



## ADOLESCENT AND YOUNG ADULT MALIGNANT HEMATOLOGY

# Psychosocial challenges and health-related quality of life of adolescents and young adults with hematologic malignancies

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**Adolescents and young adults (AYAs) occupy a unique place within the hematologic malignancy community due to the challenges they face related to their disease biology and physical, psychosocial, and economic circumstances, as well as issues related to access to care and long-term follow-up. Efforts to define age-specific (supportive) care needs and**

**targets for intervention in these areas are evolving. This review discusses the psychosocial issues AYAs with hematologic malignancies are dealing with, how these might affect their health-related quality of life, and the challenges in delivering high-quality supportive care to this underserved population. (Blood. 2018;132(4):385-392)**

## Introduction

Adolescents and young adults (AYAs) are recognized as a distinct population within the oncology/hematology community due to the unique challenges they face. When compared with pediatric and older adult oncology patients, those aged 15 to 39 years at cancer diagnosis encounter differences in tumor biology, psychosocial challenges, and issues related to access to care and long-term follow-up.<sup>1,2</sup>

AYAs typically present with hematologic malignancies (HMs) that span the spectrum from pediatric cancers (eg, acute lymphoblastic leukemia [ALL]) to adult tumors (non-Hodgkin lymphoma [NHL]), as well as tumors that are most common among their age group (Hodgkin lymphoma [HL]).<sup>3</sup> HMs form 34% of cancers diagnosed among AYAs aged 15 to 19 years (15% HL; 7% NHL; 7% ALL; 5% acute myeloid leukemia [AML]), 21% among those aged 20 to 29 years (10% HL; 6% NHL; 2% ALL; 3% AML), and 11% among 30- to 39-year olds (3% HL; 6% NHL; 1% ALL; 1% AML) in the western world.<sup>1,3-5</sup> For these patients, the 5-year overall survival varies between 50% and 95%.<sup>6</sup> Although survival in AYAs has improved over time, progress made in treatments and survival of specific tumors (eg, ALL and AML) lags behind that of children and older adults.<sup>5,6</sup> Potential reasons for the lack of progress in survival are: the diverse and incompletely understood tumor biology<sup>7</sup>; insufficient awareness of cancer risk and symptoms among patients and health care professionals (HCPs) resulting in diagnostic delays<sup>8-10</sup>; unequal access to, and low participation rates in, clinical trials<sup>1</sup>; treatment nonadherence rates of 27% to 60%<sup>11</sup>; and limited knowledge among HCPs regarding AYA treatment protocols.<sup>12</sup>

## Psychosocial challenges and needs

Adolescence, emerging adulthood, and young adulthood are complex phases of life due to the many developmental, emotional,

and social transitions.<sup>13</sup> AYAs aim to achieve several developmental milestones such as completing education, creating their own identity, establishing autonomy, forming (romantic) relationships, pursuing gainful employment, becoming financially independent, and having children.<sup>14</sup> A cancer diagnosis and treatment challenge the ability of AYAs to achieve these milestones.<sup>15</sup> Although AYA patients with an HM face challenges similar to those of older and younger patients, including short-term (eg, hair loss,<sup>16</sup> pain<sup>17</sup>) and long-term effects of cancer treatment (eg, fatigue<sup>18</sup> and cognitive problems<sup>19</sup>), the consequences are different in this phase of life and more pronounced. In the AYA population specifically, treatment decisions should include considerations of the impact of long-term and late effects of treatments.<sup>20-25</sup>

## Education, employment, and financial challenges

Employment and education provide AYAs with a sense of identity, income, and, frequently, health insurance for needed treatment and follow-up care.<sup>26,27</sup>

**Education** Cancer treatment can lead to serious disruption in educational trajectories,<sup>28,29</sup> with AYAs often missing coursework/exams at a time that is crucial to future career development.<sup>10</sup> Educational settings are an important place for AYAs to develop supportive social networks<sup>30</sup> and develop a stable sense of self-worth.<sup>10</sup> AYAs describe cancer as a major disruption in the pursuit of educational opportunities due to absenteeism, inability to complete exams, and the feeling of being "left behind."<sup>28</sup> A recent Dutch study showed that AYA lymphoma survivors (45% HL; 55% NHL) more often had a lower educational level compared with a normative population (27% vs 3%).<sup>31</sup> AYAs often receive inadequate educational support during treatment (help with coursework, postponing exams), and indicate a need for assistance with returning to school.<sup>32</sup> Close liaison between schools and hospitals is needed.

**Employment** Employment problems are common among AYAs with cancer.<sup>33</sup> One study conducted in the United States showed that 33% of AYAs (unspecified percentage HM) vs 27% of healthy controls were not working,<sup>34</sup> whereas in another American study (9% HM), 24% of AYA patients vs 14% of controls reported unemployment due to health issues.<sup>33</sup> A more recent American study (4% leukemia, 26% HL, 24% NHL) showed that 28% of AYA cancer survivors had not returned to work 15 to 35 months after diagnosis and ~50% reported problems with returning.<sup>27</sup> AYAs who reported that their cancer treatment was “very intensive” and those who had to quit work after being diagnosed were more likely to report that cancer negatively affected their work, with more than half reporting problems with memory and attention.<sup>27</sup> AYAs with ALL more strongly believed that cancer negatively impacted their work plans compared with AYAs with other cancers.<sup>27</sup> In an English interview study, AYAs reported feeling “left behind” in their job trajectories compared with their peers, and those who had previously pursued careers involving physical abilities believed that they needed to adjust their goals as a result of their cancer. In addition, some AYAs reported discrimination from employers and job insecurity due to cancer.<sup>28</sup>

Considering that AYAs are at a stage in life when entering the workforce successfully will greatly influence their future earning and career potential, patients may benefit from the incorporation of resources into AYA programs that aid the transition from treatment to occupational pursuits.<sup>27</sup> Future research might focus on effective communication strategies between workers and employers to identify appropriate work modifications to help balance the demand of work with adverse treatment-related effects, preventing patients from quitting work altogether.

