The Mental Health Effects in Adolescent/Young Adult (AYA) Patients Coping with Cardiotoxicity Related to Cancer Treatment: A proof-of-principle study

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Abstract

Research Question: Are adolescent and young adult (AYA) cancer survivors with chemotherapy-induced cardiotoxicity at an increased risk of developing depression and anxiety than AYA cancer survivors with less severe chemotherapy-associated side effects?

Background, Significance, and Rationale for the Question: Less is known about the AYA cancer population than other cancer populations and this population has not seen the same positive trends in mortality over the last few decades when compared to cancers diagnosed in childhood or later in adulthood. As treatments continue to improve and cancer patients have longer survival periods, there has been an increased incidence of long-term chemotherapy-related side effects, of which cardiotoxic side effects are associated with the highest mortality rate. While there is research documenting the cardiotoxic side effects that may develop, less has been published regarding patient perceptions of this cardiovascular disease diagnosis and how it affects the mental and behavioral health of an AYA cancer survivor. The primary goal of this study is to provide proof-of-principle to support a larger, follow-up investigation designed to understand the psychosocial effect that a disease diagnosis with severe clinical effects by evaluating the impact that chemotherapy-induced cardiotoxic side effects may have on AYA cancer survivor cared for in an urban cancer survivorship clinic in Dallas, TX.

Materials and Methods: A prospective cohort study using semi-structured interviews in combination with surveys will be performed. Patients seen through the "After the Cancer Experience" (ACE) Survivorship program at the UT-Southwestern (UTSW) campus. A portion of these patients will have cardiotoxic side effects from chemotherapy and the remaining patients will have less severe side effects from chemotherapy. Secondary endpoint metrics will include anxiety and depression scales such as the PHQ-9 and GAD-7. All patients will be screened using these tools before and after each semi-structured interview and given the appropriate consent form. Survey data will be collected at the time of consent over telephone.

Results, Conclusions, and Impact: Recruitment posed as a major barrier to study completion as only three participants successfully enrolled and completed the study. Not enough data was collected to compare rates of anxiety and depression in cancer survivors suffering from chemotherapy-induced cardiotoxicity to less severe chemotherapy-related side effects. Initial data does suggest that survivors who underwent mental health counseling and addressed mental health concerns during cancer treatment were better equipped to cope with a late effect diagnosis later in life. This study highlighted the difficulty in recruiting cancer survivors into a research study, especially during the COVID pandemic. Future research should be done to fully assess whether certain late effect diagnoses that cancer patients develop may place them at a greater risk of developing anxiety and depression. In addition, many cancer patients may benefit from an effective mental health intervention to improve quality of life, patient satisfaction, and completeness of care that may improve long term mental health outcomes.

Research Question

Are adolescent and young adult (AYA) cancer survivors with chemotherapy-induced cardiotoxicity at a higher risk of developing depression and anxiety than AYA cancer survivors with less severe chemotherapy-associated side effects?

Hypothesis: We performed a proof-of-concept study designed ultimately to test the hypothesis that adolescent and young adult cancer survivors with chemotherapy-induced cardiotoxic side effects will demonstrate survey and interview responses consistent with increased anxiety and depression in comparison to adolescent and young adult cancer survivors with less severe chemotherapy-induced side effects. We expect this to be supported objectively by using grounded theory methodology and using survey measures pre- and post-interview to document relative measures of depression and anxiety. Depression and anxiety scores are expected to be higher in the cardiotoxic side effect population in comparison to the less severe side effect population. Themes arising from the semi-structured interview and constructed using grounded theory should be more negative in nature in the cardiotoxic side effect population in comparison to the less severe side effect population.

Introduction, Significance and Rationale

Introduction

Cancer has a profound and severe impact on the lives of both the patient and his or her family, particularly for those classified in the adolescent and young adult (AYA) population. It is estimated 80,000 young people (ages 20-39) are diagnosed with cancer each year in the United States (American Cancer Society, 2020), of which 9,000 will die. The AYA cancer group is less studied and understood when compared to the childhood or older adult populations (American Cancer Society, 2020). Survival rates of the AYA population have failed to exhibit the same improvements in survivorship as the aforementioned groups in recent decades (American Cancer Society, 2020).

Previous studies have primarily focused on the long-term psychological effects of childhood cancers and found that overall childhood cancer survivors have similar levels of psychological distress when compared to the general population (Zebrack, 2002; Langeveld, 2004). Certain risk factors, including the presence of a major medical condition or treatment with cranial radiation and/or surgery, have been correlated to poor health-related quality of life and the development of psychological distress (Zeltzer, 2009). Yet, certain protective mechanisms like acceptance, autonomy, dependency, and social relationships, including family and peers (Chou, 2009) have been linked to improved psychosocial outcomes and better quality of life. These findings are limited to pediatric cancer survivors, AYA cancer survivors, however, represent a unique population with a different set of risk factors.

As a result, more research is needed to support this growing population, as the number of cancer survivors in this group has already exceeded more than 600,000 (Barthel, 2016). Recent studies are beginning to address the distinct challenges AYA cancer patients face how it relates to their long-term psychosocial health. As an example, financial concerns, identity formation, and need for social and emotional independence (American Cancer Society, 2020) have been documented as most impactful challenges facing this group.

Similarly, the psychosocial needs of AYA cancer survivors exceeding those of their counterparts without a history of cancer (Tai, 2012) has also been established. Studies have also shown when compared to age-matched healthy controls, AYAs completing adjuvant chemotherapy 3-8 years prior are more likely to have difficulty with anxiety, sleep, marital satisfaction, and body image (Johnson, 2018). This increase in depression and anxiety rates for AYA patients has been linked to the unique age at diagnosis, which represents an integral time for the formation of individual identity and social growth (Michel, 2019). Yet, older AYA patients (25-39) are more likely to show signs of psychological distress than younger AYA patients (15-24) based on age of diagnosis (Michel, 2019). Fatigue from treatment and the psychological effects of receiving cancer treatment are also thought to be contributors to the development of depression among survivors (Sapna, 2017). The Childhood Cancer Survivor Study (CCSS), the largest cohort of adolescent and childhood cancer survivors in North America, found poor mental health to be reported by 30% of AYA cancer survivors who are, on average, 20 years post-cancer diagnosis (Yi, 2020).

The standard of care for AYA cancer varies greatly depending upon the type and staging of the cancer, including growth, extranodal involvement, and systematic spread, in addition to demographics of the patient including age, race, and sex. Anthracyclines are a type of chemotherapy originally introduced in the 1960's to treat leukemia and lymphoma. Anthracyclines produce cardiotoxicity by binding DNA and topoisomerase II to form a tertiary cleavage complex which initiates cell death pathways. They have

been shown to exhibit a dose-dependent decrease in cardiovascular function, specifically a fall in left ventricular ejection fraction (LVEF); the resulting cardiotoxicity can put these patients in a state of heart failure (Volkova, 2011; McGowan 2017). Cardiotoxicity was first observed in adult cancer patients as clinically significant congestive heart failure (CHF), presenting with pulmonary edema, fluid overload, and shortness of breath at 2.2% overall incidence (Von Hoff, 1979; McGowan 2017). When observing the effects of cumulative doses of an anthracycline called doxorubicin in the treatment of cancer, a dose-dependent effect was observed to show an incidence of cardiotoxicity at the reported rates of 3%, 7%, and 18% correlated to cumulative doses of 400, 550, and 700 mg/m^2, respectively (Von Hoff, 1979; McGowan, 2017). In a follow-up retrospective pooled analysis of three lung and breast cancer trials using doxorubicin-based therapy, cardiotoxicity was documented at higher rates of cardiotoxicity with an incidence of 4.7%, 26%, and 48% at 400, 550, and 700 mg/m^2, respectively (Swain et. al, 2003; McGowan, 2017). While Anthracycline cardiotoxicity does not yet have a universally accepted definition, one proposed model identifies four groups: development of symptomatic heart failure (2-4%), subclinical fall in LVEF (9-11%), development of arrhythmia (12%), and the rise in cardiac biomarkers (30-35%) (McGowan, 2017).

Over extended periods of time and increased doses of anthracycline therapy, the risk of developing anthracycline-induced cardiotoxicity increases, of which there are currently no treatments (Volkova, 2011). The combined effect of increased incidence and improved survival rates in the AYA population, increases the likelihood for the occurrence of health problems related to their cancer therapy, of which cardiovascular disease (CVD) is the most serious and most common. Specifically, AYA survivors who develop CVD have more than an 11-fold higher overall mortality relative to those who do not (Keegan, 2018).

Understanding AYA cancer survivors already have an increased risk for developing depression or anxiety, those experiencing anthracycline-related cardiovascular toxicity may be more likely to develop depression or anxiety than their AYA survivor peers. We hypothesize AYA cancer survivors with chemotherapy-induced cardiotoxic side effects will demonstrate survey and interview responses consistent with increased depression and anxiety in comparison to AYA cancer survivors with less severe chemotherapy-induced side effects.

Significance

AYA cancer is the most under researched population of all cancer populations within the United States (American Cancer Society, 2020). Only in recent years have greater resources and research been committed to the AYA cancer survivor population and what long-term survival looks like in these patients.

