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**Article:**

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<https://doi.org/10.1002/pon.4989>

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**Long term issues and supportive care needs of adolescent and young adult childhood brain tumour survivors and their caregivers: A systematic review**

**Running title:** Experiences of childhood brain tumour survivors and their caregivers

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**Systematic review registration:** PROSPERO: International Prospective Register of Systematic Reviews: CRD42017072865

**Word count:** 5771

## **Abstract**

**Objective:** Long term issues following diagnosis and treatment of a childhood brain tumour often become apparent as the survivor enters adolescence and young adulthood. Their caregivers may additionally face long term impacts on their emotional and psychological functioning. This review synthesised evidence on the issues and supportive care needs of adolescent and young adult (AYA) survivors of a brain tumour diagnosed in childhood and their caregivers.

**Methods:** Electronic databases were searched up until September 2017. All studies reporting on issues or needs of childhood brain tumour survivors (aged 14-39) and their caregivers were included. Narrative synthesis methods were used to summarise, integrate and interpret findings.

**Results:** 56 articles (49 studies) met the inclusion criteria. Social issues (i.e. isolation, impaired daily functioning) were most commonly reported by survivors, followed by cognitive (i.e. impaired memory and attention) and physical issues (i.e. endocrine dysfunctions and fatigue). Survivors experienced poorer social functioning, sexual functioning, and were less likely to be employed or have children, when compared to other AYA cancer survivors. Caregivers experienced reduced support as the survivor moved into young adulthood. Caregivers reported uncertainty, increased responsibilities and problems maintaining their own self well-being and family relationships. Few studies reported on supportive care needs. Survivors expressed a need for better educational support and age-specific psychosocial services.

**Conclusions:** Surviving a childhood brain tumour can be particularly challenging for AYA survivors and their caregivers. Robust structured research is needed to identify specific support needs of both survivors and their caregivers and how these can be optimally addressed.

**Keywords:** cancer, oncology, adolescent; brain tumours; caregivers; supportive care; survivors; systematic review; young adult

## **Introduction**

In children and young adults under 19 years of age, primary brain and central nervous system tumours are the most common solid tumour, with an annual age-adjusted incidence rate of 5.57 per 100,000.<sup>1</sup> With improved duration of survival,<sup>2,3</sup> more attention is required to address the potential late effects on quality of survival.

Adolescence and early adulthood is a unique and complex developmental phase characterised not only by significant physical and cognitive changes but also critical psychosocial challenges, relating to self-identity, relationships, individualisation, developing autonomy, and intimacy/sexuality.<sup>4</sup> Disruptions associated with brain cancers treatment can delay or complicate the achievement of age-appropriate 'life events'. Adolescent and young adult (AYA) survivors may therefore be particularly vulnerable to experiencing late effects or other issues.

A brain tumour affects not only the survivor but also those around them. Responsibility for caring and supporting childhood survivors in the longer term is often met by their immediate family. Neurocognitive symptoms and personality changes of the survivor importantly mark the caregivers' experience. Many caregivers feel inadequately prepared and suffer from symptoms of depression, anxiety and distress.<sup>5,6</sup>

The 2006 National Institute for Health and Clinical Excellence (NICE) guidelines promote that continuous aftercare should meet the needs of brain tumour survivors allowing for age, gender and cultural differences. The guidelines state:

“Younger patients with continuing care needs should also be carefully considered... procedures should be in place to ensure the continuing care needs of younger patients with CNS tumours are appropriately met”<sup>7</sup>

However, there is little information in the guidelines on how follow-up care should address and meet young survivors and caregivers supportive care needs.

Previous systematic reviews have focused on the experiences of AYA survivors or caregivers with mixed cancer diagnoses.<sup>8, 9</sup> Other reviews have concentrated on the experiences of children,<sup>10, 11</sup> adults,<sup>12</sup> or caregivers of adult brain tumour survivors.<sup>13</sup> To date, no systematic review has collated evidence on the experiences of AYA childhood brain tumour survivors and/or their caregivers. Given the complex developmental stages and increased occurrence of life events during adolescence and young adulthood, it is expected that the experience and impact of a childhood brain tumour on AYA survivors will be different from those still in childhood or older brain tumour survivors.

We aimed to systematically identify and narratively synthesise evidence on the issues that AYA childhood brain tumour survivors and their caregivers face and their supportive care needs. We hope that the results will help identify gaps in service provision, help clinical staff understand their role throughout the survivorship period and guide policy and service development.

## **Methods**

PRISMA guidelines<sup>14</sup> for systematic reviews were utilized as a template for the methodology. The following electronic databases were searched: Medline (Ovid), Embase (Ovid), PsycInfo (Ovid), Pubmed, CINAHL (Ebsco), and the Cochrane library (Wiley). The grey literature were searched using Web of Science and the NHS Evidence. The end date of the searches was September 2017. The searches were developed for the concepts: brain tumours, children and survivorship. Guided by an Information Specialist (RRL), the searches were developed combining subject headings and free text terms for each concept. See Supplementary Material 1 for the full search strategy.

### **Selection criteria**

Original, peer-reviewed articles were included according to the following criteria:

1. Human participants with a primary diagnosis of a brain tumour and/or a primary caregiver of a survivor. If the study had a mixed cancer participant group, brain tumour data had to be reported separately.

2. Survivors of a paediatric brain tumour, currently aged 14-39 (, or caregivers of survivors within this age range. The study sample could extend beyond these age parameters provided the results for the target age range were clearly reported.
3. Articles reporting data that focused on any issues, needs or unmet needs of brain tumour survivors and/or their caregivers.

There are contradictions across the oncology literature regarding how the AYA age group should be defined.<sup>15, 16</sup> Definitions differ greatly amongst organizations, countries and AYA literature. For this review, we set the AYA age range as 14-39.

Exclusion criteria were: articles not in English, reviews, reports on incidence of brain tumours or treatment trials / intervention programmes not covering AYA patient or caregiver issues and needs.

There was no restriction on publication date or study type. The lead investigator (EN) determined whether the articles were eligible for inclusion, with a random sample (20%) independently screened by a second reviewer (FB).