**Financial challenges** Financial toxicity of cancer treatment is especially relevant to AYAs with an HM, many of whom undergo long, costly therapies such as allogeneic hematopoietic cell transplantation, with side-effects that may prevent patients from completing education and returning to work.<sup>35</sup> An American study showed that AYAs (72% lymphoma; 28% leukemia) tend to have less productivity, greater health care expenditures, and increased likelihood of financial problems than patients diagnosed at older ages.<sup>36</sup> Another American study (4% leukemia, 27% HL, 25% NHL) showed that 65% to 70% of AYAs aged 21 to 39 years and 51% of AYAs aged 15 to 20 years reported a negative financial impact,<sup>29</sup> whereas yet another American study (unspecified percentage HM) showed that AYAs had lower household incomes compared with healthy peers.<sup>34</sup> In the same study, AYAs reported higher annual medical costs (\$7417 vs \$4247 for controls) and annual average lost productivity costs due to illness/disability of \$2200 per year. Some AYAs with cancer in the United Kingdom indicated that they need to rely on their parents or other significant others for financial support, which can result in feelings of dependency and loss of control.<sup>28</sup> In interviews, AYAs with cancer (59% HM) also describe issues with competing responsibilities and experience a lack of financial support for childcare, transportation, and elderly care,<sup>37</sup> which may also result in lower treatment compliance levels among AYAs.<sup>38</sup>

In interviews, one-third of American AYAs (59% HM) mentioned difficulties in acquiring or maintaining health insurance.<sup>37</sup> Some

lacked insurance before their diagnosis because they could not afford coverage and/or felt that they did not need coverage. Others had insurance at the time of diagnosis but worried about future insurability (because of losing employment due to treatment). Access to and affordability of insurance are sometimes also problems for AYAs who are working but do not receive coverage through their employers. This can force AYAs to seek treatment in an emergency room, a suboptimal strategy given crowding, wait times, and lack of continuity of care.<sup>39</sup> Lack of insurance may lead to missed care opportunities and subsequent economic burden including tradeoffs with education and career, using up savings, delinquency on loans, credit card debt, delay in moving out from their parents’ home, increased cohabitation, delaying marriage, and sometimes difficulty paying for basic necessities like rent and food.<sup>40</sup>

## Social relationships and functioning

Engaging in social and romantic relationships is a healthy developmental milestone of any AYA, wherein sexuality is explored and future plans to marry and have children are considered.<sup>41</sup> A cancer diagnosis can disrupt social maturation, the process by which young people develop identity, self-esteem and self-worth, social cognition, emotional regulation, and communication skills that guide them throughout the remainder of their lives.<sup>10,30,42,43</sup> Several studies showed that AYAs with cancer report greater challenges in social functioning compared with the general population.<sup>44-46</sup>

**Peer and family relationships** Cancer often forces AYAs to move home and become dependent on parents or significant others, usually after periods of time living independently. AYAs who are married or in committed relationships when diagnosed are similarly forced into dependence on a spouse or partner unexpectedly. In interviews, AYAs (59% HM) described not only the benefits of being cared for and supported, but also the challenges of feeling infantilized by their parents, significant others, or partner.<sup>37</sup> Emotional development may be negatively affected by learned decisional passivity caused by overprotective parenting.<sup>47</sup>

Furthermore, as AYAs with cancer try to deal with or discuss their illness with their parents, partner, or significant others, they may discover they have quite different coping strategies. Informal caregivers may want or need to discuss issues with the AYA that he or she does not wish to discuss, or vice versa. Some AYAs desire to protect their family members by shielding things they themselves worry about, possibly out of guilt for what their parents, significant others, or partner are going through, or because they can see how upset family members are.<sup>48</sup> Moreover, in qualitative research, AYA patients with dependents experience the drive to keep pushing forward as a function of the need to take care of others (eg, children), even when they feel sick.<sup>37</sup> This reflects the intertwined experiences of fighting cancer and being a parent/caregiver, a nonnormative challenge for an AYAs. Also, children of AYA cancer patients may go through a distressing time; behavioral problems and restricted cognitive and physical functioning are reported.<sup>49</sup>

For many AYAs, having cancer is catalytic in changing social relationships, either enhancing closeness or creating distance. From the perspective of friends, a cancer diagnosis can be a source of discomfort, responding to ill friends by avoiding them.

Isolation and alienation are commonly reported among AYAs with cancer, particularly as they miss life experiences being shared by their healthy peers.<sup>50</sup> Disruptions in the socialization process can result in impaired social skills, which may lead to diminished participation, social anxiety, and loneliness.<sup>47</sup> In other qualitative studies, AYAs frequently report difficulties maintaining or making new relationships as they feel anxious about “fitting into” their peer group again.<sup>37,51,52</sup> Changes in body image often lead to feelings of insecurity and make AYAs feel different from peers.<sup>53-59</sup> An American study showed that AYAs (27% HL, 25% NHL, 4% ALL) who reported that cancer had an impact on their close relationships were more likely to desire information on how to talk about their cancer with others.<sup>60</sup> Respectively, 27%, 29%, and 5% of the HL, NHL, and ALL patients had an information need on how to talk about their cancer experience with family and friends.<sup>60</sup>

**Marital relationships** Marriage is another important social milestone for many AYAs. An American study found that fewer AYAs (6% HM) with cancer were currently married (58 vs 64%) and more had been divorced or separated (18% vs 10%) compared with age-matched controls.<sup>61</sup> Twenty-five percent of AYAs reported that cancer negatively impacted their relationship with their spouse/significant other. It could be hypothesized that the emotional and financial burden of a cancer diagnosis could lead to marital distress. In a qualitative study (59% HM), divorced AYA patients indicated that their cancer experience catalyzed the breakups because their partners were not willing or able to support them through their disease.<sup>37</sup> AYAs also discussed challenges initiating new romantic relationships. Negative body image, low self-esteem, infertility concerns, or feelings of “abnormality” as a result of cancer and its treatment might negatively influence AYAs’ readiness and ability to engage in romantic relationships.<sup>37,62,63</sup>

Future research is needed to examine the complex and nuanced ways that cancer experiences affect relationships between AYAs and their significant others; this will ultimately help to develop (digital) social support interventions which will support AYAs in developing new social contacts and maintaining existing contacts.<sup>30</sup>

**Starting a family** Approximately 75% of AYAs who have not had children at cancer diagnosis express a wish for future biological offspring.<sup>64-67</sup> Cancer treatments have the potential to destroy reproductive cells and can place women at risk for acute ovarian failure/premature menopause and men for temporary/permanent azoospermia.<sup>68,69</sup> There are several fertility preservation options available,<sup>70,71</sup> however, counseling hematologic AYA patients about fertility threats is challenging due to the undefined risk and variable timing of gonadal failure, indeterminate likelihood and timing of gonadal recovery, and the unknown risks and efficacy of nonstandard but immediately available fertility preservation options.<sup>70</sup>

Despite the available fertility preservation options, discussion, referrals, and treatment are inconsistent, and many AYAs initiate treatment without discussion or opportunity for fertility preservation.<sup>72-76</sup> For example, an American study showed that, depending on tumor type and sex, 17% to 83% of AYA patients with HM discussed fertility preservation with their HCPs.<sup>76</sup> In qualitative research, AYAs reported false beliefs, unrealistic

expectations, and uncertainty regarding their reproductive potential and options.<sup>77,78</sup> Reproductive concerns in AYA cancer survivors have been associated with grief, low self-esteem, and an altered sense of identity<sup>79</sup>; they can negatively affect dating, social relationships, and life planning.<sup>80,81</sup> AYAs with confirmed infertility reported regret for not questioning infertility risks, guilt for their current partner or fear of never finding a partner,<sup>79</sup> and long-term distress.<sup>64</sup>