Cancer already has the possibility to have a profound negative impact on quality of life. The development of a severe disease or illness directly related to the treatment necessary to overcome cancer has been researched from a biological perspective, but not from a psychosocial perspective. Little research on how the development of a severe side effect of chemotherapy, such as dilated cardiomyopathy, can impact the quality of life of someone who has already had to overcome battling cancer. Without the development of novel medications and treatment, this population will only increase in size as survivorship continues to improve and mortality from cancer continues to decline.

As this population continues to increase, it remains important to continue to learn how to best care for patients and continuously improve quality of life.

Rationale

The long-term psychological status of AYA cancer survivors in a variety of contexts and populations has been studied, however, a gap in the literature persists as it relates to the combined impact of late effects on mental health; specifically, the relationship between diagnosis cardiovascular dysfunction as a result of treatment and risk of anxiety and depression. It has been well established AYA patients diagnosed with cancer present with unique challenges which negatively affect physical, emotional, and mental development. Yet, this population is also reported to experience depression and anxiety at similar levels to the general population. Given the continued increase in survival rate for AYA cancers, we anticipate increased incidence of cardiotoxic side effects, it is thus important to delineate the specific needs of this subgroup.

In order to best care for these patients, we require a better understanding of the AYA cancer experience, but more specifically that which follows the subsequent diagnosis of CVD diagnosis as a result of treatment. The underlying hypothesis is diagnosis of cardiotoxicity, a life-threatening late effect, as a result of treatment of life-saving treatment may impact the patient's trust of the health care system and severely alter their perspective on life. Conducting 90-minute interviews with AYA survivors with and without cardiovascular long-term side effects will provide valuable insight into this understudied population that is contextualized within the cancer population. This modality is supported in the scientific community, specifically by Phillips-Salimi & Haase (2004) who urged that a more qualitative approach should be taken in developing psychosocial interventions specifically for the AYA cancer population. The proposed study aims to fill gaps in the literature by conducting qualitative interviews to garner a greater understanding of the overarching experience for AYA cancer survivors who develop long-term side effects from non-negotiable treatment, as well as the impact is has had on their long-term psychosocial health.

Preliminary Data – none

Materials and Methods

The proposed investigation was enabled by an existing, active study where the population of patients happens to be AYA cancer survivors with chemotherapy-related cardiotoxic effects. Depression and anxiety scales were administered to help turn participant feelings and emotions into quantifiable data. Patients seen through the "After the Cancer Experience" (ACE) Survivorship program at the UT-Southwestern (UTSW) campus will be used to derive our study cohort. A portion of these patients will have cardiotoxic side effects from chemotherapy and the remaining patients will have less severe side effects from chemotherapy.

General Study Details and Resources

Subjects were selected based on stringent inclusion and exclusion criteria. The inclusion criteria for this study includes a documented diagnosis of cancer treatment related late effect, such as cardiomyopathy, congestive heart failure, peripheral neuropathy, osteopenia, gonadal dysfunction, renal failure, and respiratory dysfunction, being an active patient in the After the Cancer Experience Clinic (ACE) clinics, between the ages of 18 to 55, primary language English, ability to understand and participate in the measure collection and qualitative interview, and all patients must be willing and able to provide verbal informed consent for study participation. Patients were excluded if the patient had a cancer recurrence or a secondary cancer, patients displayed symptoms of delirium or psychosis that precludes their ability to participate in a qualitative interview, patients with intellectual disability that precludes their ability to participate in a qualitative interview or precludes their ability to provide consent, currently pregnant and speaking a language other than English. All participants were followed by the UTSW After the Cancer Experience (ACE) clinic in Dallas, TX. ACE is a high-volume, academic, outpatient family medicine clinic that utilizes Epic as the electronic health record (EHR).

REDCap encrypted cloud storage were utilized in order to store retrospective data and survey response data from every subject. All data was deidentified.

Subject Identification

Study participants were discovered within the EHR by utilizing ICD 10 codes. Patients with cardiotoxicity were identified via an audit of the ACE clinic patient appointments and the secure patient database maintained by UTSW.

Inclusion and exclusion criteria were applied to potential study participants during the initial identification selection. The target population are those who are 18 to 55 years old, males and non-pregnant females, an established diagnosis of chemotherapy-associated cardiotoxicity, and patients who are followed by a PCP at the ACE clinic. For the control group, the inclusion criteria were identical with the exception that they will have no evidence of chemotherapy-associated cardiotoxicity.

Additional Subject Stratification

Sub-stratification of study data was considered to improve the granularity of our analysis. Covariates that were considered for exploration are illustrated by the following examples: 1) age/sex; 2) duration and type of anthracycline therapy; 3) type of non-cardiotoxic chemotherapy administered; 4) functional scoring of

cardiac function assessed by echocardiography and 5) tumor type. No sub-stratification was performed in this analysis.

All patients diagnosed and treated at the ACE Clinic at UT Southwestern meeting the eligibility criteria listed above were offered the opportunity to participate. Research investigators shared the responsibility of identifying eligible patients in the ACE clinic by reviewing electronic medical records (EMRs). Only UTSW personnel approached eligible patients in person or in a private area of the clinic or hospital room. The TCU medical student approached eligible patients for enrollment by virtual means, such as by phone call or by e-mail, to explain the research aims and informed consent process. Measures, questionnaires, and interviews will not be conducted until after informed consent is obtained (Figure 2).

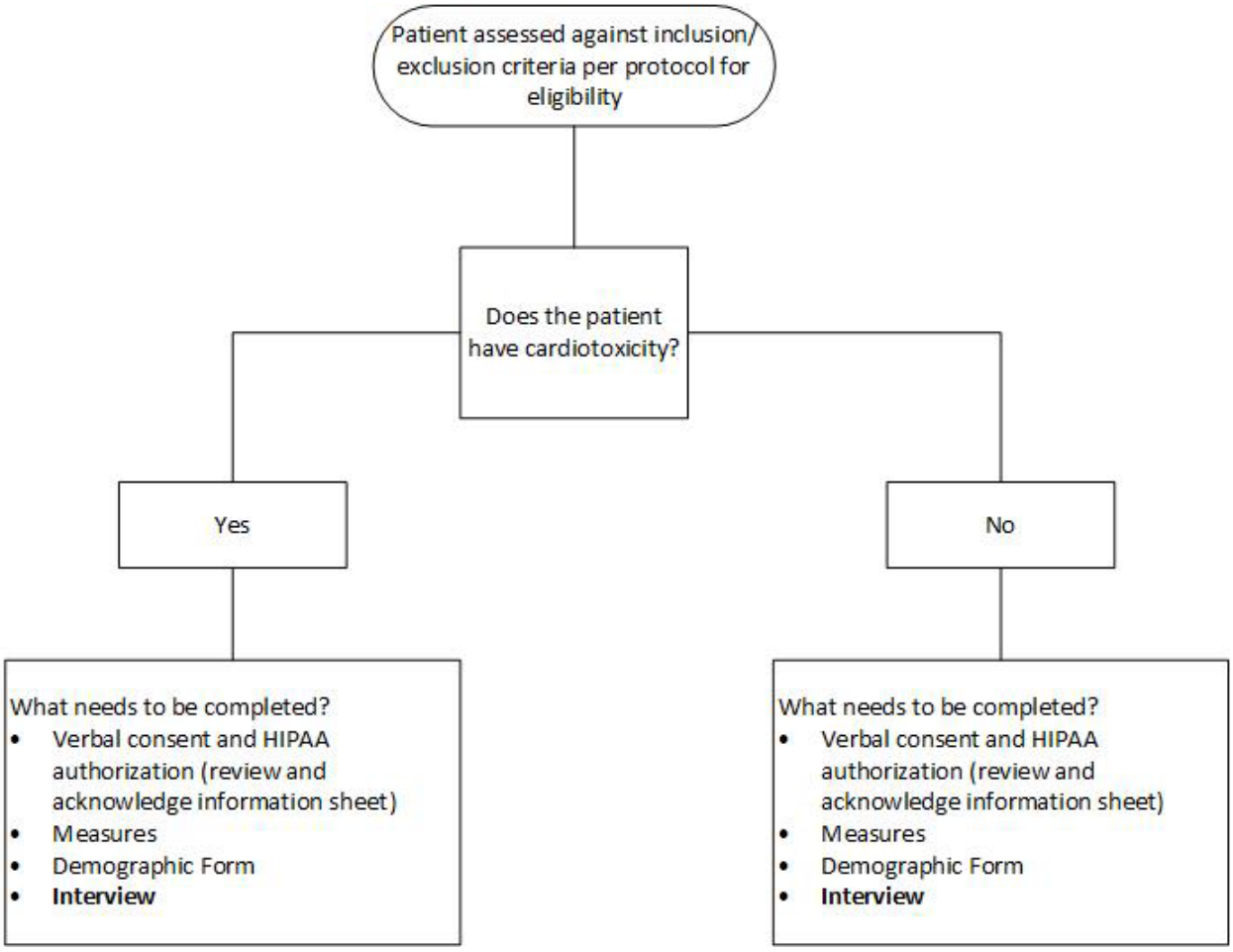


Figure 2. Flow chart of consent process for all patient groups

All patients were screened using these tools before and after each semi-structured interview and given the appropriate consent form. These interviews documented their experience, beginning from time of diagnosis up until current day. Secondary endpoint metrics included anxiety and depression scales such as the PHQ-9 and GAD-7. Survey data will be collected at the time of consent over telephone.

The following data will be collected for each participant:

Medical history

Researchers gathered and recorded the patient's diagnoses, date of cancer diagnosis, date of cancer late effect diagnosis, and time since each respective diagnosis from the electronic medical record system, EPIC.

