pain can also result from limb-removing and limb-sparing surgeries common for AYA-related cancers such as osteosarcoma. Pain education will likely only resonate with these young survivors if it addresses age-typical concerns regarding physical limitations and body image following surgery.

5. Outstanding research questions

There are a number of research questions that, if addressed, will propel this field forward.

i. What are the characteristics, impact, and time course of pain in AYA cancer survivors?

Our knowledge of pain in AYA cancer survivors is largely limited to estimates of its prevalence, especially in survivors of childhood cancer (7). Critical aspects of the AYA

survivors' pain experience are missing from our datasets. These include location, intensity, time of onset since post-primary treatment completion, interference, disability, and cognitive, affective, and social dimensions of pain (7). A fuller understanding of pain problems in AYA cancer survivors will be required to develop potent education tools.

ii. What factors predict the development of post-cancer pain across different AYA cancers?

Longitudinal data are substantially lacking. There is some evidence of differences across treatment and disease types. For example, pain seems to be more prevalent in survivors of childhood bone cancer than it is in survivors of childhood leukemia (16). However, there is little understanding of the biopsychosocial factors predicting post-cancer pain. Prediction will aid identification of in-need groups while enabling and informing early intervention.

iii. How do AYA survivors make sense of pain? We know almost nothing about how AYA

survivors assign meaning to post-cancer pain, and the distress that pain can cause. We need qualitative and quantitative studies of how AYA survivors across different disease populations attend to, interpret, and respond to pain in different body sites and with different qualities (21). Outstanding questions include how survivors attribute cause to *their* pain, and whether or not they believe it will remit. Such data will be essential for tailoring pain education content for this group.

iv. How should pain education be delivered? Many individuals travel long distances to

receive cancer treatment at specialized hospitals (31). Adolescent survivors may also move away from their survivorship care teams to attend tertiary education or pursue employment. Thus, limited access to the original oncology care team can be problematic.

Oncology care teams also have the burden of finding time to provide supportive care beyond immediate medical needs. It is thus an outstanding question as to how best to deliver pain education to AYA cancer survivors. Could education be integrated as part of routine long-term follow-up, alongside education about fertility and cardiac sequelae? Should pain education be delivered by the primary care team, catalyzing on the shift of cancer follow-up care into primary care practice (32,33)? One promising method may involve harnessing easily-accessible digital health tools such as videos (e.g., (34)) and smartphone apps (e.g., (35)), especially given the appeal of these electronic methods to AYA populations.

- v. **How can pain education be delivered within the context of the threat of disease recurrence?** A critical difference between post-cancer pain and other types of pain is the possibility that pain may reflect recurrent or new disease. The content of pain education for AYA survivors will need to integrate contemporary knowledge on symptom monitoring as a strategy for early detection (22) . Pain education will need to reflect variability between cancers in the utility of symptom monitoring as an early detection strategy, and consider healthcare professionals' level of confidence in the content within this context.
- vi. **What pain-related concepts should be targeted?** There are ongoing efforts to establish key target concepts of pain education in adults (36) and young people (37). However, we do not know whether these target concepts are equally relatable to post-cancer pain, nor whether they will resonate with AYA survivors. Concepts that may be important for this population include that pain is influenced by many factors, that there are many things

survivors can do to influence pain, and that pain is a sensible protective adaptation of an adaptable nervous system.

- vii. **Should education go beyond pain?** Should post-cancer education extend beyond pain to cover all common, and often comorbid post-cancer symptoms (e.g., fatigue)? There is growing evidence that all our bodily sensations, including but not limited to pain, fatigue, itch, stiffness and breathlessness, can be understood from a similar functional perspective of providing protection by urging protective behaviour (29,38). In line with this, similar cognitive and neural mechanisms of perception and persistence are echoed in disorders of chronic fatigue (39) and chronic itch (40). Thus, an educational approach aiming to change understanding of the biology of these sensations *in general* and their role in protection may add value.

6. Conclusions

The 2018 interdisciplinary meeting on pain education after AYA cancer, held in Adelaide Australia, successfully convened clinical and research professionals across pain science and psycho-oncology to assess clinical need, identify challenges, and prioritize issues for future research. We identified that AYAs with persistent pain and those with heightened pain-related fear have the potential to benefit from pain education. We identified a number of unique challenges of engaging AYA survivors in pain education. These include (re)conceptualizing the link between pain and threat in an uncertain environment, co-occurring sensations such as fatigue, transitions of care and health management, the changing trajectory of pain across the lifespan, and concurrent issues such as disability and body image. Finally, we identified research questions

that, if addressed, will aid the development of tailored pain education tools and interventions for AYAs living with pain after cancer.

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Box 1. A potential narrative for explaining pain to AYA cancer survivors

- Pain is an amazing method by which your body and brain protects you from danger.
- It makes total sense to have pain when your body is exposed to substantial threat.
- Our pain system is highly responsive and yours has every reason to have ramped up the sensitivity level.
- As a result, your pain system has developed a considerable safety buffer – it is now on high alert. This is an incredible, adaptive response by your nervous system to keep you as safe as possible.
- This expanded safety buffer means that you will be protected, by pain, from things that are not in fact dangerous. You can learn to identify all the things that turn your pain up and this will reduce their impact.
- You can also learn to identify things that turn your pain down and practise them so that your safety buffer operates at a helpful level, protecting you from things that are dangerous, but not from things that aren't dangerous.