Adolescents and Young Adults Living With an Uncertain or Poor Cancer Prognosis: The "New" Lost Tribe

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ABSTRACT

Historically, adolescent and young adult (AYA) patients with cancer, diagnosed for the first time at age 15 through 39 years, have often been identified as a "lost tribe" without a medical "home"; neither pediatric nor adult oncology services were able to provide age-appropriate care to this specific group. Internationally, AYA care programs are being established to bridge the gap between the age-defined healthcare worlds and to address the specific needs of AYAs with cancer. However, AYA care programs mostly focus on improving cure rates and addressing survivorship issues, and direct less attention to the unique needs of those living with an uncertain and/or poor cancer prognosis. Additionally, palliative care services are typically poorly equipped to address the age-specific needs of this group. Given that increasingly more AYAs with an uncertain and/or poor cancer prognosis are gaining life years because of novel treatments, and sometimes even face the prospect of long-term disease control, AYA care programs should address the unique palliative care needs of this "new" lost tribe within AYA oncology. This report provides a definition and description of the AYA population living with an uncertain and/or poor cancer prognosis in terms of epidemiologic, clinical, and psychosocial characteristics and challenges, and provides perspectives for future research and care initiatives. It also highlights the need to comprehensively examine the experience of AYAs who are living with uncertain and/or poor cancer prognosis to adjust best care practices for this unique group.

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"I feel a sense of hurry, rather than tiredness of life, and that is what keeps me going…. My heart is still beating, so I am moving on."

– 32-year-old woman with EGFR-positive metastatic lung cancer

Adolescents and young adults (AYAs) have historically been a neglected group by pediatric and adult oncology services, but are now recognized as a distinct population by the oncology community due to their unique needs and challenges.[1–3] The US National Cancer Institute (NCI) has defined AYA as those aged 15 to 39 years at initial cancer diagnosis,[3] but also concluded that this age range should be flexible, depending on the research question (biologic, epidemiologic, psychologic) and healthcare delivery system.[4] Quality cancer care for AYAs should be characterized by timely detection, diagnosis, and treatment initiation; adherence to treatment; and access to a multidisciplinary team of healthcare professionals knowledgeable about the biomedical and psychosocial (care) needs of AYAs.[2,5,6] Age-related issues of particular relevance to AYAs with cancer include distress about life choices, difficulties with establishing identity, impaired body image and self-esteem, social isolation, issues with intimacy and fertility, and financial hardship.[7,8] Furthermore, achievement of developmental milestones such as establishing autonomy, completing education, pursuing gainful employment and financial independence, forming (intimate) relationships, and starting a family might be delayed or not reached at all because of cancer and its treatment.[5,8,9] Historically, AYAs with cancer have often been described as a "lost tribe" without a medical "home"; neither pediatric nor adult oncology services were able to provide age-appropriate care to this specific group. Internationally, AYA programs to bridge the gap between the age-defined healthcare worlds and address the specific needs of AYAs with cancer are becoming established, but there remains widespread geographic

variation and an absence of age-focused services in some developed and developing countries.[2,3,10,11]

Most AYA programs are developed for patients whose treatment is intended to be curative.[12] However, although the overall 5-year survival rate for AYAs with cancer is approximately 80%,[13] cancer remains one of the top 5 leading causes of death in the AYA population.[14] Historically, although some AYA cancers have good survival rates even with advanced disease (eg, thyroid cancer),[15,16] standard treatments for AYAs with advanced cancer rarely extended life beyond 1 year. In recent years, the life expectancy of some patients with cancers that are common among AYAs, such as melanoma and Hodgkin lymphoma, have improved significantly following the introduction of personalized genotype-directed and immune therapies, even in patients with advanced or extended disease.[17,18] For example, the 5-year survival rate of patients with metastatic melanoma recruited to the CheckMate 067 trial was 52% in those treated with nivolumab + ipilimumab compared with 25% in those treated with ipilimumab alone.[18]

Because of the historical focus of finding a cure for cancer, the public is often unaware of how much progress has been made in helping patients live longer. AYA programs mostly focus on improving cure rates and survivorship issues; less attention is given to the unique needs of those living with an uncertain and/or poor cancer prognosis (UPCP).[12] Palliative care services are also typically poorly equipped to address the age-specific and disease-related needs of this group,[19,20] including the complex decisions AYAs need to make about their cancer care and the uncertainty they face regarding their futures.[21] It is recognized that all patients with a UPCP should have access to palliative care, focusing on the management of symptoms and facilitating psychosocial and decision-making support.[22] Unfortunately, palliative care services have traditionally been limited to care at the end of life.[23] Poort et al[24] found low rates of end-of-life discussions between specialists and AYA patients. Given that more AYA patients with a UPCP are gaining life years because of better and novel treatments, and sometimes even face the prospect of long-term disease control, AYA care programs should address the unique palliative care needs of this "new" lost tribe within AYA oncology. This report offers a definition and description of the AYA population living with a UPCP in terms of epidemiologic, clinical, and psychosocial characteristics and challenges, and provides perspectives for future research and care initiatives.