Demographics

AYA participants self-identified preferred language, ethnic/racial identity, education level, gender, employment status, marital status, occupation, annual income, household makeup, psychiatric history, and recent COVID-19 status (see Appendix E).

Researchers gathered and recorded the following demographic information from patient electronic medical record review: date of birth, age, sex, medical history, cancer diagnosis information, date of diagnosis, time since diagnosis, treatment type, insurance status (private versus public), zip code, and contact information including email and phone number. This information was recorded separately on a Data Sheet (see Appendix F).

Psychological Measures

Depression Personal Health Questionnaire – 9: (PHQ-9; Kroenke et. al, 2001) The PHQ-9 (Appendix A) is a widely used 9-item self-report screening tool used in identifying, differentiation, and assessing depression (e.g feeling down, depressed, or hopeless). Symptom frequency for the past 2 weeks is self-rated across 9 items that are scored on a 4-point Likert-type scale (0= "Not at all," 3= "Nearly every day"). The sum of these items generates a total score (Range = 0 to 27). Higher scores generally indicate greater levels of distress and cut-off scores for depression are provided. PHQ-9 scores of 5, 10, 15, and 20 represent symptoms of mild, moderate, moderately severe and severe depression, respectively (Kroenke et. al, 2001). The PHQ-9 with a cutoff score ≥7 had a sensitivity of 83% (95% confidence interval, 78%-89%) and a specificity of 61% (95% confidence interval, 59%-63%) (Hartung, 2017). PHQ-9 scores > 10 had a sensitivity of 88% and a specificity of 88% for Major Depressive Disorder (Kroenke et. al, 2001; Badr et. al, 2016). Among cancer patients, cut off scores of ≥ 8 provided a sensitivity of 93% (95% CI, 89%-95%), a specificity of 81% (95% CI, 80%-82%), a positive predictive value (PPV) of 25%, and a negative predictive value (NPV) of 99% (Thekkumpurath et. al, 2011). Good internal consistencies have been supported (alphas of .86 and .89) (Kroenke et. al, 2001). Criterion and construct validity has been supported in research (Kroenke et. al, 2001). Suicide risk is assessed in patients who respond positively to item 9 "Thoughts that you would be better off dead or of hurting yourself in some way" and will be further assessed using the C-SSRS, provided resources, and a referral will be relayed to the appropriate primary care physician or mental health provider for further follow-up.

Anxiety Generalized Anxiety Disorder Scale: (GAD-7; Donker, 2007) The GAD-7 (Appendix B) is a widely used 7-item self-report screening tool used in measuring the presence and severity of generalized anxiety symptoms. The 7 self-rated items GAD-7 are each scored 0–3 (0="not at all", 3= "nearly every day"; total score range 0–21). Scores of 5, 10, and 15 represent mild, moderate, and severe anxiety symptoms, respectively (Kroenke et. al, 2007). Reliability and validity are excellent (Cronbach's α = 0.92, AUC: 0.91). With a cut-off point of ≥ 10, sensitivity is 0.89 and specificity is 0.82 among primary care participants (Kroenke et. al, 2007). With a cut-off point of 3, sensitivity is 0.86 and specificity is 0.83 (Kroenke et. al, 2007). The authors report good internal and test–retest reliability, as well as convergent, construct, criterion, procedural, and factorial validity for the diagnosis of generalized anxiety disorder (Spitzer et. al, 2006; Kroenke et. al, 2007). A study in cancer patients found an AUC of .81 (95% CI: .79-

.82) among patients with cancer, showing adequate diagnostic accuracy for screening in this population specifically (Esser et. al, 2018).

Quality of Life Quality of Life Patient/Cancer Survivor Version: (QOL-CSV, Ferrell e. al, 2012) The QOL-CSV (Appendix C) This instrument was revised in cancer survivorship studies and includes 41 items representing the four domains of quality of life including physical well-being, psychological well-being, social well-being and spiritual well-being. The items use a 0-10 scale (0="worst outcome" 10= "best outcome") and some items involve reverse scoring (1-7, 9, 16-27, & 29-34 and 38). The measure encompasses the following 4 scales: physical well-being (e.g. "fatigue"), psychological well-being (e.g. "how much happiness do you feel"), social concerns (e.g. "amount of support from others"), and spirutal well-being (e.g. "how important to you is your participation in religious activities such as praying or going to church"). The authors report that the overall QOL-CS tool test re-test reliability was .89 with subscales of physical r=.88, psychological r=.88, social r=.81, spiritual r=.90 (Ferrell e. al, 2012). The second measure of reliability was 2 computation of internal consistency using Cronbach's alpha co-efficient as a measure of agreement between items and subscales. Analysis revealed an overall r=.93. Subscale alphas ranged from r=.71 for spiritual well-being, r=.77 for physical, r=.81 for social, and r=.89 for psychological (Ferrell e. al, 2012). The authors used several measures of validity to determine the extent to which the instrument measured the concept of QOL in cancer survivors. The first method of content validity was based on a panel of QOL researchers and nurses with expertise in oncology (Ferrell e. al, 2012). The second measure used stepwise multiple regression to determine factors most predictive of overall QOL in cancer survivors (Ferrell e. al, 2012). Seventeen variables were found to be statistically significant accounting for 91% of the variance in overall QOL (Ferrell e. al, 2012). Variables accounting for the greatest percentage were control, aches and pain, uncertainty, satisfaction, future, appearance and fatigue (Ferrell e. al, 2012). The fourth measure of validity used Pearson's correlations to estimate the relationships between the subscales of the QOL-CS and the subscales of the established FACT-G tool (Ferrell e. al, 2012). There was moderate to strong correlation between associated scales including QOL-CS Physical to FACT Physical (r=.74), QOL-CS Psych to FACT Emotional (r=.65), QOL Social to FACT Social (r=.44). The overall QOL-CS correlation with the FACT-G was .78 (Ferrell e. al, 2012). Strong evidence for the validity and reliability of this instrument has been reported (Dow et. al, 1996; Garratt et. al, 2002).

***Healthcare System Distrust Scale*:** (Shea et. al, 2008) This instrument (Appendix D) was developed to develop a scale seeking to reflect a patient's distrust of the health care system. The 9 self-rated items are each scored 1 to 5 (1= "strongly disagree", 2= "disagree", 3= "neither agree nor disagree", 4= "agree", and 5= "strongly agree"). Questions 1, 3, 6, and 7 use reverse scoring. The 9-item scale has a Cronbach's alpha of 0.83 (Shea et. al, 2008). Factor analysis demonstrated a 2-factor structure, corresponding to the domains of values and competence. The values subscale (5 items: 2, 5, 7, 8, and 9) had a Cronbach's alpha of 0.73 and the competence subscale (4 items: 1, 3, 4, and 6) had a Cronbach's alpha of 0.77 (Shea et. al, 2008).

Demographic Questionnaire: The demographic questionnaire (Appendix E) was researcher-created. Respondents will self-identify preferred language, ethnicity/race, gender, education level, employment status, annual income, household makeup, relationship status, perception of health care relationships, and information about caregiver(s) or patient. The demographic questionnaire will only be administered at initial encounter. Researchers will gather and record the following demographic information from patient electronic medical record review: date of birth, age, sex, date of cancer diagnosis, type of cancer treatment, total radiation exposure, date of cardiotoxicity diagnosis, cardiac medication history, smoking

status, drug use, body-mass index, insurance status (private versus public), zip code (for neighborhood characteristics), and patient contact information such as phone number and email address. This information will be recorded separately on a Data Sheet (Appendix F).

Qualitative Interview: Interview topics for patients included patient's overall coping/experience of cancer treatment and patient's perceptions of the health care system. (see Appendix G).

Columbia-Suicide Severity Rating Scale (C-SSRS): This scale (Appendix H) was used if a patient endorses having suicidal ideation or having thoughts or harming themselves or others. This is important to address as Suicidal ideation is predictive of or a precursor to suicidal behavior (Kessler, 1999; Posner, 2011). It has been determined that phone and in-home assessments by nonpsychiatric subspecialty staff using the C-SSRS reached conclusions that matched the conclusions of mental health professionals who followed up with participants, making this a reliable tool in evaluating suicidal ideation and deciding when a further risk assessment and work up is necessary in some participants (Lucas et. al, 2015). The C-SSRS was used to help quantify and stratify the risk of suicidality and is incorporated into the flowchart (Appendix I) that was used in this study.

Participant Interviews

Semi-structured interviews with participants were conducted by using secure video conference software, however only the audio portion will be recorded for coding. Researchers verbally reviewed consent for audio recording with participants prior to interview.

Follow-up Procedures

After the conclusion of the study, findings will be disseminated in the Adolescent/Young Adult (AYA) Patient Advisory Board where AYA cancer patients may have input regarding the generalizability of the findings. Participants were contacted by phone approximately one month +/- 7 days after their third study visit. If researchers have concerns about subjects regarding significant levels of depression, anxiety, or suicidal ideation appropriate referrals were made to primary care physicians or mental health providers.

Time and Events Table

Events Table	Before Encounter	First Visit	Second Visit	Third Visit	Follow-Up
Review EMR for eligibility	X				
Informed Consent		X			
HIPAA Release		X			
Demographic Questionnaire			X		
Battery of Measures			X	X	
Semi-Structured Interview*				X	
Phone Call Follow-Up^{+}					X

*In the case of disruptions or interviewee fatigue/side effects, interviews were allowed to take place over the course of two interview sessions totaling 1-2 hours.

