



**Study Title: COVID-19: WELL-BEING AND HRQOL IN  
CANCER PATIENTS AND SURVIVORS**

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## PROTOCOL REVISION HISTORY

<b>Version Number</b>	<b>Version Date</b>	<b>Summary of Revisions Made:</b>
N/A		

## **STATEMENT OF COMPLIANCE**

I confirm that I have read this protocol, I understand it, and I will work according to this protocol and to the ethical principles stated in the latest version of the Declaration of Helsinki, the applicable ICH guidelines for good clinical practices, and the applicable federal, state, and local laws, rules, and regulations relating to the conduct of the protocol.

I agree to inform all those who assist/collaborate with me in the conduct of this study of their responsibilities and obligations.

Once the protocol has been reviewed and approved by the Institutional Review Board (IRB) I understand that any change(s) made during the course of the study must also (first) be approved by the IRB prior to implementation, except when such modification is made to remove any immediate hazard(s) to the subject(s).

I certify that I and the study staff responsible, have received the requisite training to conduct this research protocol.

I agree to maintain adequate and accurate records in accordance with the University of Miami policies, federal, state and local laws and regulations.

I agree to maintain the confidentiality of all information received and/or developed in connection with this protocol.

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## PROTOCOL SUMMARY

Title	COVID-19: WELL-BEING AND HRQOL IN CANCER PATIENTS AND SURVIVORS
Background	<p>The coronavirus disease 2019 (COVID-19) is an infectious disease that is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As of April 9<sup>th</sup>, 2020, COVID-19 continues to be a major and catastrophic global pandemic that is impacting the lives of millions across the world. Most recent figures show over 1.5 million confirmed cases of COVID-19 across the world and almost 90 thousand deaths. In the US alone, there are over 432 thousand confirmed cases of COVID-19, and almost 15 thousand deaths. These numbers are likely to be an underestimate given limitations in testing and cause of death ascertainment. South Florida, Sylvester’s catchment area, continues to be a “hotspot” in the state of Florida with over 10,000 confirmed cases of COVID-19. Similarly, due to testing limitations, these numbers are likely significantly underestimated. Arguably, the COVID-19 pandemic has been one of the most challenging and disruptive global events experienced in several generations. While mitigation strategies have shown some promise, the COVID-19 pandemic presents a chronic and challenging public health threat that will continue to impact all communities for the foreseeable future.</p> <p>Several health conditions and populations have been determined to be at higher risk for severe illness from COVID-19. Based on available data, the Centers for Disease Control (CDC) has identified this population to include people 65 years or older, living in a nursing home or long-term care facility and individuals of all ages with underlying medical conditions such as chronic lung disease, moderate or severe asthma, serious heart conditions, diabetes, immune compromised states due to illnesses such as HIV or immunosuppressant treatments including cancer treatments, liver disease and chronic kidney disease. Cancer patients and survivors may be at elevated risk as well. Oncology providers have suggested that patients with blood malignancies may have the most significant risk. These include hematologic cancers such as non-Hodgkin lymphoma, chronic lymphocytic leukemia, acute myeloid leukemia, acute lymphoblastic leukemia, and multiple myeloma. Furthermore, patients who have received T-cell therapies, those on active chemotherapy, and patients who have undergone stem cell transplants are also compromised and should be very careful in their contacts with others. Patients being actively treated (surgery, chemotherapy, or radiation) for non-blood malignancies may also be at high risk for complications. In addition to medical complications from COVID-19 in oncology patients, both patients and survivors are already coping with multiple and chronic challenges associated with a cancer diagnosis and treatment which are likely being exacerbated by the COVID-19 pandemic. These include, but are not limited to, treatment decisions,</p>