These results emphasize that HCPs should be better educated about fertility risks and should inform AYA patients about their risks and fast-evolving opportunities for fertility preservation.<sup>72</sup>

**Sexual functioning and intimacy** AYAs may experience cancer- and treatment-related sexual dysfunctions.<sup>82</sup> Treatment can cause problems with erection, premature ejaculation, early menopause, or vaginal dryness, shrinking, and/or loss of elasticity, which can all result in discomfort during intercourse and interfere with the patients’ ability to be interested in or enjoy sex.<sup>83</sup>

An American study showed that 49% of AYAs (28% HL, 24% NHL, 4% ALL) reported negative effects on sexual function 1-year post-cancer diagnosis and 70% of those persisted in their negative perceptions 2 years after diagnosis. Those reporting a negative impact were more likely to report that their diagnosis had a negative effect on physical appearance.<sup>53</sup> A Finnish study showed that female leukemia survivors (mean age at study 20.1 years) had more restrictive images of sexuality, and their attitudes, especially those concerning sexual pleasure, were more negative than those of healthy controls.<sup>84</sup>

In addition, short- and long-term effects of treatment (eg, fatigue, graft-versus-host disease, nausea, neuropathy) may hinder intimacy and interest in sexual activity.<sup>85</sup> Patients may feel embarrassed that others see them differently because of physical changes, such as weight gain/loss, hair loss, swelling, scars, or the presence of a central line/port. All of these treatment-related effects and sexual dysfunctions accompanied by changes in self-esteem (different sense of self-worth and self-confidence) may have (enduring) negative effects on the sex lives of patients and their partners.<sup>84,86,87</sup>

One study showed that when sexual problems were not discussed, patients were likely to believe that sexual dysfunction and treatment-related damages could not be treated.<sup>86</sup> These results emphasize the need to inform about and improve post-cancer treatments addressing sexuality for AYAs and their partners.<sup>88</sup>

## Psychological issues

Several studies have shown that rates of psychological distress are significantly greater among AYAs when compared with older patients.<sup>55</sup> Older age and previous life experiences have been recognized as protective factors as they are related to highly developed coping skills.<sup>89</sup> More so than childhood cancer patients, AYAs have the cognitive capacity to understand the severity of their illness and frequently demonstrate persistent distress. A recent American study among AYAs treated for ALL, NHL, or HL showed that 23% met the criteria for anxiety, 28% for depression, and 13% for posttraumatic stress, while 46% overall demonstrated posttraumatic stress symptomatology.<sup>90</sup> Thirty-nine percent were impaired in 1 or more

psychological domains. No differences in psychological morbidity were observed between patients on-treatment and early survivors. A Dutch study showed that 69% of AYA cancer patients aged 18 to 35 years (14% HM) reported fear of recurrence/progression.<sup>87</sup>

Alterations in physical appearance, for example, scars of biopsies and central lines, weight changes, and hair loss, not only make AYAs feel different from peers but may also adversely affect maturational processes including development of self-esteem and identity.<sup>58,91</sup> Fear that the body will never return to its original appearance, of not being recognized by others, or of being mistaken for an individual of the opposite sex often leads to shame, social isolation, and regressive behaviors.<sup>15,63</sup>

Interestingly, HCPs' perceptions of their AYA patients' psychological morbidity is not related to AYA patients' own perceptions,<sup>90</sup> suggesting HCPs are not consistently assessing distress in AYA patients during clinic visits. AYAs themselves may delay reporting distress-related symptoms to providers because of a passive-avoidant coping style, an individual patient's effort to cope with the disease alone, or a fear of stigmatization following acceptance of being diagnosed with a psychological illness. Several American studies show that AYAs repeatedly report that their psychosocial needs are not met throughout the cancer experience<sup>78,92-94</sup>; for example, 41% of AYAs reported an unmet need for psychological counseling 12 months after diagnosis.<sup>92</sup>

Psychological interventions targeting adults or children are not adequate to reduce distress among AYAs.<sup>95</sup> Interventions for AYAs must manage competing demands for time such as school, work, and family.<sup>96</sup> Novel AYA-focused psychosocial interventions delivered in AYA-friendly platforms (eg, social media) are currently being evaluated.<sup>97</sup>

### End-of-life challenges

The diagnosis of advanced cancer may be particularly distressing for AYAs. Young people have had less time to learn from other adverse life experiences to help manage the consequences of advanced disease. They face many complex decisions but may lack the fully developed executive functioning and abstract thinking necessary for medical decision-making and coping with uncertainty.<sup>98</sup> During young adulthood, when new parenthood is common, fears about the welfare of children and significant others and about leaving them behind may add to distress in patients facing end of life.<sup>99,100</sup>

A Canadian interview study among AYAs aged 18 to 35 years with advanced cancer showed that patients experience their diagnosis as isolating (eg, feeling misunderstood or alienated) and unexpected (eg, cancer is a disease of older adults) and feel forcefully removed from the normal life trajectory.<sup>101</sup> In an American interview study, AYAs (20-40 years) reported anticipatory grief over their lives that have not yet been lived,<sup>102</sup> a psychological state that may be difficult for AYAs to process; they may be reluctant to face the irreversibility and progression of their disease.<sup>102</sup> This may lead to delays in the receipt of appropriate palliative and end-of-life care. An American study showed that AYAs (26% HM) who die in the hospital tend to use palliative care services very late in the disease trajectory and often undergo aggressive treatment until death is near.<sup>103</sup> Early

use of palliative care would have great use in providing physical, psychosocial, and spiritual support.

## Health-related quality of life

The combination of trying to achieve developmental milestones while coping with a life-threatening disease may have a negative impact on the health-related quality of life (HRQoL) of AYAs.<sup>104</sup> Two recent review papers show that AYAs with cancer experience worse HRQoL compared with a normative population.<sup>105,106</sup> Studies conducted among AYAs with HM support these findings.<sup>31,107-109</sup> Risk factors for poor HRQoL were low socioeconomic status, female sex, unemployment, high levels of distress, and physical symptoms.<sup>31,107,109</sup> A recent longitudinal study conducted in the United States showed that most improvements in HRQoL ( $n = 141$ ; 11% HL, 8% NHL, 26% leukemia) take place in the first year after diagnosis,<sup>110</sup> presumably once AYAs have acknowledged and adapted to new life routines that revolve around treatments and visits to clinics, hospitals, and doctors' offices. In the second year after cancer diagnosis, no significant HRQoL improvements were found. The transition from cancer patient to off-treatment survivor is often fraught with new challenges as AYA cancer survivors are confronted with survivorship concerns about their future lives.<sup>29</sup> AYA patients may therefore benefit from supportive care interventions administered during the second year following diagnosis to help those near completion of therapy (re)normalize their lives.