Definition and Epidemiology

AYAs living with a UPCP represent a minority group in oncology that has not yet been comprehensively defined. This report defines AYAs with a UPCP as those with advanced cancer for which there is no reasonable hope of cure, indicating that they will die prematurely from cancer, but have no immediate threat of death. Patients with terminal illnesses, often defined in the literature as those with a life expectancy of <3 or <6 months and poor performance status,[25] do not belong to this group. Table 1 presents the tumor types most often diagnosed and 5-year relative survival rates for AYAs with distant disease (providing a good reflection of AYAs living with a UPCP) based on data from the SEER 18 database.[26–31]

Clinical and Psychosocial Characteristics and Challenges

Research on the characteristics of AYAs with a UPCP is scarce and often focuses on issues important for the end of life; their experiences at diagnosis and (early) treatment have hardly been described in clinical research.[32,33] Onset of a cancer with an uncertain or poor prognosis is particularly distressing for AYAs. They have described their diagnoses as inconceivable, as these cancers are considered specific to older people, and are therefore unexpected and traumatic for the AYAs, as well as their families and friends.[32–34] AYAs with a UPCP face many complex decisions but often lack the life experience and fully developed executive functioning necessary for medical decision-making and coping with uncertainty.[35] Close relatives and friends often share the denial of the bad news and will be focused on treatments that will generate hope that cure is still possible.[36]

For AYAs, one of the most troublesome aspects of being diagnosed with a cancer with an uncertain and/or poor prognosis is the loss of control of their life.[36] AYAs report that their life is on hold and experience disruption of anticipated developmental milestones, while their peers are moving ahead with their own life goals.[34,37] They may also experience a sense of social isolation from peers due to a lack of understanding, and may also feel isolated within the healthcare system due to lack of identification with both AYA peers with cancer who have curative treatment goals and older patients with cancer.[34,38] A UPCP is often accompanied by continuing issues, such as symptom burden and treatment-related adverse effects, which result in loss of independence and cause AYAs to become increasingly dependent on their informal caregivers for physical, emotional, and financial support.[8,19,21,34] However, some AYAs may retain a moderately high level of performance and independency for a long time.[32] Because the perspective of a "normal" life may vanish and the future becomes uncertain, fundamental questions may emerge about the meaning of life and their limited remaining time.[34] Younger AYAs often have not lived long enough to establish clear plans for their future, whereas older AYAs feel unable to realize life goals related to careers or family planning, or

Table 1. Age-Standardized 5-Year Relative Survival Outcomes[a]

