Research Registry Protocol Title: YASU Research Registry

Research Registry Sponsor:
Young Adult Survivors United (YASU)

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List of Abbreviations:

YASU: Young Adult Survivors United
AYA: Adolescent and Young Adult
YA: Young Adult
PHQ-9: Patient Health Questionnaire-9
GAD-7: General Anxiety Disorder-7
MOS: Medical Outcomes Study
COST-FACIT: Comprehensive Score for Financial Toxicity-Functional Assessment of Chronic Illness Therapy
AYA-POST: Adolescent and Young Adult Psycho-Oncology Screening Tool

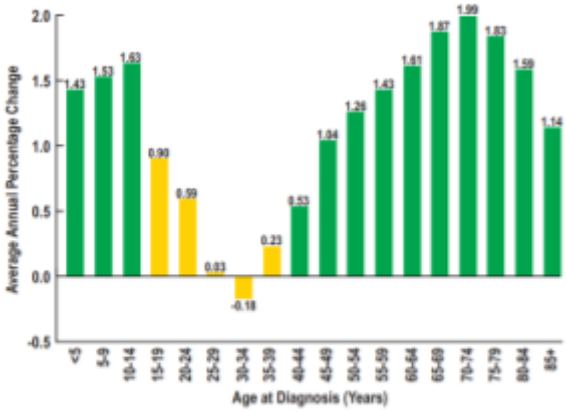
Introduction

This document is a protocol for a human research registry. This registry is to be conducted according to US standards of Good Clinical Practice in accordance with applicable Federal regulations and research policies and procedures.

Background Information and Scientific Rationale

In a 2006 landmark report, the National Cancer Institute recognized adolescents and young adults (AYAs) with cancer as a distinct subset of oncology patients, "distinguished by physiologic, developmental, and societal characteristics." (National Cancer Institute & Livestrong Young Adult Alliance, 2006) This report also showed that survival rates of AYA, ages 15-39, had not appreciably improved since the 1970s, despite improvements in both younger and older counterparts (Figure 1). While some data suggest that overall survival in AYA is now beginning to improve (Close et al., 2019), the rate of cancer in AYAs has increased by nearly 30% since the 1970s. (Scott et al., 2020) About 90,000 young adults (AYA) between the age of 15 and 39 are diagnosed with cancer each year in the United States, accounting for about 5% of all annual cancer diagnoses. (American Cancer Society, 2020)

Figure 1



Improvement in 5-Year Relative Survival, Invasive Cancer, SEER 1975-1997. Reprinted from Closing the Gap: Research and Care Imperatives for Adolescents and Young Adults with Cancer (p.5) by National Cancer Institute and LiveStrong Young Adult Alliance. Copyright 2006 by National Institutes of Health.

The AYA age range of 15-39 was chosen to be inclusive rather than exclusive and because it aligned with the lag in survival rate improvements compared to younger and older age groups. (National Cancer Institute & Livestrong Young Adult Alliance, 2006). Despite similarities, AYAs can vary widely in terms of their psychosocial development and emotional maturity– differences that may or may not correlate with chronological age. For instance, the psychosocial needs of a 15-year-old adolescent attending high school and living at home with parents differs greatly from young adults who may be living on their own, beginning careers, gaining financial independence, starting a family, raising children, or caring for aging parents.

This recognition of different developmental stages and concerns within the AYA group was the impetus for Stephanie Samolovitch, MSW to found Young Adult Survivors United (YASU) in 2020. YASU's mission is to support young adults (YAs), ages 18-39, with cancer. (*Young Adult Survivors United*, n.d.) Since 2020, YASU has been providing virtual support groups for survivors and co-survivors impacted by YA cancer. YASU also hosts regular socials, has a financial assistance program and provides respite opportunities. Since the group's

inception, close to 500 members have joined from Western Pennsylvania, across the US, and from numerous countries around the world. YASU has demonstrated the need for YA specific support. Young adults with cancer from many other states and countries have participated in YASU because there are so few resources to support these individuals. Truly, YASU is building a sustained community of support for those impacted with YA cancer.