HRQoL assessment in clinical practice throughout the disease trajectory is important as it can facilitate communication, improve symptom control and patient satisfaction, and reduce hospital admissions.<sup>111</sup> To integrate HRQoL assessments in routine clinical care, it is essential to have measures available that capture the full range of issues relevant to AYAs with HMs. Generic HRQoL instruments (eg, EORTC-QLQ-C30,<sup>112</sup> FACT-G<sup>113</sup>) do not efficiently capture the unique experiences of this group. Tumor-specific questionnaires (eg, EORTC modules for lymphoma and leukemia,<sup>114</sup> FACT-Lym<sup>115</sup>/FACT-Leu<sup>116</sup>) accompanied by age-specific questionnaires (eg, EORTC-AYA)<sup>117</sup> should be administered to assess the impact of treatments, provide optimal supportive care, and, ultimately, translate into meaningful outcomes for AYAs with HMs.

Most studies have been limited by heterogeneous study samples of AYA patients with different tumor types; subanalyses were rarely performed. Future research should explore the specific challenges of AYAs with HMs in more detail.

## Delivering quality supportive care

AYAs have often been identified as the "lost tribe"<sup>118</sup>: neither pediatric nor adult oncology/hematology departments have been able to provide age-appropriate care single-handedly to this group. In general, there is strong potential benefit from closer collaboration between pediatric and adult hematologists to improve long-term outcomes.<sup>119,120</sup> Studies show that AYAs with cancer report high levels of unmet supportive care needs,<sup>35,121</sup> especially with regard to receiving age-specific information and psychosocial supportive care.<sup>92</sup> In recent years, several AYA programs were formed in an attempt to bridge the gap and address unmet supportive care needs.<sup>2,122-125</sup>



## Multidisciplinary supportive care

As a result of the complexity of their care, the lack of experience navigating medical systems, and the variety of age-specific challenges, AYAs will likely benefit from an AYA multidisciplinary team approach. In addition to routine medical professionals, this may include specialized nurses, fertility and sexual experts, dietitians, physical therapists, psychologists, and social workers.<sup>126</sup> Early intervention by the multidisciplinary care team is essential to provide effective (psychosocial) support to AYAs including fertility and sexuality counseling, programs to maximize education and vocational functioning, concrete financial and housing support, and access to age-specific information.<sup>14</sup> Addressing physical, psychosocial, and economic challenges early in the disease trajectory will help reduce the impact of long-term effects. Supportive care for family members should also be discussed.

Given the relatively small number of AYAs as part of the whole cancer population diagnosed each year, it is not realistic to expect every hospital to possess all of the personnel, facilities, and components needed for the best treatment of AYAs, or to create their own AYA programs.<sup>127</sup> For community hospitals, an oncology clinical nurse could specialize as an AYA nurse specialist. Nurses spend ongoing and dedicated time with patients and are therefore well positioned to support and educate them. AYA specialist nurses can provide patients with developmentally appropriate educational resources and support, are critical for managing care transitions and engaging experts from other disciplines, and could function as a resource for colleagues who are less familiar with AYA age-specific needs.<sup>128</sup> In complex cases, an AYA can be referred to a center with a specialized AYA program. In larger centers, an AYA clinical nurse specialist could be introduced to improve awareness of clinical trials, assist in enrolling AYAs in these trials, promote multidisciplinary discussions and care, and provide access or referrals to age-appropriate psychosocial care or health-promoting interventions, altogether providing patients with a sense of continuity of care.<sup>127</sup>

## Inpatient and outpatient facilities

One of the most commonly expressed feelings by AYA cancer patients is that they do not belong to any specific group or place.<sup>123</sup> The health care environment can support the maintenance of a sense of normalcy by having accessible visiting hours<sup>14</sup> and availability of dedicated social space facilities (eg, to play games) to suit the age-specific needs. Studies have also shown that support received from other AYA cancer patients is incredibly important.<sup>129</sup> Inpatient wards and social space facilities within the hospital provide AYAs the opportunity to connect, share experiences, learn from each other, and feel genuinely understood.<sup>130</sup> This is particularly important for AYAs who have to undergo extensive inpatient treatments like stem cell transplantation. For the large proportion of AYAs also receiving outpatient treatment, AYA support interventions, such as face-to-face weekly meetings, online communities, and retreats, have

been shown to significantly reduce feelings of social isolation and improve knowledge and problem-solving skills.<sup>130-132</sup>

## Training and education of HCPs

HCPs and treating institutions can reasonably be expected to have knowledge of medical and supportive care opportunities for AYAs with cancer and to provide referrals to appropriate expert centers when necessary.<sup>127</sup> Currently, most HCP training programs do not address AYA-specific issues, resulting in poor recognition of AYA cancer risk and an inadequate response to their physical and psychosocial needs.<sup>2</sup> An AYA module should be required for HCPs of different disciplines.<sup>42</sup>

Several countries have made recommendations about what AYA cancer care should look like.<sup>2,133,134</sup> The current AYA programs need to be evaluated in terms of improvements in patient satisfaction, HRQoL, survival, and clinical outcomes (eg, trial participation). Studies need to provide objective evidence demonstrating the efficacy of critical components of the AYA care programs in order to create evidence-based guidelines, referral pathways, and education.<sup>127,135</sup> In addition, the AYA oncology agenda should be moved beyond high-income countries to support those in less-privileged circumstances.<sup>136</sup>

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## Authorship

Contribution: O.H. performed research, analyzed data, and wrote the paper; and P.C.H. and W.T.A.v.d.G. wrote the paper.

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## Footnote

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## REFERENCES

- Meenaghan MR, Wood WA. Challenges for cancer care delivery to adolescents and young adults: present and future. *Acta Haematol*. 2014;132(3-4):414-422.
- LIVESTRONG Young Adult Alliance. Closing the gap: research and care imperatives for adolescents and young adults with cancer. Report of the Adolescent and Young Adult Oncology Progress Review Group. No. 06-6067. Rockville, MD: US Department of Health and Human Services, National Institutes of Health, National Cancer Institute; 2006.
- Sender L, Zabokrtsky KB. Adolescent and young adult patients with cancer: a milieu of unique features. *Nat Rev Clin Oncol*. 2015; 12(8):465-480.
- Bleyer A, Montello M, Budd T, Saxman S. National survival trends of young adults with sarcoma: lack of progress is associated with lack of clinical trial participation. *Cancer*. 2005;103(9):1891-1897.
- Bleyer A, Budd T, Montello M. Adolescents and young adults with cancer: the scope of the problem and criticality of clinical trials. *Cancer*. 2006;107(suppl 7):1645-1655.