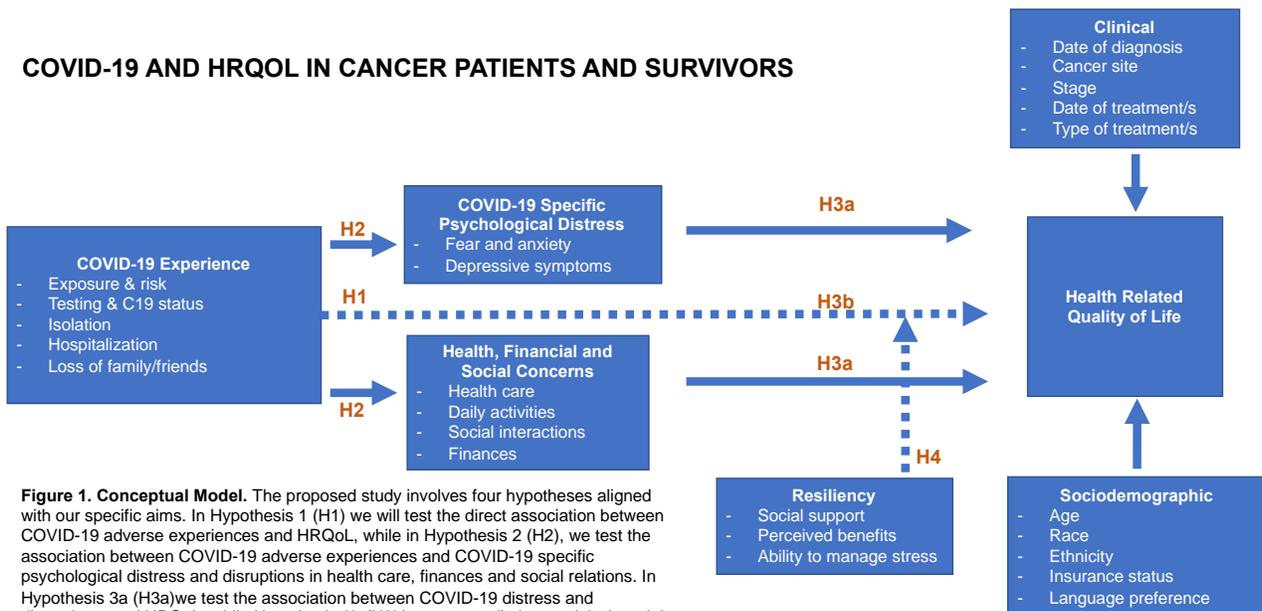
	<p>treatment-related side effects, emotional and social concerns regarding disease activity, treatment response and interpersonal disruptions. Furthermore, cancer care and follow-up can be complex, fragmented and expensive. Collectively, these chronic stressors, if left unaddressed, can significantly impact health related quality of life (HRQoL) and other patient reported outcomes (PROs). The extent to which global pandemics impact multiple aspects of HRQoL in cancer patients and survivors remains relatively unknown. Therefore, information is critically needed to guide care delivery and psychosocial programs that address unique needs and challenges faced by cancer patients and survivors.</p> <p>A robust psychosocial literature has documented the role of multiple factors on HRQoL and other PROs (e.g., symptom burden, treatment satisfaction) in cancer populations. These include psychosocial distress, and concerns about unmet needs specific to health care delivery, daily activities, social interactions and finances. Conversely, resiliency factors such as social support, perceived benefits in face of challenges, and stress management skills have been shown to favorably impact HRQoL and other PROs. This study is the first step in a line of research that will guide the development of psychosocial programs to enhance patient care and outcomes in the context of facing a global pandemic by conducting a rapid ascertainment of COVID-19 experiences and psychosocial responses in cancer patients and survivors.</p>
<p><b>Objectives</b></p>	<p><b>Primary</b></p> <p>Specific Aim 1: Administer a brief, self-report, online-based questionnaire to assess experiences during the COVID-19 pandemic (e.g., exposure, risk factors, testing, isolation, seropositivity, hospitalization, loss of family or friends); COVID-19 specific psychological distress (e.g., fear, anxiety and depressive symptoms); health, financial and social disruptions; perceived benefits and social support; and HRQoL in a convenience sample of cancer patients and survivors at Sylvester.</p> <p><b>Secondary</b></p> <p>Specific Aim 2: Evaluate the extent to which COVID-19 experiences are associated with COVID-19 specific psychological distress; health, financial and social disruptions; perceived benefits and social support; and HRQoL.</p> <p><b>Exploratory</b></p> <p>Specific Aim 3: Evaluate the extent to which resiliency factors such as social support and perceived benefits moderate the effects of COVID-19 experiences on COVID-19 specific psychological distress and HRQoL.</p>
<p><b>Endpoints</b></p>	<p>Our team, in collaboration with investigators from the MD Anderson</p>