Too often, AYAs fall into "no man's land" between pediatric and adult oncology with few options for AYA specific expertise and care. In research studies, AYA are often grouped together with pediatric or adult patients and not seen as a distinct group. This has limited our understanding of the unique needs and outcomes of those diagnosed with cancer as an AYA. To our knowledge, only two large research registries have been organized to study the AYA population.

The Childhood Cancer Survivor Study (CCSS) follows participants diagnosed up to age 20. The purpose of CCSS is to gain new knowledge about the long-term effects of cancer and therapy. As of January 2021, this study includes a cohort of 4244 AYA diagnosed between 15 and 20. While the follow-up with these individuals is in-depth, longitudinal, and ongoing, young adults (YA) diagnosed with cancer after the age of 20 are not represented in this dataset.

In 2007, the Adolescent & Young Adult Health Outcomes & Patient Experience Study (AYA HOPE) study was conducted in patients diagnosed between the ages of 15 and 39 with one of the following cancers: germ cell, Hodgkin lymphoma, non-Hodgkin lymphoma, acute lymphoblastic leukemia (ALL), or sarcoma (Ewing, osteosarcoma, or rhabdomyosarcoma). Altogether, AYA HOPE includes approximately 530 AYA cancer patients with follow-up approximately 24 months post-diagnosis. Participants were recruited from one of the following SEER cancer registries: Los Angeles, Seattle-Puget Sound, Iowa, Louisiana, Detroit, Northern California, and Greater California. This study concluded in July, 2010. AYA HOPE is an important study which provides a preliminary framework to describe the unique challenges of AYA diagnosed with cancer, (namely, financial burden, education and work, relationships and family planning, as well as physical and mental health), however many YA cancers were not represented in this dataset and only individuals from certain parts of the country were included. Furthermore, the study only includes one follow-up and the study is no longer gathering data.

There is a lack of age-relevant support and resources as well as a gap in the knowledge of the needs and outcomes of YAs with cancer. YASU has a unique opportunity to add to the literature by surveying participants in an ongoing manner from its members in Western Pennsylvania, across the country, and around the world. This dataset will help to explore the unmet needs of YAs with cancer, determine effectiveness of programming, as well as plan for future programming to serve this population. In the future, we hope to be able to also make this dataset available to other academicians and researchers interested in improving the health and wellbeing of YA survivors with cancer.

Registry Specific Aims

Through this research registry we plan to:

1. Objectively measure patient-reported symptoms (depression, anxiety, distress), perceived social support, financial toxicity and needs in survivors of young adult cancer at baseline and over time.
2. Determine effectiveness of YASU programming by examining its possible mediation on the measures of Aim 1.
3. Identify patients who may be eligible for participation in future research studies.

Registry Design

Research Design

This registry will prospectively collect data from young adult cancer survivors using electronic surveys to describe patient-reported needs and outcomes at baseline as well as changes over time. Please note that all information collected for this registry is self-reported and not confirmed.

Registry Site(s)/Location(s) and Number of Subjects

YASU website registration page: yasurvivors.org

Total number of all sites: 1
Estimated number of subjects at all sites combined: undetermined. ongoing recruitment will occur as members register with the organization.

Subject Selection

Vulnerable Populations (if applicable)

N/A

Participant Selection

Inclusion Criteria

1. Diagnosed with cancer between the ages of 18 and 39.
2. Able to speak and read English.

This registry is designed to explore the specific concerns, needs, and outcomes of those diagnosed with cancer as YAs (ages 18-39). Potential participants will be required to comprehend English as some of the surveys we will administer have not been validated in other languages. Additionally, YASUs programming is conducted in English. Without the ability to comprehend English, individuals would not be able to participate in YASU programming and we would not be able to test for possible mediation, as listed in Aim 2.

Exclusion Criteria

1. Inability to provide consent (such as neurological illness or mental incapacity)
2. Has not registered as a member of YASU

Waiver of Written Documentation of Consent or Waiver of Consent

We are applying for a Waiver of Written documentation of Consent (consent will be obtained but signatures will not be required) as this study is minimal risk and will be conducted completely electronically.