[+]This phone call follow-up will take place one month after the third visit to check in on participant

Adverse Event Monitoring

Questionnaires do not involve any medical procedures and have no inherent risks, other than potential for acute psychological discomfort and participant fatigue. However, participants could experience some degree of emotional distress due to being asked to speak about their experience with cancer treatment. The probability of this occurring was determined to be moderate and was monitored by the researchers through clinical observation and verbal check-ins during questionnaire and interview process. Additionally, any time information is collected, there is a potential risk of loss of confidentiality. Every effort will be made to keep information confidential (as described in Section 9), but this cannot be guaranteed. The probability of confidentiality breach occurring is minimal.

Statistical Analysis

Effect size was to be quantitatively evaluated. General self-reported levels of anxiety and depression were provided at initial encounter and immediately following the semi-structured interview for presence or absence of conditions and for descriptive purposes. The levels of anxiety and depression were going to be compared between participants in the presence and absence of cardiotoxicity and the themes that emerged from the qualitative interviews will also be compared.

Measures and questionnaires/data from EMRs were used to summarize and describe characteristics of the study sample both prior to interview and immediately following the interview. A researcher with expertise in qualitative methods mentored investigators in the collection of interview transcripts. Each interview was transcribed before the subsequent interview. Investigators met to debrief after each interview to discuss coding themes and initial impressions from interview. Transcripts were to be initially studied without coding in order to identify emerging themes (Bradley, Curry, & Devers, 2007). Thematic analysis was unable to be performed due to a lack of participants, however the principles of thematic analysis that were planning to be used are described as follows: investigators individually coded each interview and after a total of five interviews were to be conducted, key concepts and ideas to develop a preliminary code structure to use for subsequent interview coding. The constant comparative approach was to be utilized by investigators and apply the emerging code structure to successive transcripts and make revisions to codes as novel concepts emerge from new interviews (Glaser, 1965; Bradley, Curry, & Devers, 2007). Therefore, transcripts from each interview was coded prior to conducting the next interview to allow for analysis to be continually informed to make guided data collection (Glaser, 1965; Bradley, Curry, & Devers, 2007). Investigators were to continue this process of interviews, transcription, and analysis until thematic saturation is reached (e.g. no new ideas emerge from subsequent interviews; Glaser, 1965). Investigators were to address coding discrepancies through discussion and consulting prior notes related to coding decisions to ensure agreement in coding structure. Investigators were to consult experienced clinicians and a qualitative analyst if coding discrepancies arise and to avoid researcher bias. The finalized code structure to all of the transcripts was to be entered into NVivo 10.0 (QSR Australia) to ensure consistent and reliable code application. Investigators would then discuss and interpret themes from data by consulting a qualitative expert and using clinician support.

The anticipated AYA patient sample size was $n = 50$, however this study was able to only recruit 3 study participants. Investigators coded each transcribed interview after they were conducted and prior to the next interview with a participant of the same group (e.g. cardiotoxicity AYA group). The anticipated

sample size was determined as an estimate for when thematic saturation will be reached (e.g. no new ideas emerge from subsequent interviews; Glaser, 1965).

The study's primary aims were addressed by obtaining patient experiences firsthand pertaining to the corresponding questions on the interview guide (see Appendix G). The first study aim (evaluate prevalence of anxiety and depression in AYAs with cancer treatment-related cardiotoxicity relative to the standard AYA survivor population) was addressed by asking patients about coping with cancer treatment and side effects sustained from cancer treatment. These questions include the first questions on the interview guide: "Tell me how things have gone for you since you were diagnosed with cancer," "Tell me how things have gone for you since you were diagnosed with serious side effects related to your cancer treatment." The second primary aim (describe the impact a cardiotoxicity diagnosis related to cancer treatment has affected patient trust in the health care system) was addressed by asking patients about their perspective of their health care system and their willingness to seek medical care. These questions include the following questions in the interview guide: "Tell me about your relationship with your health care providers," and "Do you feel comfortable in a health care setting?" The interview guide was subject to change based on the responses that are provided from the interviewees, however modification to the interview guide did not occur.

ACE Patient Recruitment

Subjects fitting criteria were contacted via telephone call (Monday - Friday 9am-4pm CST, or Saturday 10am-2pm CST). This communication chronologically involved: requesting participation, explaining details of the informed consent, obtaining verbal informed consent and completion of the demographics survey.

Statistical Analysis of Demographic Survey Responses

Two major groups (+ cardiotoxicity and – cardiotoxicity) were to be compared by making unpaired comparisons, however we were unable to reach adequate levels for analysis to be made.

Statistical Analysis of Survey and Clinical Characteristics

Measures and questionnaires/data from EMRs were summarized and described characteristics of the study sample both prior to interview and immediately following the interview. A researcher with expertise in qualitative methods will mentor investigators in the collection and analysis of interview transcripts.

Power, Sample Size, and Statistical Analysis for Primary and Secondary Endpoints

The anticipated AYA patient sample size was n = 50, however the actual patient sample size was n = 3. Due to the sub-optimal amount of participants that were recruited into the study, thematic saturation was not reached and data analysis was unable to be performed. Investigators were planning to code each transcribed interview after they were conducted and prior to the next interview with a participant of the same group (e.g. cardiotoxicity AYA group). The study's primary aims were addressed by obtaining patient experiences firsthand pertaining to the corresponding questions on the interview guide (see Appendix E). The first study aim (evaluate prevalence of depression and anxiety in AYAs with cancer treatment-related cardiotoxicity relative to the standard AYA survivor population) was addressed by asking patients about coping with cancer treatment and side effects sustained from cancer treatment. These questions include the first questions on the interview guide: tell me how things have gone for you since you were diagnosed with cancer, tell me how things have gone for you since you were diagnosed with serious side effects related to your cancer treatment. The second primary aim (describe the impact a

cardiotoxicity diagnosis related to cancer treatment has affected patient trust in the health care system) was addressed by asking patients about their perspective of their health care system and their willingness to seek medical care. These questions included the following questions in the interview guide: tell me about your relationship with your health care providers, do you feel comfortable in a health care setting. However, the interview guide was subject to change based on the responses that are provided from the interviewees. If another theme arises that appears to be unrelated to these objectives, it was to be incorporated into the interview guide and examined in subsequent interviews. After each interview is conducted and transcribed, the transcription will be coded by investigators to determine which themes or categories the statements appear to be assessing. This coding process was unable to occur due to a lack of patient sample size.

Results

Demographic characteristics

This study enrolled a total 3 participants. Two females and one male participated in the study. The median age at time of study enrollment was 45 years old (IQR: 7) and the median age at time of cancer diagnosis was 16 years old (IQR: 0.75). One patient was treated with chemotherapy only while two patients were treated with chemotherapy and surgery. One patient developed peripheral neuropathy and cardiotoxicity, one patient developed only peripheral neuropathy, and one patient developed only foot drop.

Table 1: Demographics

	N	%
Gender		
Female	2	66.7%
Male	1	33.3%
Median Age		
Median Age at Enrollment	45	IQR: 7
Median Age at Diagnosis	16	IQR: 0.75
Ethnicity		
Caucasian	3	100%
Relationship Status		
Single	2	66.7%
Married/Long-term partner	1	33.3%

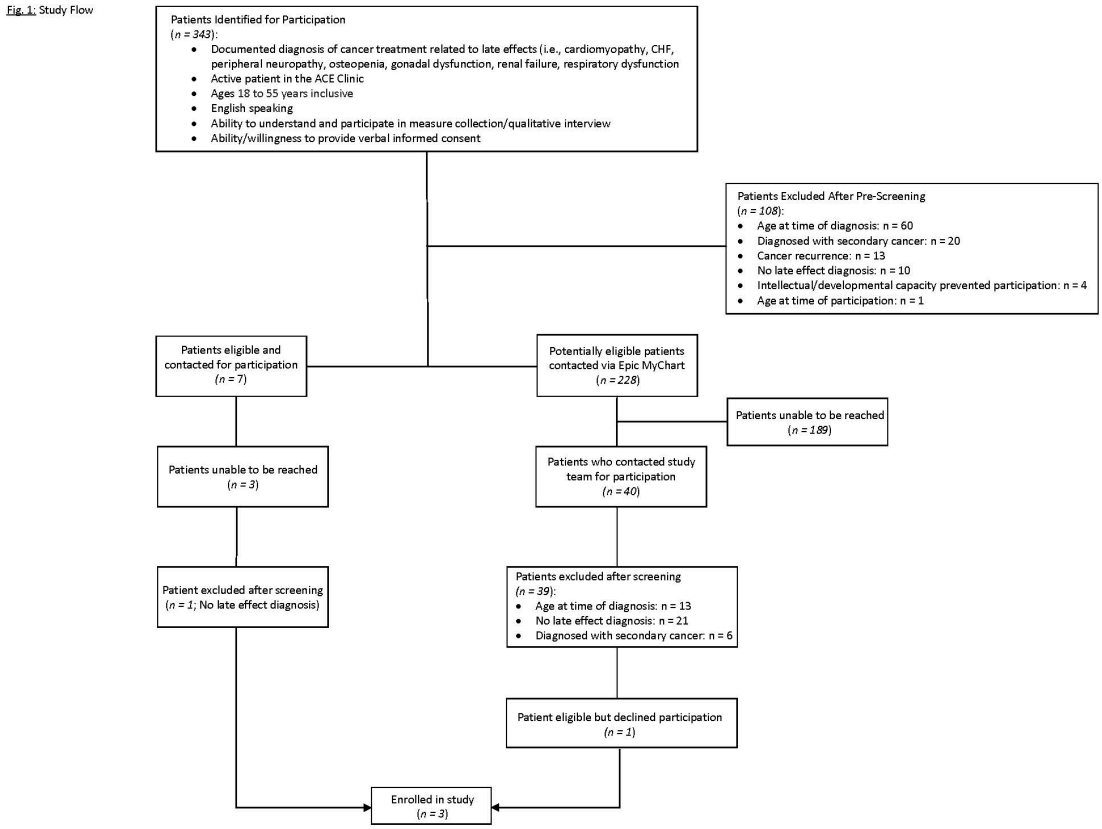
Education		
College/Undergraduate	2	66.7%
Graduate Professional Training Degree	1	33.3%
Average Income		
$25,001 - $50,000	2	33.3%
>$150,000	1	66.7%
Prior Mental Health Diagnosis		
Yes	3	100%
No	0	0%
Tobacco Use		
Yes	0	0%
No	3	100%
Alcohol Use		
Yes	3	100%
No	0	0%
Recreational Drug Use		
Yes	1	33.3%
No	2	66.7%
Treatment		
Chemotherapy only	1	33.3%
Chemotherapy with Surgery	2	66.7%
Chemotherapy Side Effect		
Cardiotoxicity	1	33.3%