#### Data extraction and Quality Assessment

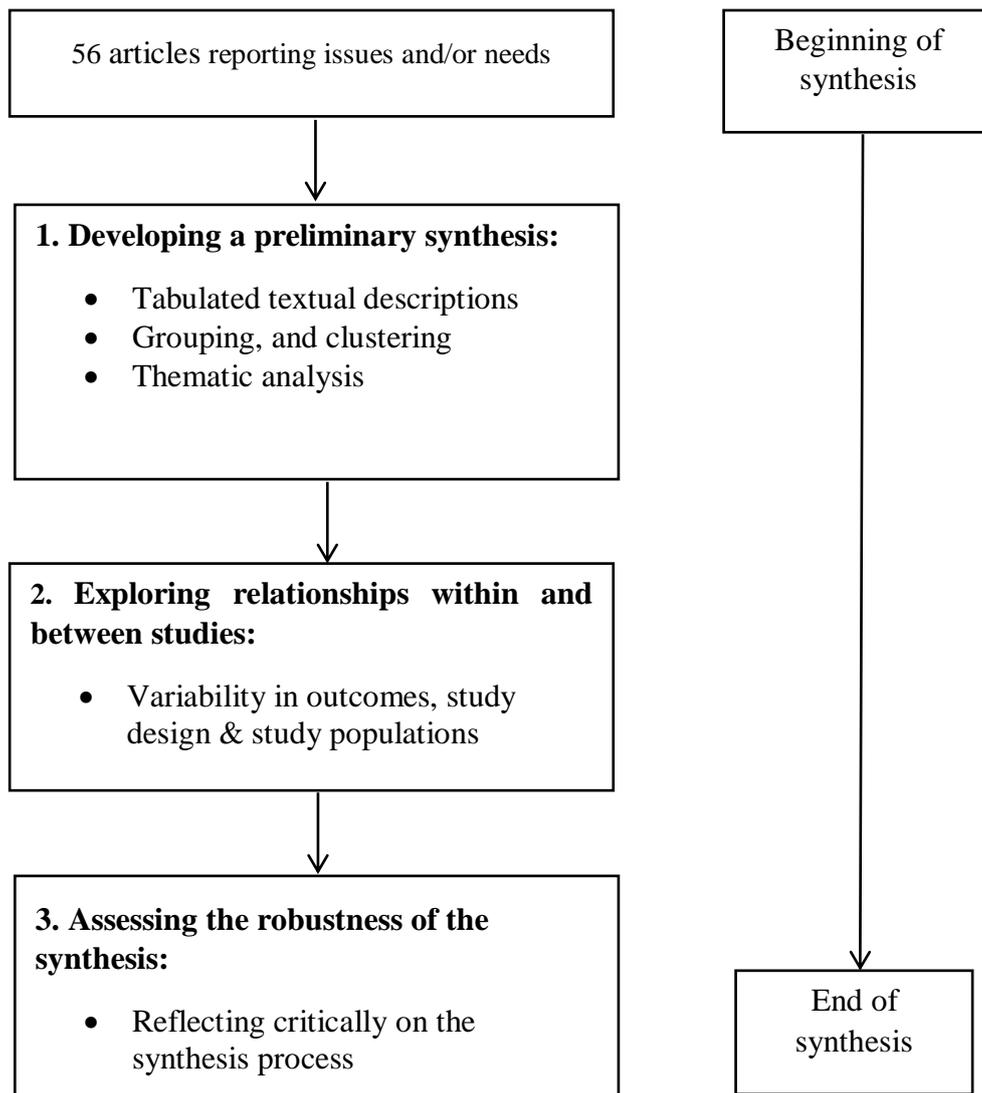
Data extraction was performed using a standardized template. Data were extracted for the study objective, design, sample-size, clinical characteristics of the survivors, measures and outcomes. All included studies were assessed using the Mixed Methods Appraisal Tool (MMAT),<sup>17</sup> which has been validated for the critical appraisal of studies with diverse designs. See Supplementary Material 2 for MMAT scores. No studies were removed because of their appraisal score but lower quality study findings should be interpreted with greater caution and in consideration of their limitations.

#### Narrative Synthesis

Narrative synthesis methods were used to summarise, integrate and interpret the findings articles included within the review. A narrative synthesis was appropriate given that there was little uniformity amongst the methods, findings, or outcomes measures used. Fig. 1. shows the processes undertaken in the narrative synthesis, guided by Popay et al.<sup>18</sup> and the Cochrane Consumers and

Communication review group handbook.<sup>19</sup> The City of Hope quality-of-life conceptual model<sup>20</sup> was adapted to map the survivors issues. The original model proposed a quality of life model for long term cancer survivors: physical wellbeing and symptoms, psychological well-being, social well-being and spiritual well-being. We added cognitive symptoms to better fit AYA brain tumour survivor issues.