	<p>Cancer Center and UCLA, has developed a comprehensive assessment of COVID-19 experiences that includes 15 objective items that assess exposure, risk factors, testing, isolation, seropositivity, symptoms, hospitalization, loss of family or friends, and loss of income. Drawing from published measures that have assessed the impact of pandemics and other major national stressors such as 9/11, a 37-item measure was developed to assess COVID-19 specific psychological distress (e.g., fear, anxiety and depressive symptoms), and health care, financial and social disruptions. Items also assess resiliency factors such as social support, perceived benefits under times of stress, and ability to manage stress. Responses are provided in a Likert like scale (from 0 to 4) where participants are asked to rank statements from “strongly disagree” to “strongly agree.” The measure provides a total score summary that indicates the degree to which the COVID-19 pandemic has negatively impacted the participant. Items that tap into resiliency are reverse scored. In addition to the summary score, based on psychometric analyses upon collection of the data, the scale is expected to yield 7 subscale scores: COVID-19 Specific Distress; Health Care Disruptions and Concerns; Disruption to Daily Activities and Social Interactions; Financial Hardship; Perceived Benefits; Functional Social Support; and Perceived Stress Management Skills. The assessment will also include the Functional Assessment of Cancer Therapy-7 (FACT-G7) which is a well-validated and commonly used measure of HRQoL in oncology. A total score provides an index of HRQoL.</p> <p><b>Electronic Health Record (EHR) Data Variables:</b> As described below, we will extract the following variables for consented participants from the electronic data warehouse (EDW) which serves as a repository of the EHR:</p> <p>Age, race, ethnicity, language preference, insurance status, date of diagnosis, date of primary treatment, date of last treatment, treatment types, cancer site, cancer stage, active disease vs. remission status and comorbidities.</p>
<p>Study Design</p>	<p>We have developed a 10-minute questionnaire that taps into how experiences during the COVID-19 pandemic (e.g., exposure, risk factors, testing, isolation, seropositivity, hospitalization, loss of family or friends, loss of income), may have impacted multiple domains of health-related quality of life (HRQoL; physical, emotional and social well-being), and other areas such as COVID-19 specific psychological distress (e.g., fear, anxiety and depressive symptoms), and disruptions to health care, finances and social interactions. The questionnaires will be administered online via email contact using a RedCap platform. Emails will be sent to Sylvester cancer patients and survivors who have consented to be contacted for research purposes and have an active email address. Data regarding clinical and sociodemographic characteristics of the respondents will be extracted from the electronic data warehouse (EDW) repository by linking the questionnaires to their medical record number (MRN).</p>

Number of Patients/Target Study Population	3000
Description of Sites/Facilities Enrolling Participants	Emails will be sent to Sylvester cancer patients and survivors in order to invite them to consent and complete the COVID-19 questionnaires.
Study duration	1 year

## 1.0 Schema

### Conceptual Model Guiding Study Hypothesis



**Figure 1. Conceptual Model.** The proposed study involves four hypotheses aligned with our specific aims. In Hypothesis 1 (H1) we will test the direct association between COVID-19 adverse experiences and HRQoL, while in Hypothesis 2 (H2), we test the association between COVID-19 adverse experiences and COVID-19 specific psychological distress and disruptions in health care, finances and social relations. In Hypothesis 3a (H3a) we test the association between COVID-19 distress and disruptions, and HRQoL, while Hypothesis 3b (H3b) tests a mediation model where it is expected that the association between COVID-19 adverse experiences and HRQoL are mediated by COVID-19 distress and disruptions. Finally, Hypothesis 4 (H4) tests whether resiliency factors moderate the relationship between COVID-19 adverse experiences, and HRQoL where participants with greater resiliency have a significantly weaker association among these measures.