6. Keegan TH, Ries LA, Barr RD, et al; National Cancer Institute Next Steps for Adolescent and Young Adult Oncology Epidemiology Working Group. Comparison of cancer survival trends in the United States of adolescents and young adults with those in children and older adults. *Cancer*. 2016;122(7):1009-1016.
7. Wood WA, Lee SJ. Malignant hematologic diseases in adolescents and young adults. *Blood*. 2011;117(22):5803-5815.
8. Dommett RM, Redaniel MT, Stevens MC, Hamilton W, Martin RM. Features of cancer in teenagers and young adults in primary care: a population-based nested case-control study. *Br J Cancer*. 2013;108(11):2329-2333.
9. Fern LA, Birch R, Whelan J, et al. Why can't we improve the timeliness of cancer diagnosis in children, teenagers, and young adults? *BMJ*. 2013;347:f6493.
10. Herbertson R, Hancock BW. Hodgkin lymphoma in adolescents. *Cancer Treat Rev*. 2005;31(5):339-360.
11. Butow P, Palmer S, Pai A, Goodenough B, Luckett T, King M. Review of adherence-related issues in adolescents and young adults with cancer. *J Clin Oncol*. 2010;28(32):4800-4809.
12. Potosky AL, Harlan LC, Albritton K, et al; AYA HOPE Study Collaborative Group. Use of appropriate initial treatment among adolescents and young adults with cancer. *J Natl Cancer Inst*. 2014;106(11).
13. Bleyer A, Barr R, Ries L, Whelan J, Ferrari A, eds. *Cancer in adolescents and young adults*, 2nd ed. Cham, Switzerland: Springer International Publishing; 2017.
14. D'Agostino NM, Penney A, Zebrack B. Providing developmentally appropriate psychosocial care to adolescent and young adult cancer survivors. *Cancer*. 2011;117(suppl 10):2329-2334.
15. Zebrack B, Isaacson S. Psychosocial care of adolescent and young adult patients with cancer and survivors. *J Clin Oncol*. 2012;30(11):1221-1226.
16. Zucchetti G, Bellini S, Bertolotti M, et al. Body image discomfort of adolescent and young adult hematologic cancer survivors. *J Adolesc Young Adult Oncol*. 2017;6(2):377-380.
17. Hughes RE, Holland LR, Zanino D, Link E, Michael N, Thompson KE. Prevalence and intensity of pain and other physical and psychological symptoms in adolescents and young adults diagnosed with cancer on referral to a palliative care service. *J Adolesc Young Adult Oncol*. 2015;4(2):70-75.
18. Poort H, Kaal SEJ, Knoop H, et al. Prevalence and impact of severe fatigue in adolescent and young adult cancer patients in comparison with population-based controls [published correction appears in *Support Care Cancer*. 2017;25(9):2919-2920]. *Support Care Cancer*. 2017;25(9):2911-2918.
19. John TD, Sender LS, Bota DA. Cognitive impairment in survivors of adolescent and early young adult onset non-CNS cancers: does chemotherapy play a role? *J Adolesc Young Adult Oncol*. 2016;5(3):226-231.
20. Singal PK, Iliskovic N, Li T, Kumar D. Adriamycin cardiomyopathy: pathophysiology and prevention. *FASEB J*. 1997;11(12):931-936.
21. Sleijfer S. Bleomycin-induced pneumonitis. *Chest*. 2001;120(2):617-624.
22. Mudie NY, Swerdlow AJ, Higgins CD, et al. Risk of second malignancy after non-Hodgkin's lymphoma: a British cohort study. *J Clin Oncol*. 2006;24(10):1568-1574.
23. Koontz MZ, Horning SJ, Balise R, et al. Risk of therapy-related secondary leukemia in Hodgkin lymphoma: the Stanford University experience over three generations of clinical trials. *J Clin Oncol*. 2013;31(5):592-598.
24. Pedersen-Bjergaard J, Andersen MK, Christiansen DH. Therapy-related acute myeloid leukemia and myelodysplasia after high-dose chemotherapy and autologous stem cell transplantation. *Blood*. 2000;95(11):3273-3279.
25. van Leeuwen FE, Klokman WJ, Veer MB, et al. Long-term risk of second malignancy in survivors of Hodgkin's disease treated during adolescence or young adulthood. *J Clin Oncol*. 2000;18(3):487-497.
26. Vetsch J, Wakefield CE, McGill BC, et al. Educational and vocational goal disruption in adolescent and young adult cancer survivors. *Psychooncology*. 2018;27(2):532-538.
27. Parsons HM, Harlan LC, Lynch CF, et al. Impact of cancer on work and education among adolescent and young adult cancer survivors. *J Clin Oncol*. 2012;30(19):2393-2400.