Figure 1 – Narrative Synthesis Process

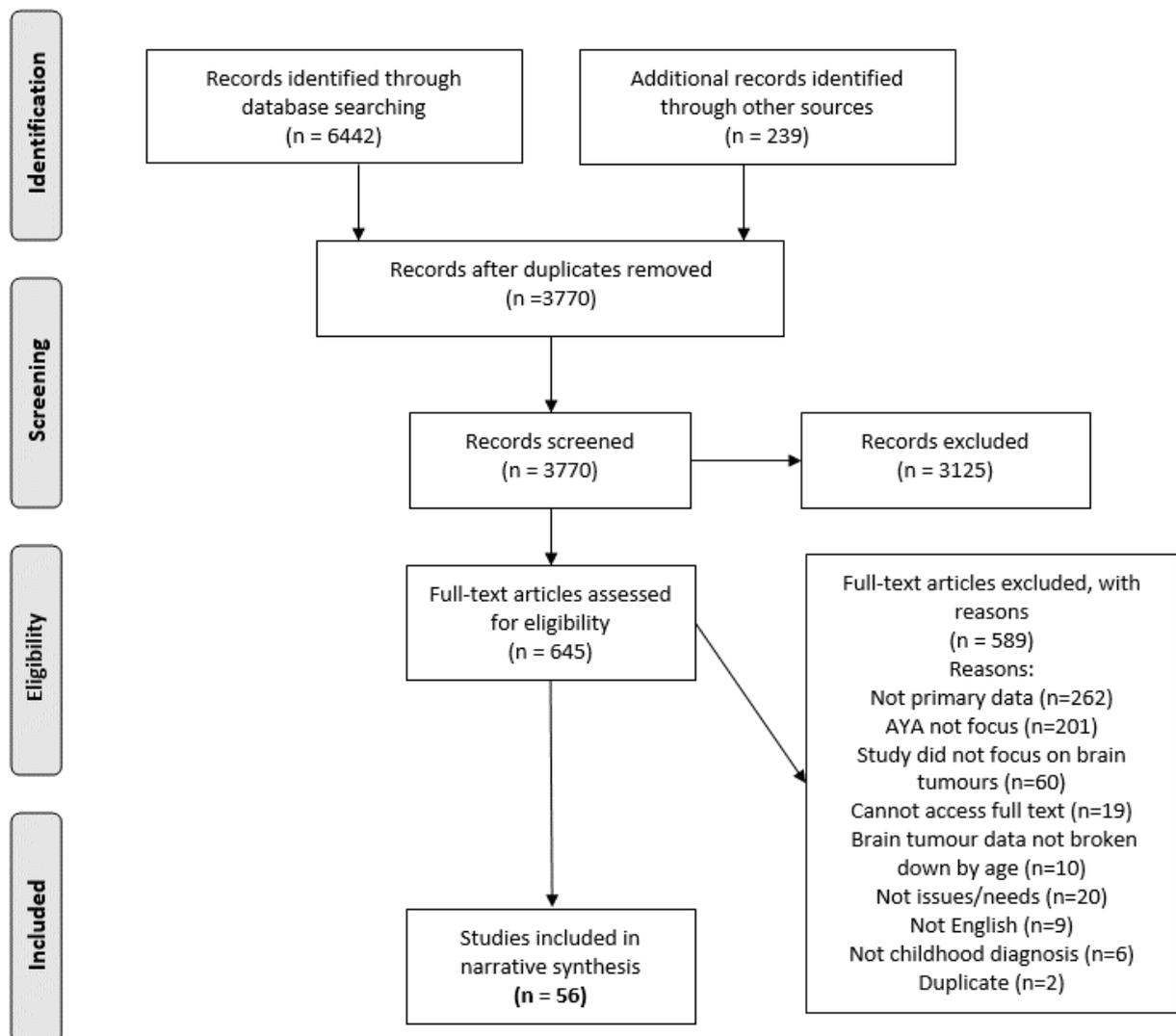


## Results

### Search Results

In total, 6642 article citations were found. 239 additional records were identified through hand searching journals and reference lists. Once duplicates were removed a total of 3770 articles remained. We excluded 3125 after reading the abstract because they did not meet the inclusion criteria. Of those remaining, 645 were retrieved in full-text, we excluded 589 because they did not meet the inclusion criteria. In total 56 articles (49 studies) remained for inclusion within the narrative synthesis. The process of searching and sifting is shown in Fig. 2.

Figure 2 – Flow chart showing selection of studies



Abbreviations: AYA = Adolescent and Young Adult

## Study characteristics

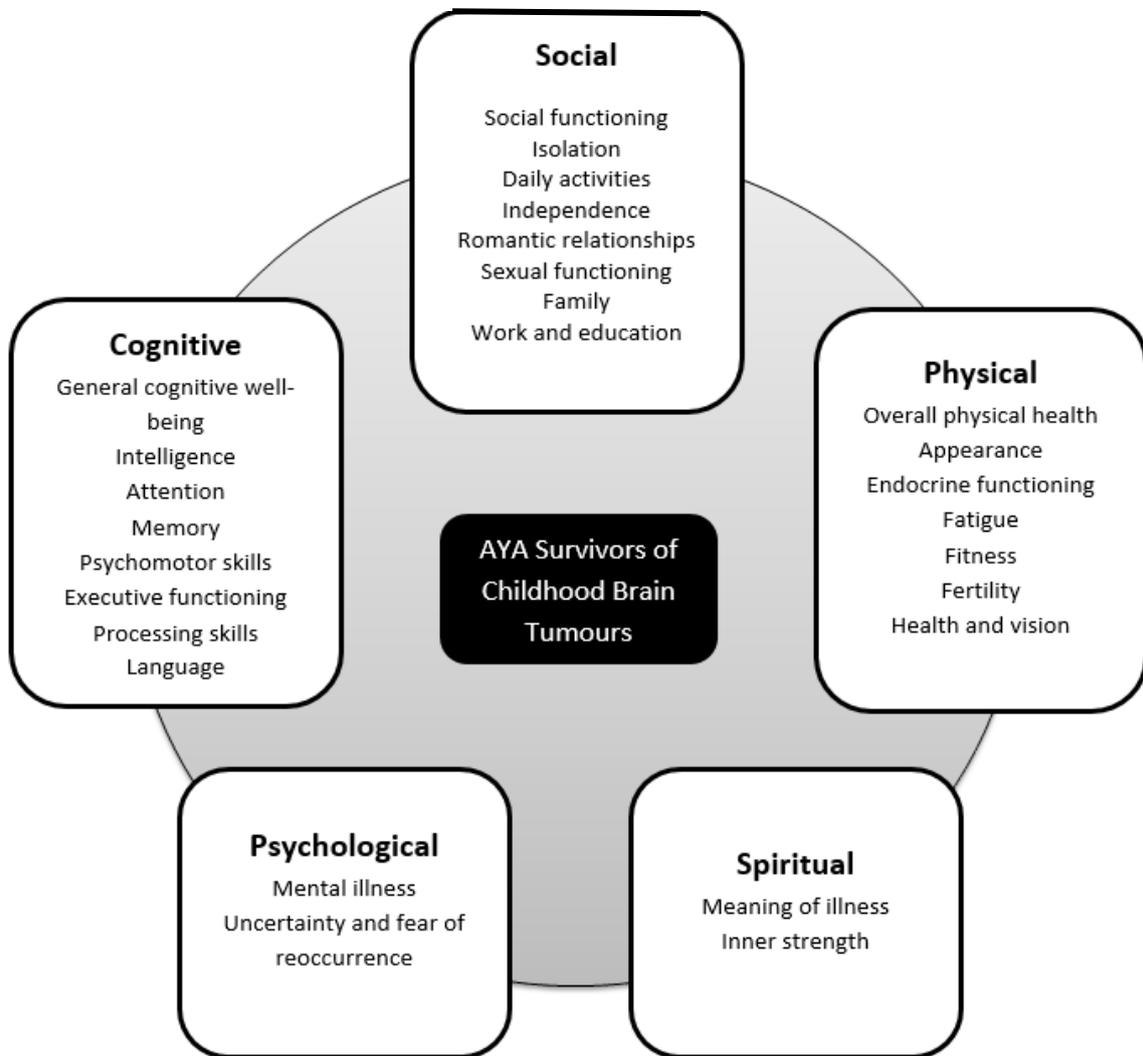
Over half of the studies had been published after 2013 (57%), and 53% of studies originated within the United States. The majority of studies (76%) reported quantitative data; five (10%) were qualitative; and seven (14%) utilised a mixed methods approach. The majority collected data from the survivors only (86%), in three studies (6%) data was solely from caregivers and in four (8%) there was data from both survivors and caregivers. In over a third of studies (35%) there was a comparison or control group.