Cancer	N[c]	Relative Survival % (Number at Risk[b]) 1 Year	2 Years	3 Years	4 Years	5 Years
5-year survival >80%						
Thyroid	741	96.8 (734)	95.2 (686)	94.6 (605)	94.2 (553)	93.1 (502)
Chronic myeloid leukemia[d]	2,363	98.3 (2,348)	95.6 (2,245)	93.9 (1,975)	91.9 (1,740)	90.4 (1,518)
Hodgkin lymphoma	5,009	97.4 (4,976)	94.9 (4,752)	92.6 (4,269)	91.2 (3,771)	90.1 (3,337)
Chronic lymphocytic leukemia[e]	448	99.1 (446)	93.6 (431)	89.4 (385)	88.2 (337)	81.1 (290)
Testis, seminoma[f]	496	92.3 (484)	86.1 (429)	84.2 (374)	83.5 (342)	83.5 (312)
Low-grade glioma[g]	1,040	98.3 (1,037)	94.7 (1,007)	90.0 (937)	86.8 (835)	82.4 (736)
Ovary, nonepithelial[h]	306	88.5 (298)	83.8 (258)	83.3 (217)	82.4 (200)	82.5 (180)
5-year survival 50%–80%						
NHL, B cell[i]	4,127	88.2 (3,990)	82.8 (3,401)	80.2 (2,930)	79.2 (2,596)	78.0 (2,324)
Testis, nonseminoma[j]	2,066	90.2 (1,998)	81.5 (1,732)	78.1 (1,426)	77.0 (1,252)	76.0 (1,106)
Burkitt lymphoma[k]	700	73.3 (656)	67.5 (460)	66.0 (385)	65.0 (330)	64.1 (282)
Myeloma	787	87.8 (778)	76.7 (710)	67.2 (599)	65.0 (525)	61.3 (442)
Acute myeloid leukemia[l]	4,910	83.1 (4,512)	69.4 (3,651)	64.1 (2,755)	61.2 (2,293)	59.4 (1,940)
Small intestine	200	73.7 (195)	65.3 (147)	59.0 (109)	57.2 (88)	56.1 (75)
NHL, T cell[m]	777	68.7 (727)	60.6 (480)	58.6 (377)	57.4 (332)	56.0 (289)
Oral cavity/pharynx	254	81.6 (252)	67.4 (196)	61.3 (141)	54.5 (116)	51.9 (97)
Acute lymphocytic leukemia[n]	4,358	82.3 (4,240)	67.0 (3,528)	58.8 (2,691)	53.9 (2,185)	51.5 (1,827)
Ovary, epithelial[o]	1,168	81.7 (1,142)	71.8 (921)	63.3 (720)	57.2 (561)	51.2 (444)
5-year survival 20%–50%						
Corpus uteri and uterus, NOS	367	74.0 (3,49)	57.7 (223)	45.4 (141)	41.5 (107)	35.3 (84)
Breast	2,341	83.9 (2,294)	63.0 (1,886)	49.5 (1,341)	40.5 (944)	34.7 (661)
Melanoma of the skin	576	58.4 (547)	39.0 (288)	33.1 (166)	30.3 (121)	29.4 (88)
Prostate	38	81.0 (38)	63.5 (29)	26.4 (20)	24.4 (9)	23.4 (7)
Pancreas	771	55.2 (706)	38.4 (309)	30.5 (175)	24.0 (119)	23.1 (84)

(continued on next page)

experience fears about the welfare of their children after they die.[34] This psychologic challenge of anticipatory grief over the life that has not yet been lived may be difficult for AYAs to process and they may be reluctant to face the irreversibility of the progression of their disease.[21] Nonetheless, it is worth mentioning that most AYAs with a UPCP continue to live full lives despite a life-limiting diagnosis.[32] AYAs try to preserve or reclaim normalcy by engaging in usual daily activities. However, physical and psychosocial challenges and the emotional burdens that accompany advanced cancer and its treatment can make it more difficult to realize this normalcy throughout the disease trajectory.[37,39,40]

Most AYAs with cancer are physically fit, apart from their cancer diagnosis, and tolerate treatment relatively well. Compared with older patients, AYAs and/or their clinicians tend to opt for more aggressive treatment, maximizing the dose intensity of chemotherapy and other treatment medications, and participating in phase I trials in order to take every opportunity to survive as long as possible with hope of cure.[36,41] A recent analysis of patients diagnosed with a metastatic soft tissue sarcoma at age 18 to 39 years showed that 21% received chemotherapy in their last month of life.[42] AYAs reported several reasons for choosing aggressive treatment options, such as their age, family pressure, desire to have more time with their loved ones and/or children, an unrealistic hope of cure, hope for a treatment breakthrough, or reluctance to decline treatments offered by their clinicians.[36] Relatively limited data about treatment efficacy in the AYA population, including the efficacy of new and experimental treatments, forces patients and clinicians to make their best guesses about the effects of additional treatments rather than making fully informed decisions. This experience of prognostic uncertainty results in patients and clinicians having to constantly balance concepts of hope and risks with limited or no evidence to guide them.[36]

Table 1. Age-Standardized 5-Year Relative Survival Outcomes[a] (cont.)

Cancer	N[c]	Relative Survival % (Number at Risk[b]) 1 Year	2 Years	3 Years	4 Years	5 Years
5-year survival <20%						
Osseous and chondromatous neoplasms	144	61.3 (141)	39.0 (89)	25.1 (50)	19.7 (27)	19.7 (16)
Cervix uteri	796	55.3 (772)	31.7 (418)	22.3 (236)	19.9 (163)	19.3 (123)
Colon and rectum	3,336	70.0 (3,242)	44.1 (2,332)	29.0 (1,365)	20.3 (824)	16.6 (536)
Lung and bronchus	2,317	52.5 (2,154)	30.4 (1,000)	22.9 (482)	18.0 (296)	16.3 (195)
Soft tissue (including heart)	976	63.4 (941)	35.7 (593)	24.7 (306)	18.4 (199)	15.6 (127)
Urinary system	625	45.7 (585)	27.5 (251)	20.2 (133)	15.6 (84)	13.8 (59)
Liver and bile duct	445	42.5 (381)	24.0 (148)	14.4 (76)	13.2 (39)	11.8 (31)
Stomach	1,446	36.4 (1,338)	17.6 (422)	13.4 (166)	10.6 (103)	9.7 (70)
Esophagus	244	36.8 (232)	15.7 (87)	13.2 (29)	11.1 (18)	4.7 (11)