Peripheral Neuropathy	2	66.7%
Footdrop	1	33.3%
Marital Status		
Single	2	66.7%
Married	1	33.3%

Recruitment strategy

Study recruitment resulted in a lack of an adequate number of research participants to reach thematic saturation and perform data analysis.

Figure 1: Recruitment strategy and efficacy



Survey Results

This study enrolled a total 3 participants. Two females and one male participated in the study. The median age at time of study enrollment was 45 years old (IQR: 7) and the median age at time of cancer diagnosis was 16 years old (IQR: 0.75). One patient was treated with chemotherapy only while two patients were treated with chemotherapy and surgery. One patient developed peripheral neuropathy and cardiotoxicity, one patient developed only peripheral neuropathy, and one patient developed only foot drop.

Table 2: Survey Outcomes, Initial

	PHQ-9, initial	GAD-7, initial	QOL	Healthcare Distrust, Values	Healthcare Distrust, Competence
Participant 1	11	11	198	12	5
Participant 2	1	1	295	4	13
Participant 3	11	6	285	10	8

Participants were re-assessed for changes in their mental health by readministering the PHQ-9 and GAD-7 at the conclusion of the study to assess if their well-being had changed as a result of their participation.

Table 3: Survey Outcomes, Final

	PHQ-9, final	GAD-7, final
Participant 1	10	17
Participant 2	0	0
Participant 3	9	6

Semi-structured interviews

Due to the intimate nature of the semi-structured interview, the transcripts of the interviews are not able to be provided to protect patient confidentiality. The nature of these interviews had several reoccurring themes emerge, including mental health care practices, identity formation, need for social and emotional independence, and lost time due to the diagnosis and treatment.

Discussion/Innovation

To date, there has been no published works detailing the relationship of cardiotoxicity induced by chemotherapy in AYA cancer survivors and its potential link to mental illnesses such as anxiety and depression. It is already well documented that AYA cancer survivors are already at an elevated risk of anxiety and depression due to a myriad of factors, such as need for mental, emotional, and physical independence, financial struggles, and fertility concerns. The themes arising from the interviews reported by the participants are consistent with literature as some of the most impactful affecting this demographic in particular. The primary goal of the proposed study is to identify if there is a sub-set of that population is at an even greater risk of developing anxiety and depression due to receiving yet another harsh and

severe diagnosis that is difficult to cope with and overcome. Unfortunately, the lack of sample size in this pilot study is not sufficient to reliably test the hypothesis.

Adequate study recruitment proved to be a major limitation of this study. However, it did prove, unequivocally, a proof of concept for this study which could then be successfully implemented as a multi-site study. While this study was unable to accomplish the aims, the study team has assessed the recruitment strategy utilized in this study to help better inform future researchers seeking to pursue research for this particular patient demographic. The recruitment strategies initially deployed dissolved due to the COVID-19 pandemic, as in-person clinical practice rapidly shifted to telehealth. Our overall experience aligns with what has been reported in the literature, as patient enrollment and recruitment have been identified as the clinical research activities most affected by the pandemic (Medidata). Specifically, the need to address new and emerging guidelines to ensure patient safety during the rapid rise in COVID-19 infection increased the likelihood that any research study would be classified as a low study priority (Williams et. al). The AACR report assessing the impact of COVID-19 on cancer research cited concern for patient care as the key factor as to why recruitment fell during COVID-19; clinicians were most concerned with addressing treatment needs directly related to the pandemic, rather than enrolling patients in research or clinical trials (Williams et. al). This was also our experience in the ACE clinic, as adapting to the threats to public health brought on by the pandemic took precedence over study recruitment.

In addition to exacerbating institutional barriers, the COVID-19 pandemic also impacted patient barriers to recruitment. The AACR report cited as many as 70% of respondents who were offered an opportunity to participate in a study declined due to fear of COVID-19 exposure (Williams et. al ,Fleury et. al). Our team observed similar reactions in potentially eligible study participants, particularly at the beginning of the pandemic. COVID-19 also has economic consequences thought to influence participation by ACE clinic patients. As highlighted in both a retrospective multi-institutional study as well as a separate retrospective review, potential lost wages and inability to miss work are key patient factors for recruitment failure (Ganz et. al, Chaudhari et. al). Specifically, the pandemic may have created new financial stressors or exacerbated preexisting financial concerns, making it even less likely for patients to agree to participate in research should it conflict with employment schedules (Ganz et. al, Chaudhari et. al, Williams et. al).

As a result, we adapted our recruitment methods in response to the COVID-related changes to clinic operations. Specifically, we incorporated a standardized message distributed through the electronic medical record (EMR) system. UT Southwestern uses EPIC (Epic Systems; Verona, WI) for its EMR, which contains the patient portal MyChart. MyChart enables patients to view aspects of their medical record and communicate with their provider in secure messages (Reich et. al). Messages were sent within MyChart to previously identified, pre-screened clinic patients not yet approached about the study. Language incorporated details about the study, its focus on mental health, and encouraged interested patients to contact the research team to participate. This approach yielded a response rate of 17.5%, with 40 of the 229 patients responding (**Figure 1**). This change in approach aligned with other literature, as transitioning data collection to telephone or virtual formats when allowable can maximize study compliance (Ganz et. al). However, while effective in increasing patient engagement, this standardized messaging approach was discontinued due to the sensitive nature of our study and its focus on mental health. Specifically, in an isolated event, a prospective participant contacted the study team via email with content that raised concerns about mental state and overall safety. Initial difficulty contacting the patient to complete a standardized suicide risk assessment (per study protocol) resulted in a decision from the study team to discontinue this recruitment approach. The patient was eventually contacted, deemed safe, and the appropriate follow-up plan implemented; however our experience highlights a limitation to this recruitment strategy, particularly for mental health-specific studies.

This study was one of the first of its kind to attempt to sub-stratify mental health outcomes in AYA cancer survivors as it pertains to a particular late side effect derived from cancer treatment. The participants' experiences in this study highlight the need for adequate mental health resources be provided

to AYA survivors during their cancer treatment to equip them with coping strategies to address future complications stemming from their cancer diagnosis.

Future Directions

Future studies should be conducted to further assess the mental health needs of AYA cancer survivors, regardless of the development of treatment side effects. The results from this study, while limited, begin to suggest that survivors with adequate counseling during cancer treatment with emphasis placed on maintaining healthy mental health practices had less anxiety and depression as well as better coping mechanisms to a late side effect diagnosis that develops later in life. Further studies should similarly seek to further elucidate this preliminary finding and characterize if the degree of side effect severity plays a role in mental health outcomes. In addition, this study highlights the difficulty in recruiting young adult cancer survivors to participate in research and that this population may need additional recruitment modalities for study recruitment to be successful. These approaches could include mailed or emailed invitation, text messaging or phone call, or when appropriate messaging through the electronic medical record system and should be implemented at the beginning of the study period. We anticipate studies, where a member of the research team familiar with patient history is involved early to identify and contact potential participants, will likely be more successful with enrollment regardless of the outreach strategy employed. Future studies should begin to highlight which recruitment modalities are most effective at recruiting AYA survivors into research, especially in light of the COVID-19 pandemic.

Conclusions

AYA cancer survivors have a unique set of circumstances specific to their age demographic. This population is receiving a cancer diagnosis during an integral time of forming individual identity and social growth. The challenging themes highlighted in these patient interviews are some of the most impactful challenges in the AYA population; these findings are consistent with literature. While prior societal norms and structural challenges previously made addressing mental health difficult, patients now seem to have greater access to mental health resources, including consistent therapy, which appears to have lessened the impact of a subsequent late effect diagnosis on the patient's overall mental health. These interviews highlight the importance of individually tailored multimodal care to address the unique needs and distinct circumstances specific to this age demographic. Specifically, neglecting mental health during treatment, can trigger previously unrecognized or repressed emotions to resurface with the emergence of a diagnosis related to cancer treatment. Early detection of mental health concerns in cancer patients may not only address the immediate mental health needs, but also better equip a patient to maintain long term positive mental health when faced with subsequent challenges and diagnoses related to cancer treatment. Based on our experience, recruitment success was most likely when initiated by a research team member with a previously established relationship with the patient. In our study, that entailed a member of the research team first identifying an eligible potential participant and then contacting them directly for enrollment. In light of COVID-19, with the continued use of telehealth and virtual medicine, researchers will need to adjust their recruitment approach to better align with service delivery and should continue to leverage and incorporate existing patient connections to ensure successful study enrollment.