## 2 INTRODUCTION

### 2.1 Study Rationale

The primary purpose of this study is to gain an understanding of how experiences during the COVID-19 pandemic (e.g., exposure, risk factors, testing, isolation, seropositivity, hospitalization, loss of family or friends, loss of income), may have impacted multiple domains of health-related quality of life (HRQoL; physical, emotional and social well-being), and other areas such as COVID-19 specific psychological distress (e.g., fear, anxiety and depressive symptoms), and disruptions to health care, finances and social interactions. We will also evaluate the extent to which resiliency factors such as social support, perceived benefits under times of stress, and ability to manage stress may buffer associations between COVID-19 experiences and HRQoL. To meet these objectives, we have developed a 10-minute questionnaire that taps into these areas and is based on prior work addressing concerns of other pandemics (e.g., H1N1) or national crises (e.g., 9/11). We also include a widely used and well-validated brief measure of HRQoL in cancer patients and survivors. The questionnaires will be administered online via email contact using a RedCap platform. Emails will be sent to Sylvester cancer patients and survivors who have consented to be contacted for research purposes and have an active email address. Data regarding clinical and sociodemographic characteristics of the respondents will be extracted from the electronic data warehouse (EDW) repository by linking the questionnaires to their medical record number (MRN). This study will provide insights into how experiences associated with the COVID-19 pandemic impact HRQoL and other experiences in our cancer patients and survivors and thus guide efforts for potential care delivery programs and interventions in the face of such pandemics that address specific needs.

### 2.2 Background

The coronavirus disease 2019 (COVID-19) is an infectious disease that is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As of April 9<sup>th</sup>, 2020, COVID-19 continues to be a major and catastrophic global pandemic that is impacting the lives of millions across the world. Most recent figures show over 1.5 million confirmed cases of COVID-19 across the world and almost 90 thousand deaths. In the US alone, there are over 432 thousand confirmed cases of COVID-19, and almost 15 thousand deaths. These numbers are likely to be an underestimate given limitations in testing and cause of death ascertainment. South Florida, Sylvester's catchment area, continues to be a "hotspot" in the state of Florida with over 10,000 confirmed cases of COVID-19. Similarly, due to testing limitations, these numbers are likely significantly underestimated. Arguably, the COVID-19 pandemic has been one of the most challenging and disruptive global events experienced in several generations. While mitigation strategies have shown some promise, the COVID-19 pandemic presents a chronic and challenging public health threat that will continue to impact all communities for the foreseeable future.

Several health conditions and populations have been determined to be at higher risk for severe illness from COVID-19. Based on available data, the Centers for Disease Control (CDC) has identified this population to include people 65 years or older, living in a nursing home or long-term care facility and individuals of all ages with underlying medical conditions such as chronic lung disease, moderate or severe asthma, serious heart conditions, diabetes, immune compromised states due to illnesses such as HIV or immunosuppressant treatments including cancer treatments, liver disease and chronic kidney disease. Cancer patients and

survivors may be at elevated risk as well. Oncology providers have suggested that patients with blood malignancies may have the most significant risk. These include hematologic cancers such as non-Hodgkin lymphoma, chronic lymphocytic leukemia, acute myeloid leukemia, acute lymphoblastic leukemia, and multiple myeloma. Furthermore, patients who have received T-cell therapies, those on active chemotherapy, and patients who have undergone stem cell transplants are also compromised and should be very careful in their contacts with others. Patients being actively treated (surgery, chemotherapy, or radiation) for non-blood malignancies may also be at high risk for complications. In addition to medical complications from COVID-19 in oncology patients, both patients and survivors are already coping with multiple and chronic challenges associated with a cancer diagnosis and treatment which are likely being exacerbated by the COVID-19 pandemic. These include, but are not limited to, treatment decisions, treatment-related side effects, emotional and social concerns regarding disease activity, treatment response and interpersonal disruptions. Furthermore, cancer care and follow-up can be complex, fragmented and expensive. Collectively, these chronic stressors, if left unaddressed, can significantly impact health related quality of life (HRQoL) and other patient reported outcomes (PROs). The extent to which global pandemics impact multiple aspects of HRQoL in cancer patients and survivors remains relatively unknown. Therefore, information is critically needed to guide care delivery and psychosocial programs that address unique needs and challenges faced by cancer patients and survivors.