Over half the studies (55%) reported data from mixed brain tumour samples. A further eight studies (16%) reported one specific brain tumour group. Fourteen studies (29%) had recruited patients with varied cancer types, but reported brain tumour data separately. See Supplementary material 2 for further description of studies.

## **Section 1: Survivor issues**

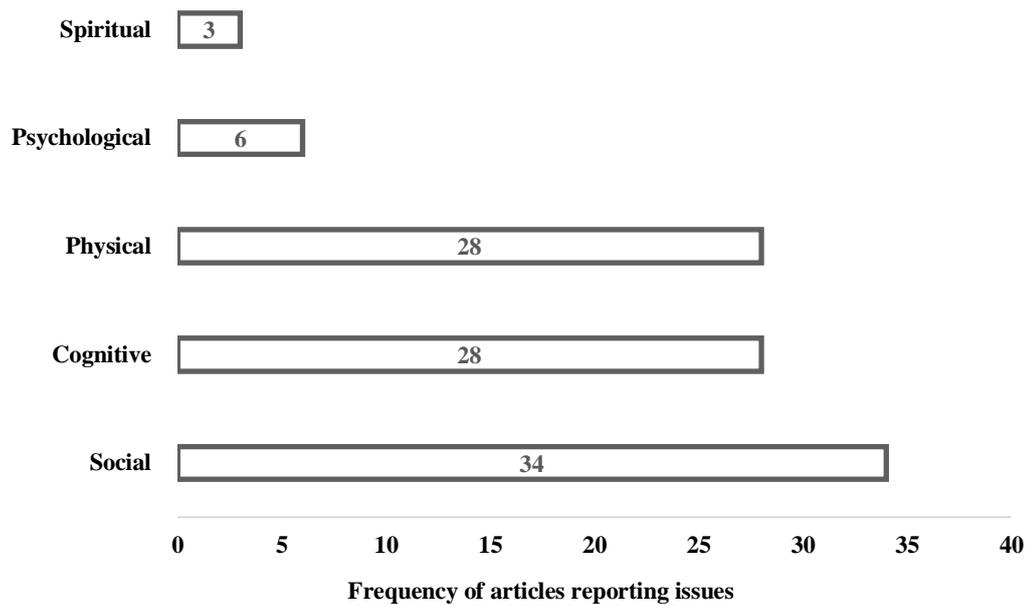
Survivor issues were derived from the main themes found in the articles and categories used in the City of Hope quality-of-life model.<sup>20</sup> The model depicts four domains: physical, psychological, social, and spiritual as priorities for assessment to ensure comprehensive quality care. The model has been adapted to illustrate the potential issues AYA brain tumour survivors may encounter which could impact on their quality of life (see Fig. 3.). The main adaptation is the addition of the cognitive wellbeing category.

Figure 3 – Adapted Quality of life Cancer survivorship model



Adapted from: Quality of Life Conceptual Model Applied to Cancer Survivors, City of Hope Beckman Research Institute 20

Figure 4 – Frequency of articles that reported survivor issues by theoretical framework theme



MMAT Scores by theme: Spiritual issues = All 75, Median = 75; Psychological = 75-100, Median = 75; Physical = 25-100, Median = 75; Cognitive = 25-100, Median = 75; Social = 25-100, Median = 75

#### Social well-being

Social well-being was the most commonly referred to theme (see Fig. 4): Thirty-four articles investigated the impact a childhood brain tumour may have on social domains of an adolescent or young adult.

Articles reported AYA survivors having impaired social functioning, expressed as e.g., avoiding social situations,<sup>21</sup> or social isolation.<sup>21-26</sup> Poorer social functioning was reported among brain tumour survivors compared to other cancer groups.<sup>27, 28</sup> Specifically, multiple studies reported a link between poorer social functioning and anti-cancer treatment and diagnosis.<sup>22, 24, 29, 30</sup> During treatment, survivors spend a long time in social isolation after which some young people found it difficult to engage with others again.<sup>24</sup> Physical issues, e.g., headaches or impaired fitness, as well as cognitive deficits were linked to social functioning,<sup>21, 31, 32</sup> and impacted on survivors' abilities to join in sports or hobbies.<sup>32</sup>

Six articles reported impaired daily functioning and/or functional living skills,<sup>22, 31, 33-36</sup> survivor restrictions ranged widely in severity,<sup>33, 34</sup> with only a small minority reporting no limitation in daily

activities.<sup>36</sup> Qualitative work linked these restrictions to impaired cognitive functioning through difficulties with reading or handling finances, or managing medications.<sup>22</sup> AYA survivors rarely lived independently,<sup>27, 35, 37, 38</sup> which was linked to feelings of frustration.<sup>25, 31, 32</sup> That said, survivors generally report close relationships with their family.<sup>21, 22, 31</sup> Poorer survivor cognitive functioning<sup>39</sup> and lower income<sup>36, 39</sup> was associated with worse family functioning.