Compliance

This research study required TCU and UTSW IRB approval and was considered minimal risk. This study will not require any consideration or approval from IACUC. All research team members completed all required CITI Training.

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Resources

This research study will be conducted under the supervision and guidance of my mentor, Dr. Keith Argenbright, who is a Family Medicine physician at Moncrief Cancer Institute. All patients who will be evaluated in this study was originally followed by Dr. Angela Orlino, Medicine-Pediatrics specialist who directs the "After the Cancer Experience" (ACE) Program, and has since transitioned to Dr. Rebecca Eary at UTSW. The personal laptop used by myself will be allowed access to EPIC and REDCap for data collection, storage, and analysis. The UTSW VPN installed and operating on my computer will be engaged for any times in which data entry or analysis is required off-site from UTSW. Any off-site visualization, entry, or analysis of data will occur privately within my residence.

APPENDICES

APPENDIX A

Personal Health Questionnaire 9

PHQ-9

Over the last 2 weeks, how often have you been bothered by any of the following problems? *(Use "✓" to indicate your answer)*	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

(For office coding: Total Score _____= _____ + _____ +_____)

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	**Somewhat difficult**	**Very difficult**	**Extremely difficult**
❑	❑	❑	❑

APPENDIX B

Generalized Anxiety Disorder 7

GAD-7

Over the last 2 weeks, how often have you been bothered by the following problems? *(Use "✔" to indicate your answer)*	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

(For office coding: Total Score T____ = ____ + ____ + ____)

Developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues, with an educational grant from Pfizer Inc. No permission required to reproduce, translate, display or distribute.

APPENDIX C

Quality of Life Patient/Cancer Survivor Version

Quality of Life Scale/CANCER PATIENT/CANCER SURVIVOR

Directions: We are interested in knowing how your experience of having cancer affects your Quality of Life. Please answer all of the following questions based on your life **at this time**.

Please circle the number from 0 - 10 that best describe your experiences:

Physical Well Being

To what extent are the following a problem for you:

1. **Fatigue**

no problem	0	1	2	3	4	5	6	7	8	9	10	**severe problem**

2. **Appetite changes**

no problem	0	1	2	3	4	5	6	7	8	9	10	**severe problem**

3. **Aches or pain**

no problem	0	1	2	3	4	5	6	7	8	9	10	**severe problem**

4. **Sleep changes**

no problem	0	1	2	3	4	5	6	7	8	9	10	**severe problem**

5. **Constipation**

no problem	0	1	2	3	4	5	6	7	8	9	10	**severe problem**

6. **Nausea**

no problem	0	1	2	3	4	5	6	7	8	9	10	**severe problem**

7. **Menstrual changes or fertility**

no problem	0	1	2	3	4	5	6	7	8	9	10	**severe problem**

8. Rate your **overall physical health**

extremely poor	0	1	2	3	4	5	6	7	8	9	10	**excellent**

Psychological Well Being Items

9. How difficult is it for you to **cope** today as a result of your disease and treatment?

not at all difficult	0	1	2	3	4	5	6	7	8	9	10 **very difficult**

10. How good is your **quality of life**?

extremely poor	0	1	2	3	4	5	6	7	8	9	10 **excellent**

11. How much **happiness** do you feel?

none at all	0	1	2	3	4	5	6	7	8	9	10 **a great deal**

12. Do you feel like you are **in control** of things in your life?

not at all	0	1	2	3	4	5	6	7	8	9	10 **completely**

13. How **satisfying** is your life?

not at all	0	1	2	3	4	5	6	7	8	9	10 **completely**

14. How is your present ability to **concentrate or to remember** things?

extremely poor	0	1	2	3	4	5	6	7	8	9	10 **excellent**

15. How **useful** do you feel?

not at all	0	1	2	3	4	5	6	7	8	9	10 **extremely**

16. Has your illness or treatment caused changes in your **appearance**?

not at all	0	1	2	3	4	5	6	7	8	9	10 **extremely**

17. Has your illness or treatment caused changes in your **self concept** (the way you see yourself)?

not at all	0	1	2	3	4	5	6	7	8	9	10 **extremely**

How distressing were the following aspects of your illness and treatment?

18. **Initial diagnosis**

not at all distressing	0	1	2	3	4	5	6	7	8	9	10	**very distressing**

19. **Cancer treatments** (i.e. chemotherapy, radiation, or surgery)

not at all distressing	0	1	2	3	4	5	6	7	8	9	10	**very distressing**

20. **Time since my treatment** was completed

not at all distressing	0	1	2	3	4	5	6	7	8	9	10	**very distressing**

21. How much **anxiety** do you have?

none at all	0	1	2	3	4	5	6	7	8	9	10	**a great deal**

22. How much **depression** do you have?

none at all	0	1	2	3	4	5	6	7	8	9	10	**a great deal**

To what extent are you <u>fearful</u> of:

23. **Future diagnostic tests**

no fear	0	1	2	3	4	5	6	7	8	9	10	**extreme fear**

24. **A second cancer**

no fear	0	1	2	3	4	5	6	7	8	9	10	**extreme fear**

25. **Recurrence** of your cancer

no fear	0	1	2	3	4	5	6	7	8	9	10	**extreme fear**

26. **Spreading (metastasis)** of your cancer

no fear	0	1	2	3	4	5	6	7	8	9	10	**extreme fear**

Social Concerns

27. How distressing has illness been for your **family**?

not at all	0	1	2	3	4	5	6	7	8	9	10	**a great deal**

28. Is the amount of **support** you receive from others sufficient to meet your needs?

not at all	0	1	2	3	4	5	6	7	8	9	10	**a great deal**

29. Is your continuing health care interfering with your **personal relationships**?

not at all	0	1	2	3	4	5	6	7	8	9	10	**a great deal**

30. Is your **sexuality** impacted by your illness?

not at all	0	1	2	3	4	5	6	7	8	9	10	**a great deal**

31. To what degree has your illness and treatment interfered with your **employment**?

no problem	0	1	2	3	4	5	6	7	8	9	10	**severe problem**

32. To what degree has your illness and treatment interfered with your **activities at home**?

no problem	0	1	2	3	4	5	6	7	8	9	10	**severe problem**

33. How much **isolation** do you feel is caused by your illness or treatment?

none	0	1	2	3	4	5	6	7	8	9	10	**a great deal**

34. How much **financial burden** have you incurred as a result of your illness and treatment?

none	0	1	2	3	4	5	6	7	8	9	10	**a great deal**

Spiritual Well Being

35. How important to you is your participation in **religious activities** such as praying, going to church?

not at all important	0	1	2	3	4	5	6	7	8	9	10	**very important**

36. How important to you are other **spiritual activities** such as meditation?

not at all important	0	1	2	3	4	5	6	7	8	9	10	**very important**

37. How much has your **spiritual life** changed as a result of cancer diagnosis?

less important	0	1	2	3	4	5	6	7	8	9	10	**more important**

38. How much **uncertainty** do you feel about your future?

not at all uncertain	0	1	2	3	4	5	6	7	8	9	10	**very uncertain**

39. To what extent has your illness made **positive changes** in your life?

none at all	0	1	2	3	4	5	6	7	8	9	10	**a great deal**

40. Do you sense a **purpose/mission** for your life or a reason for being alive?

none at all	0	1	2	3	4	5	6	7	8	9	10	**a great deal**

41. How **hopeful** do you feel?

not at all hopeful	0	1	2	3	4	5	6	7	8	9	10	**very hopeful**

APPENDIX D

Health Care System Distrust Scale

1. The Health Care System does its best to make patients' health better

Strongly Disagree Disagree Neither agree nor disagree Agree Strongly Agree

2. The Health Care System covers up its mistakes

Strongly Disagree Disagree Neither agree nor disagree Agree Strongly Agree

3. Patients receive high quality medical care from the Health Care System

Strongly Disagree Disagree Neither agree nor disagree Agree Strongly Agree

4. The Health Care System makes too many mistakes

Strongly Disagree Disagree Neither agree nor disagree Agree Strongly Agree

5. The Health Care System puts making money above patients' needs

Strongly Disagree Disagree Neither agree nor disagree Agree Strongly Agree

6. The Health Care System gives excellent medical care

Strongly Disagree Disagree Neither agree nor disagree Agree Strongly Agree

7. Patients get the same medical treatment from the Health Care System, no matter what the patient's race or ethnicity

Strongly Disagree Disagree Neither agree nor disagree Agree Strongly Agree

8. The Health Care System lies to make money

Strongly Disagree Disagree Neither agree nor disagree Agree Strongly Agree

9. The Health Care System experiments on patients without them knowing

Strongly Disagree Disagree Neither agree nor disagree Agree Strongly Agree

APPENDIX E

Demographic Questionnaire

Thank you for participating in our research study! Please circle the response that is most true for you. The following questions will be used to describe our study sample and all of your responses will be de-identified. You do not have to answer any questions you do not want to, but we ask that you respond truthfully. We will not look at this information until we have analyzed all the interviews. Please ask the research assistant if you have any questions.