28. Grinyer A. The biographical impact of teenage and adolescent cancer. *Chronic Illn*. 2007;3(4):265-277.
29. Bellizzi KM, Smith A, Schmidt S, et al; Adolescent and Young Adult Health Outcomes and Patient Experience (AYA HOPE) Study Collaborative Group. Positive and negative psychosocial impact of being diagnosed with cancer as an adolescent or young adult. *Cancer*. 2012;118(20):5155-5162.
30. Warner EL, Kent EE, Trevino KM, Parsons HM, Zebrack BJ, Kirchhoff AC. Social well-being among adolescents and young adults with cancer: a systematic review. *Cancer*. 2016;122(7):1029-1037.
31. Husson O, Prins JB, Kaal SE, et al. Adolescent and young adult (AYA) lymphoma survivors report lower health-related quality of life compared to a normative population: results from the PROFILES registry. *Acta Oncol*. 2017;56(2):288-294.
32. Goodall S, King M, Ewing J, Smith N, Kenny P. Preferences for support services among adolescents and young adults with cancer or a blood disorder: a discrete choice experiment. *Health Policy*. 2012;107(2-3):304-311.
33. Tai E, Buchanan N, Townsend J, Fairley T, Moore A, Richardson LC. Health status of adolescent and young adult cancer survivors. *Cancer*. 2012;118(19):4884-4891.
34. Guy GP Jr, Yabroff KR, Ekwueme DU, et al. Estimating the health and economic burden of cancer among those diagnosed as adolescents and young adults. *Health Aff (Millwood)*. 2014;33(6):1024-1031.
35. Barata A, Wood WA, Choi SW, Jim HS. Unmet needs for psychosocial care in hematologic malignancies and hematopoietic cell transplant. *Curr Hematol Malig Rep*. 2016;11(4):280-287.
36. Kent EE, Forsythe LP, Yabroff KR, et al. Are survivors who report cancer-related financial problems more likely to forgo or delay medical care? *Cancer*. 2013;119(20):3710-3717.
37. Kent EE, Parry C, Montoya MJ, Sender LS, Morris RA, Anton-Culver H. "You're too young for this": adolescent and young adults' perspectives on cancer survivorship. *J Psychosoc Oncol*. 2012;30(2):260-279.
38. Rytting ME, Jabbour EJ, O'Brien SM, Kantarjian HM. Acute lymphoblastic leukemia in adolescents and young adults. *Cancer*. 2017;123(13):2398-2403.
39. Olson EJ. No room at the inn: a snapshot of an American emergency room. *Stanford Law Rev*. 1994;46(2):449-501.
40. Collins SR, Robertson R, Garber T, Doty MM. Young, uninsured, and in debt: why young adults lack health insurance and how the Affordable Care Act is helping: findings from the Commonwealth Fund Health Insurance Tracking Survey of Young Adults, 2011. *Issue Brief (Commonw Fund)*. 2012;14:1-24.
41. Horwitz AV, White HR. The relationship of cohabitation and mental health: a study of a young adult cohort. *J Marriage Fam*. 1998;60(2):505-514.
42. Nass SJ, Beaupin LK, Demark-Wahnefried W, et al. Identifying and addressing the needs of adolescents and young adults with cancer: summary of an Institute of Medicine workshop. *Oncologist*. 2015;20(2):186-195.
43. Huitt W, Dawson C. Social development: why it is important and how to impact it. Educational Psychology Interactive. Valdosta, GA: Valdosta State University, 2011. <http://www.edpsycinteractive.org/papers/socdev.pdf>. Accessed 29 November 2017.
44. Geue K, Sender A, Schmidt R, et al. Gender-specific quality of life after cancer in young adulthood: a comparison with the general population. *Qual Life Res*. 2014;23(4):1377-1386.
45. Smith AW, Bellizzi KM, Keegan TH, et al. Health-related quality of life of adolescent and young adult patients with cancer in the United States: the Adolescent and Young Adult Health Outcomes and Patient Experience study. *J Clin Oncol*. 2013;31(17):2136-2145.
46. Husson O, Zebrack BJ, Aguilar C, Hayes-Lattin B, Cole S. Cancer in adolescents and young adults: who remains at risk of poor social functioning over time? *Cancer*. 2017;123(14):2743-2751.
47. Nass SJ, Patlak M. Identifying and addressing the needs of adolescents and young adults with cancer: workshop summary. Washington, DC: National Academies Press, 2014.
48. Zebrack BJ, Chesler MA. Quality of life in childhood cancer survivors. *Psychooncology*. 2002;11(2):132-141.
49. Visser A, Huizinga GA, van der Graaf WT, Hoekstra HJ, Hoekstra-Weebers JE. The impact of parental cancer on children and the