In romantic relationships, AYA survivors see themselves as less valuable mates to a prospective partner.<sup>40</sup> Survivors were likely to be sexually inactive.<sup>27, 31, 35, 41-43</sup> Reduced sexual activity was found when compared to other cancer groups<sup>27, 41, 43</sup> and the general population.<sup>31</sup> Survivors of a childhood brain tumour were also less likely to have children compared to general population controls<sup>44</sup> and other cancer survivors.<sup>45, 46</sup>

Many AYA survivors need assistance to perform well in school.<sup>31, 38, 46</sup> Education experiences were often described as problematic: including missing school, cognitive difficulties - feeling misunderstood, facing bullying and social isolation.<sup>24, 25, 32</sup> Survivors were more likely to be unemployed later in life when compared to age and gender matched controls<sup>46-48</sup> and other cancer survivors,<sup>27, 49</sup> with reported unemployment rates varying from 8-70%.<sup>27, 33, 35-39, 46-51</sup> Issues in attaining or keeping a job included fatigue, poor concentration, physical issues (e.g., epilepsy), cognitive difficulties, and poor social skills.<sup>22, 31, 32</sup> Some survivors had sheltered work, a setting in which people with disabilities receive services and training to develop work-related skills and behaviours.<sup>37, 38, 47</sup> AYA survivors were found to have significantly lower levels of vocational identity and career readiness (i.e. ability to perform work tasks, social skills) when compared to AYA non-cancer survivors.<sup>52</sup> Vocational identity is an integral part of human development, especially for adolescents. This process includes the formation of career: objectives, goals, aspirations and plans. Financial difficulties were also common in AYA brain tumour survivors.<sup>39, 53, 54</sup> AYA survivors were more likely than other cancer groups to be receiving disability benefits.<sup>54</sup>

## Cognitive well-being

Different aspects of cognitive deficits were reported in 28 articles. Overall, in these articles, cognitive functioning was found to be impaired. AYA brain tumour survivors are often at higher risk of cognitive issues than other cancer survivors.<sup>27, 49, 53, 55</sup> Impaired memory seemed to be the most common cognitive issue.<sup>21-26, 35, 39, 47, 48, 56-59</sup> Qualitative findings<sup>21-24, 31, 47, 56</sup> established that impaired memory was a daily issue. Memory issues were innate in how survivors' and their caregivers assessed their ability to self-care and meet developmental milestones, such as living independently,<sup>22</sup> making friendships,<sup>23</sup> and educational achievements.<sup>31</sup> For some memory loss was described as an invisible effect.<sup>24</sup> Unlike physical effects, invisible effects may go undetected and mean the appropriate additional support may not be offered.

Attentional deficits were particularly challenging because of their consequent impact on the development of other cognitive abilities, social functioning and academic achievement.<sup>21, 35, 48, 57, 59</sup> Evidence suggested that AYA survivors scored lower in Intelligence Quotient (IQ) scores and had limited mathematical skills.<sup>29, 33, 34, 47-49, 55, 58, 60</sup> AYAs scored lower in IQ testing than population controls.<sup>34, 60</sup>

Many survivors presented with poor processing speeds,<sup>21, 23, 37, 39, 48, 59, 61</sup> leading to poorer physical and/or mental health,<sup>37</sup> social functioning<sup>21, 23</sup> and health-related quality of life.<sup>37, 39</sup> Similarly language and vocabulary issues were challenging.<sup>31, 35, 55, 60</sup> Compared to matched healthy controls, brain tumour survivors scored significantly lower in verbal assessments.<sup>31, 46, 60, 61</sup>

Some survivors suffered from impaired motor skills.<sup>31, 34, 35, 37, 46, 48</sup> Motor deficits contributed to social isolation and vocational limitation by restricting the types of activities open to survivors (i.e. playing sports or writing).<sup>31, 35</sup>

Executive functions are a diverse set of cognitive processes broadly conceptualised according to four primary domains: decision making, planning (e.g. organisation), purposive action (e.g. set shifting-the ability to move back and forth between tasks), and effective performance (e.g., preservation, goal maintenance). Survivors experienced poor executive functioning including: planning/organising,<sup>34, 48</sup>

preservation,<sup>34</sup> set shifting,<sup>34, 35, 48</sup> and flexibility.<sup>48</sup> Survivors self-reported less executive dysfunction in comparison to when their mothers reported symptoms (by proxy). This may be problematic as survivors who perceive fewer executive functioning difficulties may not pursue help or support, such as neuro-rehabilitation programmes, which may have a negative effect on other long term functional outcomes.<sup>62</sup>

### Physical well-being

Survivors had impaired general physical health.<sup>21, 27, 28, 30, 31, 46, 53</sup> More specifically symptoms included: poor mobility,<sup>21, 31, 38, 46</sup> poor physical functioning,<sup>22, 30</sup> reduced bone mineral density,<sup>63, 64</sup> hearing and/or vision issues,<sup>21, 23, 25, 31, 38, 46, 65</sup> and poor fitness levels.<sup>31, 55</sup>

At a time when physical appearance becomes increasingly more salient, AYA survivors reported having issues with their appearance.<sup>22, 24, 27, 31, 32, 38</sup> Visible effects after the tumour and treatment included –small stature, hair loss, weight issues and scars.<sup>22, 24, 31, 32</sup> Parents of survivors described that issues with body image contributed to starting/maintaining peer relationships because survivors worried they looked different from their peers.<sup>32, 38</sup>

AYA survivors' commonly had endocrine dysfunctions.<sup>21, 23, 31, 37, 38, 49, 58, 66-69</sup> More specifically, growth hormone deficiency was reported in 22-97% of survivors.<sup>33, 38, 49, 66, 67, 69</sup> Other frequently reported endocrine disorders included hypothyroidism,<sup>33, 67, 69</sup> hypogonadism<sup>31, 33, 69</sup> and cortisol deficiency.<sup>30</sup> Issues with endocrine functioning during adolescence could impact on growth and development, weight gain, reproductive processes, and mood.