Abbreviations: AYA, adolescent and young adult; NHL, non-Hodgkin lymphoma; NOS, not otherwise specified.
[a]Total number in database. Total number included in relative survival analyses can be different because of censored cases.
[b]Number at risk includes those still at risk at the different years' follow-up in the relative survival analyses.
[c]All AYAs aged 15–39 years at time of their first diagnosis with malignant distant cancer (diagnosed between 2001–2015), according to SEER Summary Stage 2000 (≥1998)27 were included. The Ann Arbor staging was used for including stage III and IV Hodgkin lymphoma and NHL.28 Cancer type was defined using the site recode ICD-O-3/WHO 2008,p with exception of osseous and chondromatous neoplasms, because these tumors were classified using the AYA site recode/WHO 2008.29,30 Analyses were performed with STATA, version 16.1 (StataCorp LLP). Relative survival was determined using the Ederer II approach and with expected survival probabilities from the US Annual Life Table 1970–2017.31 Age-standardization of outcomes was performed with weights based on the International Cancer Survival Standard 3. End of follow-up was determined by year of death or 2016. Patients with >1 diagnosis or with incomplete survival data were excluded (n=5,630; 11%).
[d]Includes ICD-O-3: 9863, 9875, 9876.
[e]Includes ICD-O-3: 9670, 9823.
[f]Includes ICD-O-3: 9061, 9062, 9064.
[g]Includes ICD-O-3: grade II astrocytoma (9400, 9410, 9411, 9420), oligodendroglioma (9450), mixed glioma (9382).
[h]Includes ICD-O-3: sex cord stromal tumors (8590, 8620, 8622, 8631, 8670), germ cell tumors (9060, 9064, 9070, 9080, 9081, 9082).
[i]Includes ICD-O-3: 9591, 9596, 9671, 9673, 9675, 9678–9680, 9684, 9688–9690, 9695, 9698, 9699, 9735, 9737, 9738.
[j]Includes ICD-O-3: 9065, 9070, 9071, 9080, 9081, 9082, 9084, 9085, 9100, 9101.
[k]Includes ICD-O-3: 9867, 9826.
[l]Includes ICD-O-3: 9727, 9840, 9861, 9865–9867, 9869, 9871–9874, 9891, 9895–9898, 9910, 9911, 9920, 9945, 9946.
[m]Includes ICD-O-3: 9702, 9705, 9708, 9709, 9714, 9716–9719, 9827.
[n]Includes ICD-O-3: 9728, 9729, 9811–9818, 9835–9837.
[o]Includes ICD-O-3: serous tumors (8020, 8021, 8050, 8120, 8260, 8441, 8442, 8450, 8460–8462, 9014), endometrioid tumors (8380, 8381), mucinous tumors (8470, 8471, 8480, 8481), clear cell tumors (8310), carcinosarcoma (8980, 8950, 8951), carcinoma, NOS (8010, 8046, 8140, 8440), mixed tumors (8255, 8323).
[p]Several ICD-O-3 histology codes were historically used but are no longer represented in the 2016 WHO guidelines. These former histology codes have been included, because many diagnoses were registered prior to 2010 using these codes.

Based on prognosis and type of treatment, 3 distinct subgroups of AYAs with a UPCP can be identified: (1) traditional survivors, or patients undergoing standard established treatment with an life expectancy of 1 to 5 years; (2) low-grade glioma (LGG) survivors, or patients with an LGG with a life expectancy of 5 to 10 years; and (3) new survivors, or patients with a UPCP undergoing novel treatment(s).