Registry Procedures

Specific Training

After IRB approval and prior to study initiation, the PI will meet with members of the YASU organization to explain the registry and procedures for consent and data collection and their roles and duties including answering any questions or concerns that may arise. Besides an email sent to current YASU members inquiring about their interest in research registry participation, the consent for new members and ongoing surveys for those who consent to participate will be automatically triggered and sent (using Salesforce) so we do not anticipate needing significant involvement from YASU organizational staff members for ongoing study management.

Recruitment of participants

YASU members who have already registered with the organization will receive an email providing an overview of the registry at a time point after IRB approval for the registry has been secured. No previous data they provided will be used in the research registry. Only information that they provide in the future will be used. Any new members registering with YASU will be provided with this information at the time of registering with the organization If the member would like to participate in the research registry, they may access a webpage (data security measures are discussed later in the protocol) which will provide an overview of the purpose of the study and expectations. Potential participants will be informed that their participation in the registry is voluntary and will not in any way change their relationship with the YASU organization. Potential participants will be given as much time as they need to review the study description and will be provided with the PI's and/or a YASU staff member's email to answer any questions they may have before providing consent via the webpage. Additionally, for any current members, we will offer a virtual session to describe the study and

provide a forum for questions, should they so choose. Potential participants will not be required to attend the virtual session; they may also choose to email the PI or YASU staff members with questions, if they prefer.

Participants will be offered two levels of consent. They will be asked to enter the registry for research purposes. They will also choose to opt-in or opt-out of consenting to future contact [for further follow-up or for invitation to participate in additional research studies]. “Opting-in” to future contact will allow us to use the contact information they provided to YASU to facilitate future contact (e.g. name, email address, phone numbers, mailing address) for researchers who have received approval from YASU. Participants will provide consent electronically by certifying they have read the information sheet and either agree or do NOT agree to participate in the registry. They will also either choose to agree to future contact for research or NOT agree to future contact for research.

Data Collection Schedule

Cancer survivors will be asked for consent at the time of registration with YASU or (in the case of those who have already registered) with an email sent to describe study and providing an opportunity to give consent and participate in the registry. Baseline and annual follow-up data will be collected according to the table below. In addition, participation in organizational sponsored programs (e.g., socials, support groups, financial assistance) will be recorded and included in the research registry.

	Instrument		Assessment Time Points	
		# Items (Approx. time)	Baseline	6 mos., then Yearly
Demographics Race Gender DOB Address			 ✔ ✔ ✔ ✔	
Disease and treatment information Age at Diagnosis Type of cancer Stage Treatment			 ✔ ✔ ✔ ✔	
Change in disease or treatment	Compared to a year ago, is your health: better, about the same, or worse [If better or worse, then allow free text to explain why]			✔
Depression	PHQ-9	9 (2 min)	✔	✔
Anxiety	GAD-7	7 (1-2 min)	✔	✔
Distress	Distress Thermometer (included in AYA-POST)	1 (30 sec)	✔	✔
Needs Assessment	AYA Psycho-Oncology Screening Tool (AYA-POST)	50 (5 min)	✔	
Financial Toxicity	COST – FACIT (Ver 2)	12 (3 min)	✔	✔
Social support survey instrument	MOS Social Support Survey Instrument	19 (5 min)	✔	✔

Baseline= day of enrollment in the program

Surveys completed ±2 weeks from targeted timeframe

Registry Duration

Registry enrollment will be ongoing. Participants will remain active in the registry until they voluntarily withdraw or expire. Any data that has been provided up until that point will continue to be included in the registry.

Data Management and Quality Plan

Data De-identification

Participants will be assigned a unique identifier instead of using their names, however other unique identifiers may still be included in the dataset (e.g., zip code and date of birth). The unique identifier will automatically be assigned by Salesforce based on the order of enrollment in the research registry. For instance, the first person to enroll in the research registry would be assigned 0001, the second would be assigned 0002, and so on. A spreadsheet will automatically be created in Salesforce when YASU members enroll in the research registry which will link the unique identifier to the participants. This spreadsheet will be stored in Salesforce separately from the registry dataset. The PI and YASU staff members may be granted access to this information as well as future research collaborators. We plan to keep this linking information available indefinitely. The link between the subject's identity and the assigned registry number may be broken if it becomes necessary to clarify survey responses or if survey responses require reaching out to the individual to provide resources (e.g., reporting on the PHQ-9 plans to harm or kill themselves or others).