Many survivors experienced increased levels of fatigue as adolescents and young adults.<sup>21, 23, 26, 27, 31, 32, 53, 67, 70, 71</sup> In comparison to other cancer survivors, brain tumour survivors were more likely to report difficulty with tiredness and fatigue.<sup>26, 53</sup> Whilst fatigue is reported as a physical issue following the cancer survivorship model, it is also a common symptom of many cognitive and psychological problems. Survivors expressed how fatigue had stopped them doing hobbies/sports and socialising.<sup>38</sup>

Regarding fertility, childhood brain tumour survivors fell pregnant significantly less often than healthy peers.<sup>44</sup> That said, brain tumour survivors' desire to have children was significantly lower than healthy peers of the same age.<sup>44</sup> For some fertility was not currently an issue, especially for adolescents, but it was something they were anxious about facing in the future.<sup>32</sup>

#### Psychological well-being

Survivor mental health did not differ from general population controls.<sup>25, 46</sup> However, one article found that AYA brain tumour survivors reported significantly poorer mental health than other cancer survivors.<sup>28</sup> Another reported that AYA brain tumour survivor had poorer psychological functioning than other cancer survivors.<sup>27</sup> The most frequent psychological problems for survivors were internalising problems and withdrawal.<sup>29</sup> Psychotic symptoms (i.e. mood dysfunction, delusional thinking and hallucinations) were diagnosed in a small number of survivors, with antipsychotic medication having little effect.<sup>72</sup>

Despite improvements in recurrence-free survival rates for children diagnosed with brain tumours, AYA survivors still worry about recurrence. In two qualitative studies participants expressed that the anxiety of whether the tumour was going to return, was one of the realities of living as a survivor.<sup>25, 56</sup> In some cases the uncertainty of recurrence negatively affected survivors' ability to plan for the future or feel engaged in life.<sup>25, 56</sup> Both studies highlight that the fear of recurrence may become an issue as survivors enter young adulthood; especially if they feel unable to plan a future, they may not reach the same developmental milestones.

#### Spiritual well-being

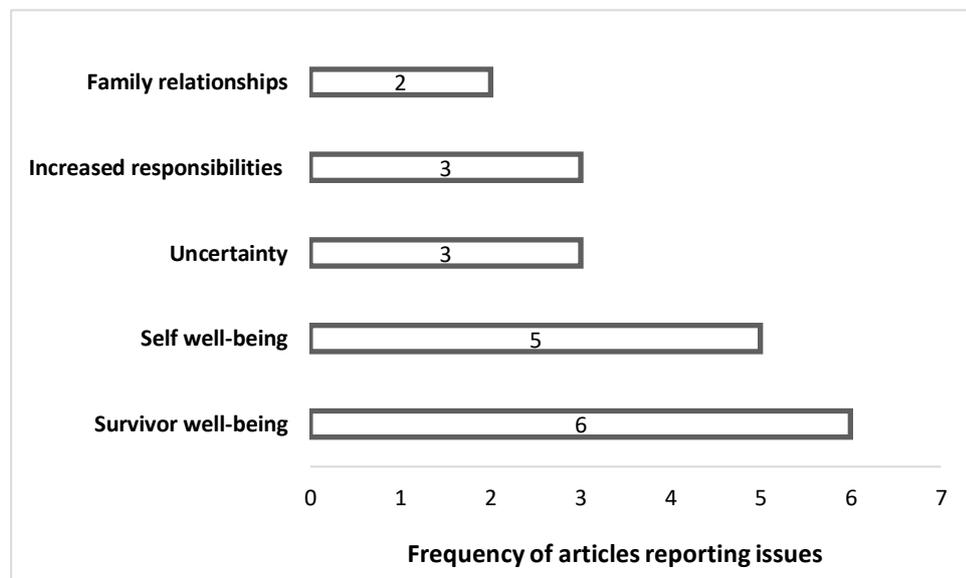
Compared to other AYA cancer survivors, brain tumour survivors had significantly poorer optimism, self-esteem and vitality.<sup>28</sup> However, survivors were not less resilient.<sup>27</sup> The way survivors viewed the meaning of their illness differed vastly.<sup>22, 25, 31</sup> Some focused on the negative effects of illness, seeing themselves as 'losers' for their deficits. Some survivors said they were treated differently because of their cancer history, and felt that others pitied them.<sup>31</sup> Yet in the same study half of survivors described at least one positive consequence of surviving a brain tumour on their world view.<sup>31</sup> Some

survivors positively viewed their experience of surviving a brain tumour, feeling it had made them more mature and were trying to move beyond the illness.<sup>25</sup>

## Section 2: Caregiver Issues

Eight articles reported caregivers' issues,<sup>21, 23, 24, 30, 32, 36, 73, 74</sup> four focused specifically on studying the role of the family caregiver.<sup>30, 36, 73, 74</sup> Caregiver participants consisted of parents (mothers and fathers),<sup>21, 30, 75</sup> mothers only<sup>23, 36, 73, 74</sup> and mixed family members (including grandparents).<sup>24</sup> Caregiver issues had five themes (see Fig. 5): Survivor well-being; Uncertainty; Increased responsibilities; Self-well-being and Family relationships.

Figure 5 – Frequency of articles that reported caregiver issues by theme



MMAT Scores by theme: Family relationships = All 75, Median = 75; Increased responsibilities = All 75, Median = 75; Uncertainty = All 75, Median = 75; Self well-being = 75, Median = 75; Survivor well-being = 75, Median = 75

### Survivor well-being

Parents were concerned about the survivor's well-being. Caregivers worried that survivors had limited social life and that they weren't accepted into social groups.<sup>24, 32, 36, 73</sup> They acknowledged that survivors' lives were fundamentally different to others their age because of the brain tumour and worried if they would ever recover their previously existing social network.<sup>32</sup> Parents were not only

worried about survivors' current issues but about potential issues in the future.<sup>30</sup> In particular their ability to find a romantic partner<sup>21, 30</sup> and have children.<sup>32</sup> Others feared that their potentially forever-dependent children might outlive them.<sup>30</sup>

### Uncertainty

Uncertainty was a common theme, especially regarding the survivors' future health.<sup>30, 32</sup> Like seen in survivor reports, the threat of relapse was a pressing issue. In some cases this threat stopped parents from planning future activities, and instead they lived very much in the present.<sup>30, 32</sup> Another source of uncertainty came from whether their child would ever reach independence.<sup>32, 74</sup> In one study the majority of parents believed their child would never be independent.<sup>74</sup> Some worried about leaving them alone in the house or their ability to be financially independent.<sup>32</sup>