Questions about you:

1. What is your preferred language?
    a) English
    b) Spanish
    c) Other (please list):_____

2. Are you of Hispanic, Latinx, or of Spanish origin?
    a) Yes
    b) No

3. How would you describe yourself?
    a) American Indian or Alaska Native
    b) Asian
    c) Black or African American
    d) Native Hawaiian or Other Pacific Islander
    e) White
    f) Other (please list):_____

4. To which gender identity do you most identify?
    a) Female
    b) Male
    c) Transgender female
    d) Transgender male
    e) Other (please list):_____
    f) Prefer not to answer

5. What is your current marital status?
    a) Married/Long-term Partner
    b) Single
    c) Separated
    d) Divorced
    e) Widowed

a) Other (please list):_____

6. Please list the persons currently living in your (primary) household and their relationship to you:

_____
_____
_____
_____
_____

7. What is the highest level of education you have completed?
    a) Less than seventh grade
    b) Junior high school (9th grade)
    c) Partial high school (10th or 11th grade)
    d) High school graduate (whether private preparatory or public school)
    e) Partial college (at least one year)
    f) Associates degree or specialized training
    g) Standard college or university graduation
    h) Graduate professional training (graduate degree)
    i) Other (please list):_____

8. Please check the category that tells us your approximate total family income for YEAR. Consider all sources of income, including earnings, public government assistance, child support alimonies, support from other members of your household who regularly contribute to your household, etc.
    a) _____ _Less than $10,000
    b) _____ $10,001 to $15,000
    c) _____ $15,001 to $25,000
    d) _____ $25,001 to $50,000
    e) _____$50,001 to $75,000
    f) _____$75,001 to $100,000
    g) _____$100,001 to $150,000
    h) _____ more than $150,000.

9. What is your current work status (select all that apply):
    a) Working full-time outside of the home
    b) Working part-time outside of the home
    c) Full-time Homemaker
    d) Unemployed
    e) Temporarily laid off, on leave (FMLA), or between jobs
    f) Disabled
    g) Retired
    h) Student
    i) Other (please list):_____

9.a. Please list your current occupation if employed: _____

10. Have you become unemployed/left your job within the past year?
    a. Yes
    b. No

10.a. If you answered "Yes" to #10, was it because of side effects from cancer-associated treatment?
    a) Yes
    b) No

11. Have you been diagnosed or treated for any past psychiatric medical condition, including depression, anxiety, or bipolar disorder?
    a) Yes
    b) No

11.a. If you answered "Yes" to #11, what year were you diagnosed or begin receiving treatment? (please specifiy if you are answering year of diagnosis or treatment)
    c) Year:_____

12. Do you smoke tobacco (cigarettes, cigars, vape, etc.)?
    a) Yes
    b) No

If you do smoke, when did you start and how frequently do you smoke?
    12.a. Year_____
    12.b. Frequency
        i. Less than once a month
        ii. A few times per month
        iii. Weekly
        iv. Daily
        v. Multiple times per day

13. Do you drink alcohol?
    a) Yes
    b) No

If you do drink, on average how many drinks do you have per week? _____

14. Do you use recreational drugs?
    a) Yes
    b) No

13.a. If you do use recreational drugs, what drugs do you use?
    c) _____

Health Care Questions:

15. Prior to your cancer diagnosis, how often would you attend health care appointments, planned and unplanned, annually?
    a) 0
    b) 1-5
    c) 6-10
    d) 10-20
    e) 20+

16. After your diagnosis relating to side effects from your cancer treatment, how often would you attend health care appointments, planned and unplanned, annually
    a) 0
    b) 1-5
    c) 6-10
    d) 10-20
    e) 20+

17. As a result of your changes in health, did you move in with a parent(s)/caregiver(s)?
    a) Yes
    b) No

    If yes, did you live with your parent(s)/caregiver(s):
    16.a. before cancer diagnosis?
        i. Yes
        ii. No
    16.b. before cancer treatment-related side effect diagnosis?
        iii. Yes
        iv. No

18. On a scale of 1 to 10 (1 = not close at all, 10 = extremely close), how close would you say you are with your health care providers?
    1 2 3 4 5 6 7 8 9 10

19. On a scale of 1 to 10 (1 = never, 10 = always), rate your likelihood to approach your health care team when you have a question regarding your health.
    1 2 3 4 5 6 7 8 9 10

20. At any time in the past 4 weeks, have you been tested for COVID-19, other than as a requirement for a medical procedure?
    a) Yes

b) No

19.a. If yes, were your results:

(1) Positive (2) Negative (3) Unknown

21. At any time in the past 4 weeks, have you been exposed to anyone who tested positive for COVID-19?
    a) Yes
    b) No

22. At any time in the past 4 weeks, have you been in a gathering of more than 50 people?
    a) Yes
    b) No

23. Prior to this appointment, have you obtained medical care in the past 4 weeks?
    a) Yes
    b) No

22.a. If yes, how would you rate that experience?

1- Poor 2- Fair 3- Good 4- Excellent

24. At any time in the past 4 weeks, did you delay getting medical care because of the coronavirus pandemic?
    a) Yes
    b) No

25. Please describe the prevention behaviors you practice to reduce your risk of contracting coronavirus:

_____
_____
_____
_____
_____

APPENDIX E

Data Sheet

The following data will be collected from AYA patient's Electronic Medical Records.

Patient Information:

1) Date of Birth
2) Age
3) Sex
4) Medical history
5) Cancer diagnosis
6) Date of cancer diagnosis
7) Type of treatment
8) Long term chemotherapy side effect diagnosis
9) Date of long term chemotherapy side effect diagnosis (cardiotoxicity, nephrotoxicity, peripheral neuropathy, etc.)
10) Primary care physician (if available)
11) Mental health provider (if available)
12) Body Mass Index (BMI)
13) Insurance (private vs. public)
14) Zip code of residence
15) Phone number
16) Email

Phone call follow up data will be recorded here one month after the last study visit including:

1) Have you received a new diagnosis pertaining to your mental health not present at enrollment (with date)?
2) How have you been feeling since your participation in this study?
3) Have you had COVID-19?
4) Have you had the COVID-19 vaccine? If no, why not?

APPENDIX F

Interview Guide – AYA Form

Orientation statement: Our goal with this study is to understand how adolescents and young adults cope during cancer treatment and beyond. Our hope is that by talking directly to patients, we can gain a better understanding and in turn help those who are struggling after beating cancer. There are no right or wrong answers—you are the expert in your life and in your experience.

1) Tell me how things have gone for you since you were diagnosed with cancer.
    a. Has anything happened during this time that has changed things for you? If so, what?
    b. What kind of things did you do to get through this time?
    c. How did you do that?
    d. What were some challenges you encountered and how did you handle it?
    e. How did it feel to overcome cancer?

2) Tell me how things have gone for you since you were diagnosed with serious side effects related to your cancer treatment.
    a. What kind of things are you doing/have you done to get through this time?
    b. How did you do that?
    c. How has this diagnosis affected you in your daily life?
    d. How does living with this diagnosis compare to when you were living with cancer?

3) Tell me about your relationship with your health care providers.
    a. How would you describe the care you receive?
    b. What have they done that has been helpful/not helpful?
    c. Do you feel comfortable in a health care setting?
    d. Do you feel in control of the care you receive?

4) What impact has COVID-19 had on your everyday living?
    a. How has COVID-19 affected your access to health care?
    b. How has COVID-19 affected your relationships with your health care providers?

5) What else should I know about your experience with cancer that I haven't asked?
    a. What is important for me to know about your experiences with cancer?

APPENDIX H

SAFE-T Protocol with C-SSRS (Columbia Risk and Protective Factors) - Recent

Step 1: Identify Risk Factors

C-SSRS Suicidal Ideation Severity	Mont
1) Wish to be dead *Have you wished you were dead or wished you could go to sleep and not wake up?*	
2) Current suicidal thoughts *Have you actually had any thoughts of killing yourself?*	
3) Suicidal thoughts w/ Method (w/no specific Plan or Intent or act) *Have you been thinking about how you might do this?*	
4) Suicidal Intent without Specific Plan *Have you had these thoughts and had some intention of acting on them?*	
5) Intent with Plan *Have you started to work out or worked out the details of how to kill yourself? Do you intend to carry out this plan?*	
C-SSRS Suicidal Behavior: *"Have you ever done anything, started to do anything, or prepared to do anything to end your life?"* Examples: Collected pills, obtained a gun, gave away valuables, wrote a will or suicide note, took out pills but didn't swallow any, held a gun but changed your mind or it was grabbed from your hand, went to the roof but didn't jump; or actually took pills, tried to shoot yourself, cut yourself, tried to hang yourself, etc. If "YES" Was it within the past 3 months?	Lifeti Past Mont

Activating Events:
□ Recent losses or other significant negative event(s) (legal, financial, relationship, etc.)
□ Pending incarceration or homelessness
□ Current or pending isolation or feeling alone

Treatment History:
□ Previous psychiatric diagnosis and treatments
□ Hopeless or dissatisfied with treatment
□ Non-compliant with treatment
□ Not receiving treatment
□ Insomnia