Data Confidentiality, Storage, and Retention

Registry documentation and data will be stored electronically within Salesforce. Salesforce contributes to keeping ePHI secure in the Salesforce Covered Services by implementing security safeguards that apply to all customers by default such as:

- Continually monitoring the services for security violations
- Encrypting all data in transit
- Storing user passwords in the SHA-256 one-way hash format
- Enabling audit logging that allows system administrators to track certain change activity in the Salesforce Covered Services
- Providing customer administrators with configurable tools to maintain strict password security policies which govern access
- Providing customer administrators with configurable tools to define user profiles and permission sets governing data visibility
- Providing customer administrators with configurable tools to define a company-wide sharing model, a role hierarchy, and security rules governing data access
- Providing customer administrators with configurable tools for field level history monitoring and retention.

Data Quality

Source data verification is not necessary for this research registry because the electronic surveys *are* the source data. Prior to data analysis, data will be checked for anomalies or outliers which might suggest invalid data entry by participants.

Data Sharing

Original records including identifiable data will be available to members of the research team and YASU organization for an indefinite period of time. Data may be shared with other researchers/groups with objectives inside or outside the primary aims of this study. In order to be granted access to our dataset, the outside researcher would need to secure IRB approval from an IRB for their proposed study and then would sign a YASU-provided confidentiality agreement. Datasets shared with researchers outside of YASU will not include identifiers. This new data may be made available to the general public via the Internet and an open database. This information will not have participants name or other personally identifiable information included (i.e. it will be de-identified).

Future research collaborators outside of YASU may use the registry to contact participants for other studies and may have access to the linked Salesforce spreadsheet to screen for candidates. Outside researchers who wish to use contacts from the YASU research registry in recruitment for their study will be required to secure IRB approval for their proposed study and to complete the YASU-provided confidentiality agreement prior to any possible participant contact information being shared. Once IRB-approval has been received and the agreement is completed, the PI (and/or YASU executive director) may grant the requestor access to the requested information.

Registry Data Points

All data will be collected via electronic survey as described earlier.

Initial baseline demographics will be collected at the time of registry enrollment and will include self-reported date of birth, race, gender, and address.

Disease and treatment information will be collected via self-report at the time of consent to the research registry. Self-reported information that will be collected include age at diagnosis, type of cancer, stage, and treatment received.

Patient Health Questionnaire 9 (PHQ-9) (Pfizer, 2010): The PHQ-9 is a 9-item self-reported instrument designed to assess depressive symptoms. For each of the questions, individuals choose one of the following responses regarding how they have been feeling in the past two weeks: Not at all (0), Several days (1), More than half the days (2), or nearly every day (3). The responses can be summed together to yield a total score from 0-27, with higher scores indicating more depressive symptoms. The PHQ-9 will be completed electronically via survey at baseline and annually.

Generalized Anxiety Disorder (GAD-7) (Pfizer, 2010): The GAD-7 is a self-administered 7-item instrument to measure anxiety symptom severity. Like the PHQ-9, individuals think about how they have been feeling in the past two weeks and choose from the following answers: Not at all

(0), Several days (1), More than half the days (2), or nearly every day (3). Total scores range from 0-21, with higher scores indicating greater anxiety symptom severity.

Adolescent and Young Adult Pyscho-Oncology Screening Tool (AYA-POST) (Patterson et al., 2022): The AYA-POST provides a psychosocial screening and assessment for people diagnosed with cancer. The tool comprises a distress thermometer and age-specific needs assessment. The distress thermometer quantifies the amount of self-reported distress an individual has experienced over the past week ranging from 0 (no distress) to 10 (high distress). The needs assessment identifies areas of distress or concern in the following categories: practical, family, emotional, social, physical, information, and other (which allows for free response).