Traditional Survivors

Traditional survivors include AYAs with leukemia, lymphoma, or metastatic tumors in the breast, colon and rectum, ovary, or testis (germ cell), treated with radiotherapy, chemotherapy, or hormone therapy. Although median overall survival for patients with these cancers is generally well described, it is based on studies with a significantly older median patient age.[33] As a young patient with colorectal cancer described her care experience: "You treat me like I am a 70-year-old patient. Where are treatments that address the isssues relevant to my age?"[43] These traditional survivors are typically treated with one treatment after another, switching regimen whenever the disease progresses, and eventually running out of options. Because these patients are constantly on treatment, they often do not have time without adverse effects and clinic appointments, and treatments become part of their normal routine.[44,45]

LGG Survivors

Primary brain and central nervous system tumors are the third most common cancer and the third most common cause of cancer death in AYAs.[46] Gliomas account for 29% to 35% of the brain tumors, with approximately two-thirds comprising LGGs.[47] LGGs encompass a heterogeneous group of diffuse, slow-growing glial brain tumors.[48] Despite the fact that LGGs remain a major contributor to morbidity and mortality in AYAs, this young patient group is not often specifically studied

in neuro-oncology. Initial treatment of many LGGs is surgical resection, although some are unresectable from the outset.[49] Evidence indicates that, after tumor resection, high-risk patients benefit from immediate adjuvant radiotherapy and chemotherapy, whereas watchful waiting or surveillance is a reasonable option for low-risk patients.[49] When progression is not expected to occur rapidly, delaying postoperative treatment is particularly attractive because the significant adverse effects associated with additional therapies can be postponed without compromising survival outcomes.[49] Despite intensive treatment, tumor recurrence inevitably occurs in most patients with diffusely infiltrating LGGs, and often develops into a high-grade glioma. Patients with progressive low-grade or dedifferentiated gliomas will eventually die of tumor progression.[50,51] Depending on histology, tumor size, and neurologic deficits, 82% of AYAs with an LGG survive ≥5 years (Table 1).[50] However, prolonged survival is often accompanied by cognitive decline caused by tumor infiltration, tumor-related epilepsy, radiation damage, psychologic stress, or a combination of these factors.[50,52] Up to 90% of patients with LGGs may experience long-term cognitive deficits, including impairments in memory, attention, communication, and executive functioning, which can hamper daily functioning, achievement of developmental milestones, and health-related quality of life.[50,53,54] LGGs and their management can affect all aspects of life, and due to the cognitive deterioration over time, this cancer can impact daily life even more severely than most other AYA cancers.[54] The disease has a significant impact on informal caregivers as well, as they have to cope with the burden of cancer, the psychologic consequences, the physical and cognitive deterioration of their child or partner for a relatively long time, and a possible reversal of roles.[51,55]

New Survivors

New survivors can been characterized by patients receiving novel therapies, including immunotherapy or targeted therapy, which have significantly improved outcomes.[15,56] Typical examples of new AYA cancer survivors are patients with advanced melanomas, lung cancer, or recurrent leukemias and lymphomas. Because of the novelty of some therapies, long-term adverse effects have not yet been well described, and prognostic information is often lacking.[33,45] The uncertain prognosis forces this new AYA survivor population to focus on scan results to monitor disease progression, and many of these patients do not plan their lives beyond the next clinical outcome assessment.[44] Uncertainty about the effectiveness of therapy and the anxiety of running out of treatment options is an enormous emotional burden.[33,36] In daily life, anxiety about scan results and the rollercoaster of emotions associated with alternating good and bad results, and everything in between, influence important life choices, such as relationships and career plans. Because these novel therapies are not effective for every patient, the reality is that only a small number of AYAs with advanced cancer will survive considerably longer, and it remains unknown who those survivors are.[56] Patients who do survive longer than expected typically have few "patient peers," because their peers either die or transfer into long-term follow-up care. Patients are also often confronted with difficulties relating to the expense of accessing novel treatments, which is a burden in itself.[45]

Future Perspectives

It is important to note that the SEER database is limited, because no data are available from AYAs who experienced disease progression at a later stage. Furthermore, the SEER data may not be fully representative of the entire AYA population living with a UPCP; differences in access to effective healthcare and treatment ethics exist between countries, for example. To be able to develop personalized (supportive) care programs and interventions, we need not only insight into the epidemiologic characteristics of this new lost tribe but also an understanding of the needs, challenges, preferences, and everyday experiences of AYAs with a UPCP.