Other:
□ _____
□ _____
□ _____

Clinical Status:
□ Hopelessness
□ Major depressive episode
□ Mixed affect episode (e.g. Bipolar)
□ Command Hallucinations to hurt self
□ Chronic physical pain or other acute medical problem (e.g. CNS disorders)

□ Highly impulsive behavior
□ Substance abuse or dependence
□ Agitation or severe anxiety
□ Perceived burden on family or others
□ Homicidal Ideation
□ Aggressive behavior towards others
□ Refuses or feels unable to agree to safety plan
□ Sexual abuse (lifetime)
□ Family history of suicide

□ **Access to lethal methods:** Ask <u>specifically</u> about presence or absence of a firearm in the home or ease of accessing

Step 2: Identify Protective Factors (Protective factors may not counteract significant acute suicide risk factors)

Internal:	**External:**
□ Fear of death or dying due to pain and suffering	□ Belief that suicide is immoral; high spirituality
□ Identifies reasons for living	□ Responsibility to family or others; living with family
□ _____	□ Supportive social network of family or friends
□ _____	□ Engaged in work or school

Step 3: Specific questioning about Thoughts, Plans, and Suicidal Intent – (see Step 1 for Ideation Severity and Behavior)

C-SSRS Suicidal Ideation Intensity (with respect to the most severe ideation 1-5 identified above)	**Mon**
Frequency ***How many times have you had these thoughts?*** (1) Less than once a week (2) Once a week (3) 2-5 times in week (4) Daily or almost daily (5) Many times each day	
Duration ***When you have the thoughts how long do they last?*** (1) Fleeting - few seconds or minutes (4) 4-8 hours/most of day (2) Less than 1 hour/some of the time (5) More than 8 hours/persistent or continuous (3) 1-4 hours/a lot of time	
Controllability ***Could/can you stop thinking about killing yourself or wanting to die if you want to?*** (1) Easily able to control thoughts (4) Can control thoughts with a lot of difficulty (2) Can control thoughts with little difficulty (5) Unable to control thoughts (3) Can control thoughts with some difficulty (0) Does not attempt to control thoughts	
Deterrents ***Are there things - anyone or anything (e.g., family, religion, pain of death) - that stopped you from wanting to die or acting on thoughts of suicide?*** (1) Deterrents definitely stopped you from attempting suicide (4) Deterrents most likely did not stop you (2) Deterrents probably stopped you (5) Deterrents definitely did not stop you (3) Uncertain that deterrents stopped you (0) Does not apply	
Reasons for Ideation ***What sort of reasons did you have for thinking about wanting to die or killing yourself? Was it to end the pain or stop the way you were feeling (in other words you couldn't go on living with this pain or how you were feeling) or was it to get attention, revenge or a reaction from others? Or both?***	

(1) Completely to get attention, revenge or a reaction from others (2) Mostly to get attention, revenge or a reaction from others (3) Equally to get attention, revenge or a reaction from others and to end/stop the pain	(4) Mostly to end or stop the pain (you couldn't go on living with the pain or how you were feeling) (5) Completely to end or stop the pain (you couldn't go on living with the pain or how you were feeling) (0) Does not apply	
	Total Score	

Step 4: Guidelines to Determine Level of Risk and Develop Interventions to LOWER Risk Level

"The estimation of suicide risk, at the culmination of the suicide assessment, is the quintessential **clinical judgment**, since no study has identified one specific risk factor or set of risk factors as specifically predictive of suicide or other suicidal behavior."
From The American Psychiatric Association Practice Guidelines for the Assessment and Treatment of Patients with Suicidal Behaviors, page 24.

RISK STRATIFICATION	TRIAGE
High Suicide Risk □ Suicidal ideation with intent or intent with plan **in past month** (C-SSRS Suicidal Ideation #4 or #5) **Or** □ Suicidal behavior **within past 3 months** (C-SSRS Suicidal Behavior)	□ **Initiate local psychiatric admission process** □ **Stay with patient until transfer to higher level of care is complete** □ **Follow-up and document outcome of emergency psychiatric evaluation**
Moderate Suicide Risk □ Suicidal ideation with method, **WITHOUT plan, intent or behavior** **in past month** (C-SSRS Suicidal Ideation #3) **Or** □ Suicidal behavior more than 3 months ago (C-SSRS Suicidal Behavior Lifetime) **Or** □ Multiple risk factors and few protective factors	□ **Directly address suicide risk, implementing suicide prevention strategies** □ **Develop Safety Plan**
Low Suicide Risk □ Wish to die or Suicidal Ideation **WITHOUT method, intent, plan or behavior** (C-SSRS Suicidal Ideation #1 or #2) **Or** □ Modifiable risk factors and strong protective factors **Or** □ No reported history of Suicidal Ideation or Behavior	□ **Discretionary Outpatient Referral**

Step 5: Documentation

Risk Level :

[ ] High Suicide Risk

[ ] Moderate Suicide Risk

[ ] Low Suicide Risk

Clinical Note:

□ Your Clinical Observation

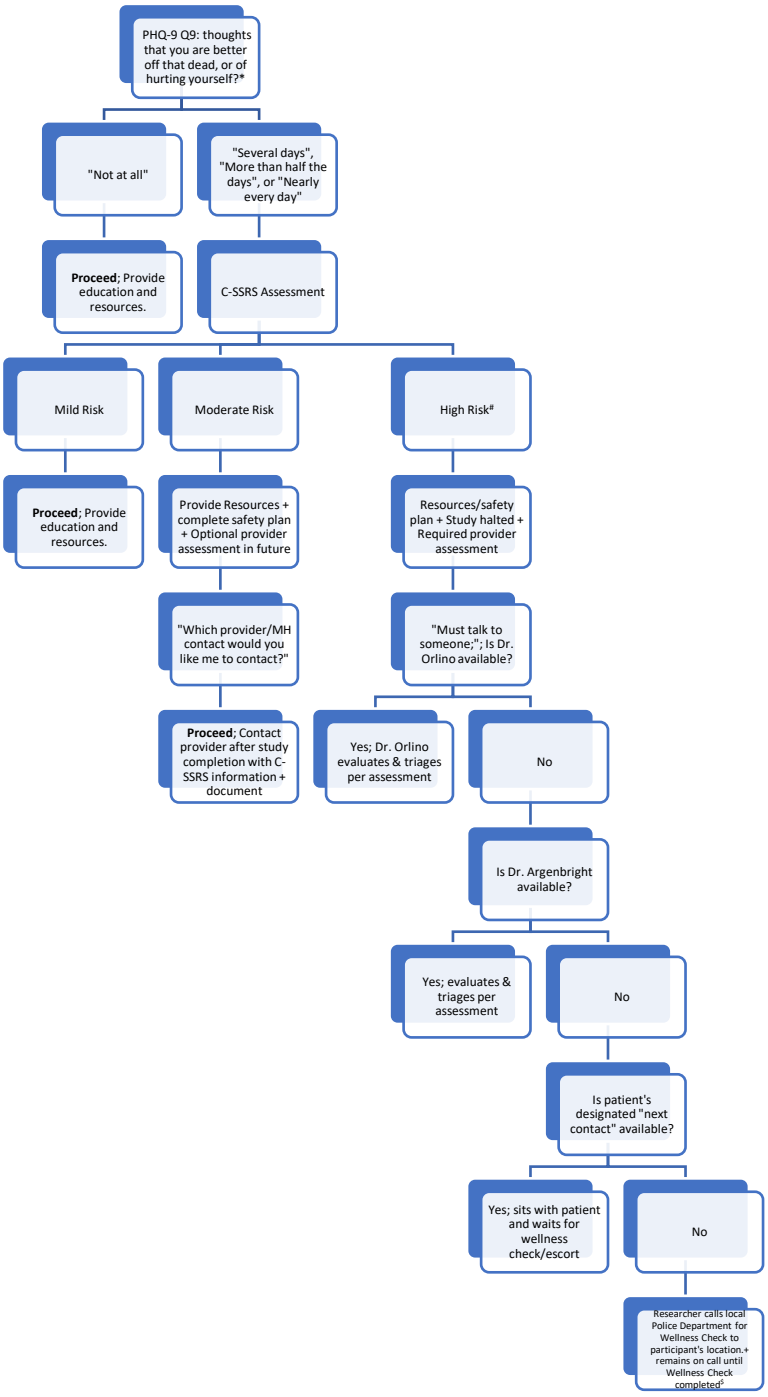
- Relevant Mental Status Information
- Methods of Suicide Risk Evaluation

- Brief Evaluation Summary
  - Warning Signs
  - Risk Indicators
  - Protective Factors
  - Access to Lethal Means
  - Collateral Sources Used and Relevant Information Obtained
  - Specific Assessment Data to Support Risk Determination
  - Rationale for Actions Taken and Not Taken

- Provision of Crisis Line 1-800-273-TALK(8255)
- Implementation of Safety Plan (If Applicable)

APPENDIX I

SUICIDAL IDEATION WORK UP[+]



[+]PCP, Primary Mental Health provider, location, and patient's designated "next contact" will be collected prior to PHQ-9 administration

*****This flowchart could also be initiated by any thoughts or feelings of suicidal ideation or harming themselves or others during the semi-structured interview, not just the PHQ-9

[#]If at any point during the "High Risk" flowchart contact is lost with the patient, 911 will be contacted for a wellness check

[$]Can also call Zale Lipshy, inpatient psychiatric triage line, at 214-645-4115.