COmprehensive Score for financial Toxicity-Functional Assessment of Chronic Illness Therapy (COST-FACIT) (Version 2) (FACITgroup, 2017): The COST-FACIT is a 12-item patient reported measure of financial distress for cancer patients. The measure provides a summary score for financial toxicity. Scores range from 0-44 with higher scores indicating better financial wellbeing.

MOS Social Support Survey Instrument (Sherbourne & Stewart, 1992): The Social Support Survey is a self-administered, multidimensional social support survey that was specifically developed for patients with chronic health conditions. This 19-item measure consists of four separate social support subscales (emotional/informational support; tangible support; affectionate support; positive social interaction) and an overall functional social support index. Higher scores in the subscale and the overall support index indicate more support.

Statistical Analysis Plan

Aim 1 is to describe patient-reported symptoms (depression, anxiety, distress), perceived social support, financial toxicity and needs in survivors of young adult cancer at baseline and over time. Baseline data will be summarized using descriptive statistics appropriate to the variable's level of measurement. Repeated measures analysis of variance will be used to measure changes over time.

Aim 2 is to determine effectiveness of YASU programming by examining its possible mediation on the measures of Aim 1. This will be assessed via mediation analysis suited to longitudinal data, such as a natural effect models (Mittinty & Vansteelandt, 2020).

Once data are gathered we will determine whether to exclude missing data pair-wise or whether we plan to impute missing values, depending on the variable and the amount of missing data within and between cases.

Potential Risks and Benefits

Potential Benefits

There are no direct benefits to subjects for participating in this research registry. However, information regarding needs and wellbeing of young adult cancer survivors may result from this registry.

Potential Risks

This research represents a registry documenting the needs and outcomes of young adult cancer survivors. The most likely risk posed to participants would be a breach of confidentiality if someone other than the research team obtained access to the data.

We do not anticipate that completing registry surveys will increase the risk of depression or suicide, however these things may be reported on the depressive symptom measure. Resources for those that report suicidality will be provided including a suicide hotline and links to mental health resources.

Mitigation of Risks

Security measures in place to prevent breach of confidentiality from happening (e.g. using Salesforce, an application that upholds HIPAA privacy and security measures; employing features such as limiting access to identifiable data to only users that are associated with the registry).

Participants' responses to the depression inventory scale (PHQ-9) will be monitored. Resources for those that report suicidality will be provided including a suicide hotline and links to mental health resources.

Provisions to Protect the Privacy Interest of Registry Participants

All precautions will be taken to make sure that only authorized individuals will be accessing subject research records. The collection of sensitive information about subjects is limited to the amount necessary to achieve the aims of the research registry, so that no unneeded sensitive information is being collected.

Early Withdrawal of Subjects

Investigator Withdrawal of Subjects

Research registry participants will continue to be surveyed annually. If a participant does not complete surveys within the 4-week "grace period" (±2 weeks from targeted timeframe) the survivor will not be withdrawn from the registry, but these surveys will be considered as missing data in the data set.

Subject Request for Withdrawal from Registry

Patients wishing to withdraw their data from the research registry will be directed to contact the principal investigator. From the point of withdrawal, no further data will be collected from the patient or their medical records. However, any data collected up to the point of withdrawal will be maintained for integrity of the research registry. Patients will be made aware of their rights in the consent.

Data Collection and Follow-up for Withdrawn Subjects

Patients who withdraw from the registry will have their data maintained in the research database up to the point of withdrawal. This data will be included in subsequent analysis.

Adverse Event Reporting

Adverse Events

N/A; This is an observational registry that does not include a planned intervention or exposure.

Ethical Considerations

N/A

Sharing of Results with Subjects

Individual participant results will not be shared with subjects or others. General results from aggregate data may be shared with participants.

Funding Source

Staunton Farm Foundation (07/01/23-06/30/24)
Elsie H. Hillman Foundation (07/01/23-06/30/25)

Subject Stipends or Payments

Participants will be given a $15 Amazon gift card for completion of the initial set of surveys and a $10 Amazon gift card for subsequent survey sets (e.g., 6 month, 12 month, and 24 month follow-ups).

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