### Increased responsibilities

Caregivers had increased responsibilities, tasks that usually healthy AYAs handle independently. Qualitative findings described parents assisting survivors in: everyday tasks (i.e. cooking meals, managing finances and promoting hygiene); managing medications, education; arranging social contacts; and support with hobbies and leisure activities.<sup>24, 32, 73</sup> In some cases parents decided to home school the survivor because they felt they needed extra assistance and support.<sup>24, 32</sup>

### Self-Well-being

Five studies reported diminished caregiver well-being.<sup>23, 30, 32, 36, 73</sup> Parents revealed that because of their caregiving demands, they had less time and energy to dedicate to maintaining self. Parents described feeling fatigued,<sup>32, 73</sup> having problems maintaining their own social relationships,<sup>23, 30, 73</sup>; and not being able to pursue their own careers.<sup>73</sup> Their social lives declined because caring became their main priority, meaning they had less time to engage in social and leisure activities, thereby limiting their social world.<sup>23, 30</sup> Caregiver health plays a major role in family life, one study highlighted the direct association between caregiver well-being and better family functioning.<sup>36</sup>

## Family relationships

The pressure of keeping healthy family relationships, whilst caring for a young brain tumour survivor, could prove to be challenging for caregivers. Families of children who have survived a brain tumour may face issues that make family management more difficult. For some caregivers their marriage had suffered – causing separation.<sup>21, 30</sup> Strain was noted because of the added pressure of caring for the survivor and also because of discrepancies between partners about how best to care for their child.<sup>30</sup> For others the diagnosis, treatment, and late-effects had brought them closer together.<sup>21</sup> Parents worried about their relationships with survivors' siblings, anxious they felt alone or as if they “got the short end of the stick”.<sup>21</sup>

## **Section 3: Supportive care needs**

### Survivor Needs

Only three studies aimed to specifically identify survivor needs.<sup>23, 56, 76</sup> AYA needs differed from those of paediatric and older adult survivors, including the need for age-specific social resources. AYA brain tumour survivors were more likely to value social activities and support groups, compared to other cancer groups.<sup>76</sup> Social activities and support groups were favoured above informational mailing, weekend retreats, informational workshops or individual counselling.<sup>76</sup> Social resource recommendations included creating several arenas for peer support.<sup>56</sup> Parents highlighted that their child needed more opportunities to merely “hang out” with peers.<sup>21</sup> When an AYA social support programme was evaluated survivors relayed positive experiences.<sup>23</sup> Participation in the programme provided survivors with “something to look forward to”, a regular social activity, important in addressing some of the social isolation issues. Furthermore, including the use of social media as a part of the programme was recognised as a manageable and satisfying way to decrease isolation within the survivors.

Some survivors felt the current health care delivery did not meet all their needs. Many were unsure how to discuss issues with physicians, and others felt the information they received was inadequate because the medical staff communicated solely with their parents.<sup>47, 56</sup> Providing survivors with age-

specific resources about late effects and psychosocial challenges at each follow-up appointment may be helpful.<sup>56</sup>

Several studies stressed the need for comprehensive follow-up services for childhood survivors.<sup>31, 37, 38, 50, 69, 70</sup> The importance of follow-up in a survivorship clinic to offer coordinated, multidisciplinary care that can address the multiple issues/needs of survivors of brain tumours while addressing caregiver needs and family functioning was highlighted. One study stressed that health professionals should be mindful that many survivors may define themselves as healthy and will not necessarily identify late-effects caused by their illness/treatment.<sup>31</sup> Findings specifically identified careful follow up of endocrine function,<sup>69</sup> liver function,<sup>70</sup> and health related quality of life.<sup>37, 50</sup>

The stress of keeping up with their classmates in an environment that was not equipped to handle their needs proved difficult for many young survivors.<sup>24</sup> Regarding educational support, survivors described needing: extra time to complete assignments/exams, more one-on-one help, and extra encouragement.<sup>24, 32</sup> Some survivors said that by appearing more “normal” meant that they were not always recognised as needing additional support with their academic work.<sup>24</sup> Throughout survivor narratives, the paradox of wanting special considerations within the classroom yet not wanting to be different or singled out among their peers was strongly evident. Another study concluded that academic/vocational goals and expectations must be observed over time, as learning needs may change.<sup>22</sup>

#### Caregiver needs

Parents consistently reported that there was not enough support available for themselves or the survivor during adolescence and young adulthood. Parents felt that when their child was undergoing treatment they had support, but that support declined as they moved further away from the treatment.<sup>30, 32</sup> Regarding useful support services, parents expressed that parent support groups and survivorship education classes would be most helpful. Other services mentioned were parental health and self-care classes and practical support such as financial assistance.<sup>21</sup>

Two articles highlighted that different caregivers and families deal with survivorship differently and will have different needs.<sup>30, 74</sup> One study found that clinicians find it challenging to tailor interventions to family and caregiver needs, as tools to assess family functioning and caregiver coping are not available.<sup>30</sup> Nuanced communication is needed, not only during treatment, but also into survivorship with specific approaches to meet caregiver needs and provide coping skills to manage stressful situations.<sup>30, 74</sup>

## **Discussion**

This systematic review revealed that AYA brain tumour survivors can encounter various social, cognitive, physical, psychological and spiritual issues which have the potential to significantly impact upon their wellbeing. Social, cognitive and physical issues were the most frequently reported - with poor social functioning being the most pressing. A childhood diagnosis of a brain tumour appeared to inhibit or change how AYAs interact with family, friends and employers as well as how they cope with unexpected and unwanted changes in areas ranging from employment stability to romantic relationships. Survivors miss out or struggle with achieving key life-events including: independence, educational achievements and becoming parents.

Cognitive deficits meaningfully contribute to these poor social outcomes. Survivors experience neurocognitive late effects across multiple domains that often hinder their independence - and are associated with poorer social functioning. This is compounded by growing concerns about their physical issues as they move into adolescence and young adulthood.