Based on available literature, García-Rueda et al[57] created a model to understand the experience of patients living with advanced cancer. They identified the common desire of patients to live normally while being aware of the approach of death, and described living with advanced cancer as a unique process. During this process, patients experience suffering, which can affect every aspect of their lives (ie, physical, psychosocial, emotional, spiritual). Patients try to reduce this suffering and find (new) meaning in life through internal processing, such as adapting to change or staying positive. Each patient experiences this process differently, depending on the person's personality, available social support, and the aggressiveness and progression of the cancer. The impact of the patient's disease on the family dynamics, the importance of the support network, and the healthcare context are also included in this model. Moreover, the study highlights the diversity of the advanced cancer population and emphasizes a focus on the individual and their personal cancer journey rather than on the disease. This model could serve as a starting point to study the specifics of AYAs living with a UPCP. A scoping review found several knowledge gaps in the literature on the experience of AYAs with advanced cancer, including their experience within the healthcare system; their relationships with children, partners, parents, and other AYA patients; and the impact of sociodemographic factors (ie, sex, race, socioeconomic status, sexual orientation) on their experiences.[33] These findings

were supported by an integrative literature study, showing a lack of evidence on the everyday experience of AYAs with advanced cancer.[32] Although these AYA patients can have similarities to children or adults with advanced cancer, they may have unique concerns related to age, life stage, and family dynamics that have not yet been identified.

These investigators all call for more research into the experiences of AYA patients with advanced cancer so that person-centered care initiatives can be developed to improve their lives in a meaningful way.[32,33,57] Existing clinical practice guidelines highlight the need for early integration of supportive and palliative care in standard oncology care for AYAs in order to meet the unique medical, psychosocial, and supportive care needs of these patients and their families.[58] An integrated palliative care service with early engagement can provide open discussion around advanced care planning,[58] which can be defined as "a process that supports [patients] at any age or stage of health in understanding and sharing their personal values, life goals, and preferences regarding future medical care."[59] Advanced care planning needs to be seen as an ongoing process embedded within standard healthcare and, particularly for AYAs with a UPCP, should be implemented early in the disease trajectory.[59] Importantly, the introduction of supportive care rather than palliative care terminology allows the introduction of relevant concepts and discussions in a less stigmatized way. Speaking the right language at the right moment, although crucial for all patients with cancer, is of utmost importance in this precious phase of life for AYAs with a UPCP. The dynamics and fluctuating characteristics of life-limiting cancers and life circumstances of AYAs demand a patient-centered approach and the revisiting and revision of patients' wishes over time.[60]

With limited empirical literature available on the topic of this new lost tribe, it is clear that research is needed to comprehensively examine the experiences of AYAs with a UPCP to adjust best care practices for this unique group.

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References

1. Meeneghan MR, Wood WA. Challenges for cancer care delivery to adolescents and young adults: present and future. Acta Haematol 2014; 132:414–422.
2. 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;28:4850–4857.
3. 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. Accessed February 8, 2021. Available at: https://www.livestrong.org/sites/default/files/what-we-do/reports/ayao_prg_report_2006_final.pdf
4. Smith AW, Seibel NL, Lewis DR, et al. Next steps for adolescent and young adult oncology workshop: An update on progress and recommendations for the future. Cancer 2016;122:988–999.
5. Coccia PF, Pappo AS, Beaupin L, et al. Adolescent and young adult oncology, version 2.2018, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2018;16:66–97. To view the most recent version of these guidelines, visit NCCN.org
6. Zebrack B, Mathews-Bradshaw B, Siegel S. Quality cancer care for adolescents and young adults: a position statement. J Clin Oncol 2010; 28:4862–4867.
7. D'Agostino NM, Penney A, Zebrack B. Providing developmentally appropriate psychosocial care to adolescent and young adult cancer survivors. Cancer 2011;117(Suppl):2329–2334.
8. Zebrack BJ. Psychological, social, and behavioral issues for young adults with cancer. Cancer 2011;117(Suppl):2289–2294.
9. Arnett JJ. Emerging adulthood. A theory of development from the late teens through the twenties. Am Psychol 2000;55:469–480.
10. Saloustros E, Stark DP, Michailidou K, et al. The care of adolescents and young adults with cancer: results of the ESMO/SIOPE survey. ESMO Open 2017;2:e000252.
11. Li CK, Dalvi R, Yonemori K, et al. Care of adolescents and young adults with cancer in Asia: results of an ESMO/SIOPE/SIOP Asia survey. ESMO Open 2019;4:e000467.
12. Park EM, Rosenstein DL. Living with advanced cancer: unmet survivorship needs. N C Med J 2014;75:279–282.
13. Close AG, Dreyzin A, Miller KD, et al. Adolescent and young adult oncology-past, present, and future. CA Cancer J Clin 2019;69:485–496.
14. Sender L, Zabokrtsky KB. Adolescent and young adult patients with cancer: a milieu of unique features. Nat Rev Clin Oncol 2015;12: 465–480.
15. Bleyer A, O'Leary M, Barr R, Ries LAG, eds. Cancer epidemiology in older adolescents and young adults 15 to 29 years of age, including SEER incidence and survival: 1975–2000. National Cancer Institute, NIH Pub. No. 06-5767; Bethesda, MD, 2006.
16. Bleyer A. Latest estimates of survival rates of the 24 most common cancers in adolescent and young adult Americans. J Adolesc Young Adult Oncol 2011;1:37–42.
17. Connors JM, Jurczak W, Straus DJ, et al. Brentuximab vedotin with chemotherapy for stage III or IV Hodgkin's lymphoma. N Engl J Med 2018; 378:331–344.
18. Larkin J, Chiarion-Sileni V, Gonzalez R, et al. Five-year survival with combined nivolumab and ipilimumab in advanced melanoma. N Engl J Med 2019;381:1535–1546.
19. Pritchard S, Cuvelier G, Harlos M, et al. Palliative care in adolescents and young adults with cancer. Cancer 2011;117(Suppl):2323–2328.
20. Wiener L, Weaver MS, Bell CJ, et al. Threading the cloak: palliative care education for care providers of adolescents and young adults with cancer. Clin Oncol Adolesc Young Adults 2015;5:1–18.
21. Clark JK, Fasciano K. Young adult palliative care: challenges and opportunities. Am J Hosp Palliat Care 2015;32:101–111.
22. World Health Organization. WHO Definition of Palliative Care. Accessed September 14, 2019. Available at: https://www.who.int/cancer/palliative/definition/en/
23. Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. N Engl J Med 2010;363: 733–742.
24. Poort H, Zupanc SN, Leiter RE, et al. Documentation of palliative and end-of-life care process measures among young adults who died of cancer: a natural language processing approach. J Adolesc Young Adult Oncol 2019;9:100–104.