- family: a review of the literature. *Cancer Treat Rev*. 2004;30(8):683-694.
50. Levin Newby W, Brown RT, Pawletko TM, Gold SH, Whitt JK. Social skills and psychological adjustment of child and adolescent cancer survivors. *Psychooncology*. 2000;9(2):113-126.
  51. Evan EE, Zeltzer LK. Psychosocial dimensions of cancer in adolescents and young adults. *Cancer*. 2006;107(suppl 7):1663-1671.
  52. Zebrack B, Chesler MA, Kaplan S. To foster healing among adolescents and young adults with cancer: what helps? What hurts? *Support Care Cancer*. 2010;18(1):131-135.
  53. Wettergren L, Kent EE, Mitchell SA, et al; AYA HOPE Study Collaborative Group. Cancer negatively impacts on sexual function in adolescents and young adults: The AYA HOPE study. *Psychooncology*. 2017;26(10):1632-1639.
  54. Moules NJ, Estefan A, Laing CM, et al. "A tribe apart": sexuality and cancer in adolescence. *J Pediatr Oncol Nurs*. 2017;34(4):295-308.
  55. Sansom-Daly UM, Wakefield CE. Distress and adjustment among adolescents and young adults with cancer: an empirical and conceptual review. *Transl Pediatr*. 2013;2(4):167-197.
  56. Aubin S, Perez S. The clinician's toolbox: assessing the sexual impacts of cancer on adolescents and young adults with cancer (AYAC). *Sex Med*. 2015;3(3):198-212.
  57. Tindle D, Denver K, Lilley F. Identity, image, and sexuality in young adults with cancer. *Semin Oncol*. 2009;36(3):281-288.
  58. Evan EE, Kaufman M, Cook AB, Zeltzer LK. Sexual health and self-esteem in adolescents and young adults with cancer. *Cancer*. 2006;107(suppl 7):1672-1679.
  59. Larouche SS, Chin-Peuckert L. Changes in body image experienced by adolescents with cancer. *J Pediatr Oncol Nurs*. 2006;23(4):200-209.
  60. Kent EE, Smith AW, Keegan TH, et al. Talking about cancer and meeting peer survivors: social information needs of adolescents and young adults diagnosed with cancer. *J Adolesc Young Adult Oncol*. 2013;2(2):44-52.
  61. Kirchhoff AC, Yi J, Wright J, Warner EL, Smith KR. Marriage and divorce among young adult cancer survivors. *J Cancer Surviv*. 2012;6(4):441-450.
  62. Fosså SD, Dahl AA. Fertility and sexuality in young cancer survivors who have adult-onset malignancies. *Hematol Oncol Clin North Am*. 2008;22:291-303.
  63. Olsen PR, Lorenzo R. Supportive care. *Prog Tumor Res*. 2016;43:16-26.
  64. Schover LR. Patient attitudes toward fertility preservation. *Pediatr Blood Cancer*. 2009;53(2):281-284.
  65. Geue K, Richter D, Schmidt R, et al. The desire for children and fertility issues among young German cancer survivors. *J Adolesc Health*. 2014;54(5):527-535.
  66. Goodwin T, Elizabeth Oosterhuis B, Kiernan M, Hudson MM, Dahl GV. Attitudes and practices of pediatric oncology providers regarding fertility issues. *Pediatr Blood Cancer*. 2007;48(1):80-85.
  67. Levine J, Canada A, Stern CJ. Fertility preservation in adolescents and young adults with cancer. *J Clin Oncol*. 2010;28(32):4831-4841.
  68. Murphy D, Orgel E, Termuhlen A, Shannon S, Warren K, Quinn GP. Why healthcare providers should focus on the fertility of AYA cancer survivors: it's not too late! *Front Oncol*. 2013;3:248.
  69. Lee SJ, Schover LR, Partridge AH, et al; American Society of Clinical Oncology. American Society of Clinical Oncology recommendations on fertility preservation in cancer patients [published correction appears in *J Clin Oncol*. 2006;24(36):5790]. *J Clin Oncol*. 2006;24(18):2917-2931.
  70. Loren AW. Fertility issues in patients with hematologic malignancies. *Hematology Am Soc Hematol Educ Program*. 2015;2015:138-145.
  71. Loren AW, Mangu PB, Beck LN, et al; American Society of Clinical Oncology. Fertility preservation for patients with cancer: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol*. 2013;31(19):2500-2510.
  72. Benedict C, Thom B, Kelvin JF. Fertility preservation and cancer: challenges for adolescent and young adult patients. *Curr Opin Support Palliat Care*. 2016;10(1):87-94.
  73. Forman EJ, Anders CK, Behera MA. A nationwide survey of oncologists regarding treatment-related infertility and fertility preservation in female cancer patients. *Fertil Steril*. 2010;94(5):1652-1656.
  74. Neal MS, Nagel K, Duckworth J, et al. Effectiveness of sperm banking in adolescents and young adults with cancer: a regional experience. *Cancer*. 2007;110(5):1125-1129.
  75. Ginsberg JP, Ogle SK, Tuchman LK, et al. Sperm banking for adolescent and young adult cancer patients: sperm quality, patient, and parent perspectives. *Pediatr Blood Cancer*. 2008;50(3):594-598.
  76. Shnorhavorian M, Harlan LC, Smith AW, et al; AYA HOPE Study Collaborative Group. Fertility preservation knowledge, counseling, and actions among adolescent and young adult patients with cancer: a population-based study. *Cancer*. 2015;121(19):3499-3506.
  77. Benedict C, Shuk E, Ford JS. Fertility issues in adolescent and young adult cancer survivors. *J Adolesc Young Adult Oncol*. 2016;5(1):48-57.
  78. Zebrack BJ, Block R, Hayes-Lattin B, et al. Psychosocial service use and unmet need among recently diagnosed adolescent and young adult cancer patients. *Cancer*. 2013;119(1):201-214.
  79. Crawshaw M, Sloper P. A qualitative study of the experiences of teenagers and young adults when faced with possible or actual fertility impairment following cancer treatment. Executive summary. York, United Kingdom: Department of Social Policy and Social Work, University of York; 2006.
  80. Carpentier MY, Fortenberry JD. Romantic and sexual relationships, body image, and fertility in adolescent and young adult testicular cancer survivors: a review of the literature. *J Adolesc Health*. 2010;47(2):115-125.
  81. Halliday LE, Boughton MA, Kerridge I. Mothering and self-othering: the impact of uncertain reproductive capability in young women after hematological malignancy. *Health Care Women Int*. 2014;35(3):249-265.
  82. Stanton AM, Handy AB, Meston CM. Sexual function in adolescents and young adults diagnosed with cancer: a systematic review. *J Cancer Surviv*. 2018;12(1):47-63.
  83. Zhou ES, Falk SJ, Bober SL. Managing premature menopause and sexual dysfunction. *Curr Opin Support Palliat Care*. 2015;9(3):294-300.
  84. Puukko LR, Hirvonen E, Aalberg V, Hovi L, Rautonen J, Siimes MA. Sexuality of young women surviving leukaemia. *Arch Dis Child*. 1997;76(3):197-202.
  85. Flynn KE, Jeffery DD, Keefe FJ, et al. Sexual functioning along the cancer continuum: focus group results from the Patient-Reported Outcomes Measurement Information System (PROMIS®). *Psychooncology*. 2011;20(4):378-386.
  86. Bober SL, Varela VS. Sexuality in adult cancer survivors: challenges and intervention. *J Clin Oncol*. 2012;30(30):3712-3719.
  87. Thewes B, Kaal SEJ, Custers JAE, et al. Prevalence and correlates of high fear of cancer recurrence in late adolescents and young adults consulting a specialist adolescent and young adult (AYA) cancer service. *Support Care Cancer*. 2018;26(5):1479-1487.
  88. Perz J, Ussher JM, Gilbert E; Australian Cancer and Sexuality Study Team. Feeling well and talking about sex: psycho-social predictors of sexual functioning after cancer. *BMC Cancer*. 2014;14(1):228.
  89. Jones WC, Parry C, Devine S, Main DS, Okuyama S, Tran ZV. Prevalence and predictors of distress in posttreatment adult leukemia and lymphoma survivors. *J Psychosoc Oncol*. 2015;33(2):124-141.
  90. Muffy LS, Hlubocky FJ, Khan N, et al. Psychological morbidities in adolescent and young adult blood cancer patients during curative-intent therapy and early survivorship. *Cancer*. 2016;122(6):954-961.
  91. Zeltzer LK. Cancer in adolescents and young adults psychosocial aspects. Long-term survivors. *Cancer*. 1993;71(suppl 10):3463-3468.
  92. Keegan TH, Lichtensztajn DY, Kato I, et al; AYA HOPE Study Collaborative Group. Unmet adolescent and young adult cancer survivors information and service needs: a population-based cancer registry study. *J Cancer Surviv*. 2012;6(3):239-250.
  93. DeRouen MC, Smith AW, Tao L, et al; AYA HOPE Study Collaborative Group. Cancer-related information needs and cancer's impact on control over life influence health-related quality of life among adolescents and young adults with cancer. *Psychooncology*. 2015;24(9):1104-1115.
  94. Zebrack BJ, Corbett V, Embry L, et al. Psychological distress and unsatisfied need