Identified problems were frequently more prevalent, or more intense, than in other cancer groups, making it more likely that brain tumour survivors will have poorer overall well-being: Similar to the findings of the present review, a recent review reported poorer quality of life outcomes in paediatric brain tumour patients than those diagnosed with other cancers,<sup>77</sup> emphasising that brain tumour supportive care should be disease-specific and tailored to individual needs.

The majority of identified studies focused on only survivor's experiences rather than their caregivers'. Yet our findings highlight that caregivers may experience momentous stress related to the pressures associated with their caring responsibilities. These pressures can take their toll on well-being, especially when support is not available. Caregivers indicated that support had declined as they moved further away from the survivor's treatment into long term survivorship.

There was little data reported that specifically focused on the supportive care needs and/or unmet needs of AYA childhood brain tumour survivors. Equally none of the studies included in our review assessed the needs of the AYA survivor's caregiver. In a sample of mixed cancer survivors (not just those living beyond a diagnosis of a brain tumour),<sup>78</sup> over 50% of AYA survivors indicated that they had unmet needs in relation to information and services. Based on the current review, it would be reasonable to expect that this percentage would be higher for brain tumour survivors because of the higher prevalence and complexity of late morbidities. However, it is still unclear what these specific needs are and whether they are currently being met.

### Limitations

There are several limitations to the research reported in this review. First, the quality of the evidence varied per study, as reflected in the MMAT scores (see Supplementary Table), and thus, findings should be interpreted with caution. Second, the majority of the studies involve a cross-sectional design. This is problematic as adolescence is a period of rapid development and change - behavioural patterns are established, cognitive functions mature, physical changes occur, and complex social relationships develop. Future research should focus on collecting longitudinal data that will allow us to examine if and when survivors and caregivers issues/needs change as they progress into adulthood. Third, in the majority of studies with caregiver participants, the views of the mothers dominated the sample, with very little representation from fathers. Fourth, in three studies survivors had been treated up to four decades ago, these results may not be relevant to survivors who have been treated more recently.<sup>26, 49, 66</sup> Older treatment periods may present varying treatment effects and therefore issues and needs, whilst different levels of supportive care may have been available. Finally, this is a relatively new area of study, and the majority of the studies included in this review have been conducted in the

United States. Therefore, additional studies are needed in other countries to identify specific issues and needs that might be culturally tied or dependent upon differences across health and social care systems.

There are limitations specific to our systematic review. First, due to the inclusion criteria, some studies with important findings were excluded from this review. For example, the set age criteria (14-39) meant that studies with participants outside this parameter were excluded, even if the majority of the participants were aged 14-39.<sup>79, 80</sup> Second, we appreciate that some potentially relevant articles may have been missed for the following reasons: only 20% of the abstracts were reviewed by a second reviewer, and we were not able to access all full-texts. We also appreciate that new evidence is constantly emerging and the review does not include any articles published after the last search date (September 2017). Third, in some studies brain tumour survivors were only a small percentage of the study population. Although some data were reported separately, allowing us to include the study within the review, this data was not always very detailed. Finally, only studies published in English were used due to resource limitations and time constraints.

#### Clinical implications

Currently, there is insufficient knowledge of what AYA brain tumour survivors specifically need from supportive care. Only a small number of studies in the review addressed unmet supportive care needs. Despite the numerous studies reporting survivor issues, it is known that the presence of issues is not always related to the need for, or uptake of supportive interventions.

Our systematic review shows that AYA survivors often experience many unique long term issues as a consequence of the diagnosis and treatment of a childhood brain tumour. These issues are different to older survivors and those still in childhood. Their priorities and unique life events mean that the late effects of treatment impact their lives differently to other age groups. Adolescence is a period of trying to gain independence, but the review highlights that survivors can find this difficult – emotionally and practically. For example, impaired daily functioning and cognitive issues were integral to their ability to self-care and gain independence. Unlike children, AYAs have to make

important decisions about their education and future careers. AYAs also start to plan for the future, with romantic relationships considered a critical developmental task marking one's entry into adulthood, alongside starting a family. Therefore, it is important that this group is provided with age-specific information, support and resources that guide them through adolescent life events, such as further education, learning to drive, paid work and relationships. Supportive services should be mindful that adolescence and young adulthood is a period of constant change and that the need for information and support may change rapidly, meaning regular reviews may be necessary. Information, support and resources should be brain-tumour specific, as experiences of brain tumour survivors differ significantly to those with other cancers.

Furthermore, we recommend that caregivers' unique needs are considered by long-term follow up teams and support services. They too face unique challenges and should have access to information, support and resources for caring for an adolescent childhood brain tumour survivor.

#### Future research

Significant gaps exist in our understanding of the unique needs of adolescent and young adult brain tumour survivors and their caregivers. The extent to which unmet needs are related to tumour and treatment characteristics requires further research. With new research constantly emerging, regular updates of this literature review will be necessary. From the systematic review, three areas of future research are identified. First, studies are needed to describe the needs and more importantly unmet needs of both AYA childhood brain tumour survivors and their caregivers. Increasing our understanding of the unmet needs will help to develop more targeted and effective supportive care models. Second, descriptive studies are needed to fully investigate survivor and caregiver expectations for supportive care and how these expectations comply with the current use of long term follow-up care and supportive services. Third, existing research seems to be omitting the perspectives of the healthcare professionals. Their input would be valuable in regard to the development and evaluation of effective interventions to support AYA survivors and their caregivers. Subsequent to the results from descriptive studies, evidence based programmes and services need to be modified and/or developed to address both AYA survivor and caregiver unmet and desired supportive care needs.

## **Conclusions**

Surviving a childhood brain tumour can be particularly challenging for AYA survivors (aged 14-39) and their caregivers. Many of their issues are unique when compared to other cancer diagnosis and age groups. Survivors and caregivers continue to report long term issues and unmet needs throughout follow-up. More research is needed on the specific unmet supportive care needs of both survivors and their caregivers and how support services can best meet these needs. Understanding their unmet needs and recognising what services are required due to the late effects of treatment is critical to improving their quality of survival.

**Acknowledgments:** Funding for this work was provided by Ellie’s Fund and Yorkshire Cancer Research – Grant Ref Number: L389FB (PI: FB)

**Conflict of Interest:** None declared

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