25. Hui D, Nooruddin Z, Didwaniya N, et al. Concepts and definitions for "actively dying," "end of life," "terminally ill," "terminal care," and "transition of care": a systematic review. J Pain Symptom Manage 2014; 47:77–89.
26. SEER*Stat Databases: November 2018 submission. Incidence - SEER 18 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2018 Sub (2000–2016 varying). SEER web site. Accessed April 2, 2020. Available at: https://seer.cancer.gov/data-software/documentation/seerstat/nov2018/
27. National Cancer Institute; Surveillance, Epidemiology, and End Results Program. SEER Summary Staging Manual 2000. Accessed April 2, 2020. Available at: https://seer.cancer.gov/tools/ssm/ssm2000/
28. National Cancer Institute; Surveillance, Epidemiology, and End Results Program. Lymphomas – Ann Arbor Staging (1983–2015). Accessed April 2, 2020. Available at: https://seer.cancer.gov/seerstat/variables/seer/ajcc-stage/ann-arbor/
29. National Cancer Institute; Surveillance, Epidemiology, and End Results Program. Site Recode ICD-O-3/WHO 2008 Definition. Accessed April 2, 2020. Available at: https://seer.cancer.gov/siterecode/icdo3_dwhoheme/
30. National Cancer Institute; Surveillance, Epidemiology, and End Results Program. AYA Site Recode/WHO 2008 Definition. Accessed April 2, 2020. Available at: https://seer.cancer.gov/ayarecode/aya-who2008.html
31. National Cancer Institute; Surveillance, Epidemiology, and End Results Program. Expected Survival Life Tables. Accessed April 2, 2020. Available at: https://seer.cancer.gov/expsurvival/
32. Lundquist DM, Berry DL. Experiences of adolescents and young adults living with advanced cancer: an integrative review. Oncol Nurs Forum 2019;46:451–458.
33. Drake EK, Urquhart R. The experiences of young adults living with metastatic/advanced cancer: a scoping review. J Adolesc Young Adult Oncol 2020;9:145–156.
34. Knox MK, Hales S, Nissim R, et al. Lost and stranded: the experience of younger adults with advanced cancer. Support Care Cancer 2017;25: 399–407.
35. Casey BJ, Tottenham N, Liston C, et al. Imaging the developing brain: what have we learned about cognitive development? Trends Cogn Sci 2005;9:104–110.
36. Figueroa Gray M, Ludman EJ, Beatty T, et al. Balancing hope and risk among adolescent and young adult cancer patients with late-stage cancer: a qualitative interview study. J Adolesc Young Adult Oncol 2018;7: 673–680.
37. Schapmire TJ, Head BA, Faul AC. Just give me hope: lived experiences of Medicaid patients with advanced cancer. J Soc Work End Life Palliat Care 2012;8:29–52.
38. Trevino KM, Fasciano K, Block S, et al. Correlates of social support in young adults with advanced cancer. Support Care Cancer 2013;21:421–429.
39. Ngwenya N, Kenten C, Jones L, et al. Experiences and preferences for end-of-life care for young adults with cancer and their informal carers: a narrative synthesis. J Adolesc Young Adult Oncol 2017;6:200–212.
40. Lundquist DM, Berry DL, Boltz M, et al. Wearing the mask of wellness: the experience of young women living with advanced breast cancer. Oncol Nurs Forum 2019;46:329–337.
41. McVeigh TP, Sundar R, Diamantis N, et al. The role of genomic profiling in adolescents and young adults (AYAs) with advanced cancer participating in phase I clinical trials. Eur J Cancer 2018;95:20–29.