- for psychosocial support in adolescent and young adult cancer patients during the first year following diagnosis. *Psychooncology*. 2014;23(11):1267-1275.
95. Richter D, Koehler M, Friedrich M, Hilgendorf I, Mehnert A, Weißfogel G. Psychosocial interventions for adolescents and young adult cancer patients: a systematic review and meta-analysis. *Crit Rev Oncol Hematol*. 2015;95(3):370-386.
  96. Rabin C, Simpson N, Morrow K, Pinto B. Intervention format and delivery preferences among young adult cancer survivors. *Int J Behav Med*. 2013;20(2):304-310.
  97. Sansom-Daly UM, Wakefield CE, Bryant RA, et al. Online group-based cognitive-behavioural therapy for adolescents and young adults after cancer treatment: a multicenter randomised controlled trial of Recapture Life-AYA. *BMC Cancer*. 2012;12(1):339.
  98. Clark JK, Fasciano K. Young adult palliative care: challenges and opportunities. *Am J Hosp Palliat Care*. 2015;32(1):101-111.
  99. Fernandes C, Muller R, Rodin G. Predictors of parenting stress in patients with haematological cancer. *J Psychosoc Oncol*. 2012;30(1):81-96.
  100. Krauel K, Simon A, Krause-Hebecker N, Czimbalmos A, Bottomley A, Flechtner H. When a parent has cancer: challenges to patients, their families and health providers. *Expert Rev Pharmacoecon Outcomes Res*. 2012;12(6):795-808.
  101. Knox MK, Hales S, Nissim R, et al. Lost and stranded: the experience of younger adults with advanced cancer. *Support Care Cancer*. 2017;25(2):399-407.
  102. Trevino KM, Maciejewski PK, Fasciano K, et al. Grief and life disruption in young adults with advanced cancer. *J Adolesc Young Adult Oncol*. 2012;1(4):168-172.
  103. Keim-Malpass J, Erickson JM, Malpass HC. End-of-life care characteristics for young adults with cancer who die in the hospital. *J Palliat Med*. 2014;17(12):1359-1364.
  104. Zebrack BJ. Psychological, social, and behavioral issues for young adults with cancer. *Cancer*. 2011;117(suppl 10):2289-2294.
  105. Quinn GP, Gonçalves V, Sehovic I, Bowman ML, Reed DR. Quality of life in adolescent and young adult cancer patients: a systematic review of the literature. *Patient Relat Outcome Meas*. 2015;6:19-51.
  106. Sodergren SC, Husson O, Robinson J, et al; EORTC Quality of Life Group. Systematic review of the health-related quality of life issues facing adolescents and young adults with cancer. *Qual Life Res*. 2017;26(7):1659-1672.
  107. Mattson MR, Demshar RK, Daly BJ. Quality of life of young adult survivors of hematologic malignancies. *Cancer Nurs*. 2013;36(2):E1-E7.
  108. Oerlemans S, Nijziel MR, van de Poll-Franse LV. Age-related differences in quality of life among patients with diffuse large B-cell lymphoma. *Cancer*. 2015;121(16):2857-2858.
  109. Kent EE, Sender LS, Morris RA, et al. Multilevel socioeconomic effects on quality of life in adolescent and young adult survivors of leukemia and lymphoma. *Qual Life Res*. 2013;22(6):1339-1351.
  110. Husson O, Zebrack BJ, Block R, et al. Health-related quality of life in adolescent and young adult patients with cancer: a longitudinal study. *J Clin Oncol*. 2017;35(6):652-659.
  111. Basch E, Spertus J, Dudley RA, et al. Methods for developing patient-reported outcome-based performance measures (PRO-PMs). *Value Health*. 2015;18(4):493-504.
  112. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*. 1993;85(5):365-376.
  113. Cella DF, Tulsky DS, Gray G, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. *J Clin Oncol*. 1993;11(3):570-579.
  114. van de Poll-Franse L, Oerlemans S, Bredart A, et al. International development of four EORTC disease-specific quality of life questionnaires for patients with Hodgkin lymphoma, high- and low-grade non-Hodgkin lymphoma and chronic lymphocytic leukaemia. *Qual Life Res*. 2018;27(2):333-345.
  115. Hlubocky FJ, Webster K, Beaumont J, et al. A preliminary study of a health related quality of life assessment of priority symptoms in advanced lymphoma: the National Comprehensive Cancer Network-Functional Assessment of Cancer Therapy-Lymphoma Symptom Index. *Leuk Lymphoma*. 2013;54(9):1942-1946.
  116. Cella D, Jensen SE, Webster K, et al. Measuring health-related quality of life in leukemia: the Functional Assessment of Cancer Therapy-Leukemia (FACT-Leu) questionnaire. *Value Health*. 2012;15(8):1051-1058.
  117. Sodergren SC, Husson O, Rohde GE, et al. A life put on pause: an exploration of the health-related quality of life issues relevant to adolescents and young adults with cancer [published online ahead of print 22 March 2018]. *J Adolesc Young Adult Oncol*. doi: 10.1089/jayao.2017.0110.
  118. Michelagnoli MP, Pritchard J, Phillips MB. Adolescent oncology—a homeland for the “lost tribe”. *Eur J Cancer*. 2003;39(18):2571-2572.
  119. Juliusson G, Hough R. Leukemia. *Prog Tumor Res*. 2016;43:87-100.
  120. Curran E, Stock W. How I treat acute lymphoblastic leukemia in older adolescents and young adults [published correction appears in *Blood*. 2015;126(15):1868]. *Blood*. 2015;125(24):3702-3710.
  121. Smith AW, Parsons HM, Kent EE, et al; AYA HOPE Study Collaborative Group. Unmet support service needs and health-related quality of life among adolescents and young adults with cancer: the AYAs HOPE study. *Front Oncol*. 2013;3:75.
  122. Albritton K, Bleyer WA. The management of cancer in the older adolescent. *Eur J Cancer*. 2003;39(18):2584-2599.
  123. Ferrari A, Thomas D, Franklin AR, et al. Starting an adolescent and young adult program: some success stories and some obstacles to overcome. *J Clin Oncol*. 2010;28(32):4850-4857.
  124. Lewis I, Morgan S. Models of care and specialized units. In: Bleyer WA, Barr RD, eds. *Cancer in adolescents and young adults*. New York, NY: Springer Verlag; 2007:341-352.
  125. Husson O, Manten-Horst E, van der Graaf WT. Collaboration and networking. *Prog Tumor Res*. 2016;43:50-63.
  126. Zebrack B, Bleyer A, Albritton K, Medearis S, Tang J. Assessing the health care needs of adolescent and young adult cancer patients and survivors. *Cancer*. 2006;107(12):2915-2923.
  127. Zebrack B, Mathews-Bradshaw B, Siegel S; LIVESTRONG Young Adult Alliance. Quality cancer care for adolescents and young adults: a position statement. *J Clin Oncol*. 2010;28(32):4862-4867.
  128. Daniel CL, Emmons KM, Fasciano K, Fuemmeler BF, Demark-Wahnefried W. Needs and lifestyle challenges of adolescents and young adults with cancer: summary of an Institute of Medicine and Livestrong Foundation Workshop. *Clin J Oncol Nurs*. 2015;19(6):675-681.
  129. Hollis R, Morgan S. The adolescent with cancer—at the edge of no-man's land. *Lancet Oncol*. 2001;2(1):43-48.
  130. Roberts CS, Piper L, Denny J, Cuddeback G. A support group intervention to facilitate young adults' adjustment to cancer. *Health Soc Work*. 1997;22(2):133-141.
  131. Beale IL, Kato PM, Marin-Bowling VM, Guthrie N, Cole SW. Improvement in cancer-related knowledge following use of a psychoeducational video game for adolescents and young adults with cancer. *J Adolesc Health*. 2007;41(3):263-270.
  132. Zebrack BJ, Oeffinger KC, Hou P, Kaplan S. Advocacy skills training for young adult cancer survivors: the Young Adult Survivors Conference at Camp Mäka-Dream. *Support Care Cancer*. 2006;14(7):779-782.
  133. Fernandez C, Fraser GA, Freeman C, et al. Principles and recommendations for the provision of healthcare in Canada to adolescent and young adult-aged cancer patients and survivors. *J Adolesc Young Adult Oncol*. 2011;1(1):53-59.
  134. Palmer S, Thomas D. A practice framework for working with 15-25 year old cancer patients treated within the adult health sector. Melbourne, Australia: OnTrac@PeterMac Adolescent and Young Adult Cancer Service; 2008.
  135. Ferrari A, Barr RD. International evolution in AYA oncology: current status and future expectations. *Pediatr Blood Cancer*. 2017;64(9):e26528.
  136. Barr RD, Ferrari A, Ries L, Whelan J, Bleyer WA. Cancer in adolescents and young adults: a narrative review of the current status and a view of the future. *JAMA Pediatr*. 2016;170(5):495-501.