42. Younger E, Husson O, Asare B, et al. Treatment patterns and clinical outcomes of adolescents and young adults with metastatic soft tissue sarcomas: a specialist centre experience. J Adolesc Young Adult Oncol 2019.
43. Lidington E, van der Graaf WTA, Younger E, et al. Identifying unmet needs in patients diagnosed with cancer as young adults aged 25-39: a qualitative study of an underserved population. Presented at the 3rd Global Adolescent and Young Adult Cancer Congress; December 4–8, 2018; Sydney, Australia.
44. Lobb EA, Lacey J, Kearsley J, et al. Living with advanced cancer and an uncertain disease trajectory: an emerging patient population in palliative care? BMJ Support Palliat Care 2015;5:352–357.
45. Langbaum T, Smith TJ. Time to study metastatic-cancer survivorship. N Engl J Med 2019;380:1300–1302.
46. Ostrom QT, Gittleman H, de Blank PM, et al. American brain tumor association adolescent and young adult primary brain and central nervous system tumors diagnosed in the United States in 2008-2012. Neuro-oncol 2016;18(Suppl 1):i1–50.
47. Diwanji TP, Engelman A, Snider JW, et al. Epidemiology, diagnosis, and optimal management of glioma in adolescents and young adults. Adolesc Health Med Ther 2017;8:99–113.
48. Baumert BG, Hegi ME, van den Bent MJ, et al. Temozolomide chemotherapy versus radiotherapy in high-risk low-grade glioma (EORTC 22033-26033): a randomized, open-label phase 3 intergroup study. Lancet Oncol 2016;17:1521–1532.
49. Geurts M, van den Bent MJ. On high-risk, low-grade glioma: what distinguishes high from low? Cancer 2019;125:174–176.
50. Shields LB, Choucair AK. Management of low-grade gliomas: a review of patient-perceived quality of life and neurocognitive outcome. World Neurosurg 2014;82:e299–309.
51. Taphoorn MJ, Sizoo EM, Bottomley A. Review on quality of life issues in patients with primary brain tumors. Oncologist 2010;15:618–626.
52. Taphoorn MJ, Klein M. Cognitive deficits in adult patients with brain tumours. Lancet Neurol 2004;3:159–168.
53. Taphoorn MJ. Neurocognitive sequelae in the treatment of low-grade gliomas.Semin Oncol 2003:30;45–48.
54. Papageorgiou GI, Razis ED. CNS tumors in adolescents and young adults: the need for a holistic specialized approach. JCO Oncol Pract 2020;16: 155–162.
55. Edvardsson T, Ahlström GJ. Being the next of kin of a person with a low-grade glioma. Psychooncology 2008;17:584–591.
56. Kumar RS, Messina JL, Sondak EK, Reed D. Treating melanoma in adolescents and young adults: challenges and solutions. Clin Oncol Adolesc Young Adults 2015;5:75–86.
57. García-Rueda N, Carvajal Valcárcel A, Saracíbar-Razquin M, et al. The experience of living with advanced-stage cancer: a thematic synthesis of the literature. Eur J Cancer Care (Engl) 2016;25:551–569.
58. Donovan KA, Knight D, Quinn GP. Palliative care in adolescents and young adults with cancer. Cancer Contr 2015;22:475–479.
59. Sudore RL, Lum HD, You JJ, et al. Defining advance care planning for adults: a consensus definition from a multidisciplinary Delphi panel. J Pain Symptom Manage 2017;53:821–832.e1.
60. Zadeh S, Pao M, Wiener L. Opening end-of-life discussions: how to introduce Voicing My CHOiCES™, an advance care planning guide for adolescents and young adults. Palliat Support Care 2015;13:591–599.