A robust psychosocial literature has documented the role of multiple factors on HRQoL and other PROs (e.g., symptom burden, treatment satisfaction) in cancer populations. These include psychosocial distress, and concerns about unmet needs specific to health care delivery, daily activities, social interactions and finances. Conversely, resiliency factors such as social support, perceived benefits in face of challenges, and stress management skills have been shown to favorably impact HRQoL and other PROs. This study is the first step in a line of research that will guide the development of psychosocial programs to enhance patient care and outcomes in the context of facing a global pandemic by conducting a rapid ascertainment of COVID-19 experiences and psychosocial responses in cancer patients and survivors.

The study team is led by Dr. Frank J. Penedo who has extensive expertise in psychosocial oncology, cancer survivorship, psychosocial assessment and intervention in cancer patients, and cancer care delivery. Dr. Michael Antoni brings strong and relevant expertise in medical oncology and psychosocial oncology.

## **2.3 Risk/Benefit Assessment**

### **Known Potential Risks**

The topic addressed would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation.

The survey will only be conducted with Sylvester patients. No questions requiring mandatory reporting or regarding documentation status are asked.

Minimal risk is anticipated as a result of answering the survey questions. Though we regard the risks of participating in this study to be low, we will make sure to handle any situations sensitively and empathetically as a result of the COVID-19 subject matter. Research staff is required to complete UM-mandated training on the Protection of Human Research Participants. Certificates for all research staff will be kept on file in the lab supervisor's office. Since the risks associated with participating in this survey are relatively low and easily

managed, and since the benefits for participants are potentially substantial, we feel that the balance of risks-to-benefits is reasonable.

### **Known Potential Benefits**

The participants will not receive any direct benefit from the proposed research, but others may benefit from the knowledge obtained.

### **Assessment of Potential Risks and Benefits**

To minimize risk of the consented participant's clinical data link to measure responses, a unique identifier is assigned within RedCap form once the patient signs the informed consent. At this point the patient has provided their consent and filled out the questionnaire. Their medical record number will be hidden after entry so that it is not displayed to all users. Medical record number entry is required to link the selected clinical data but this field will be hidden except to key personnel (e.g. statistician, study lead) with the designated user rights.

Ultimately, this research seeks to develop, enhance/or guide the psychosocial management of cancer patients and survivors during a pandemic, natural disaster or other chronic unforeseen naturalistic stressors.

## **3 OBJECTIVES AND ENDPOINTS**

### **3.1 Objectives**

#### **Primary Objectives**

**Specific Aim 1:** Administer a brief, self-report, online-based questionnaire to assess experiences during the COVID-19 pandemic (e.g., exposure, risk factors, testing, isolation, seropositivity, hospitalization, loss of family or friends); COVID-19 specific psychological distress (e.g., fear, anxiety and depressive symptoms); health, financial and social disruptions; perceived benefits and social support; and HRQoL in a convenience sample of cancer patients and survivors at Sylvester.

#### **Secondary Objective**

**Specific Aim 2:** Evaluate the extent to which COVID-19 experiences are associated with COVID-19 specific psychological distress; health, financial and social disruptions; perceived benefits and social support; and HRQoL.

#### **3.1.1 Exploratory Objective**

**Specific Aim 3:** Evaluate the extent to which resiliency factors such as social support and perceived benefits moderate the effects of COVID-19 experiences on COVID-19 specific psychological distress and HRQoL.

### **3.2 Endpoints**

#### **3.2.1 Primary Endpoints**

The questionnaire will assess exposure, risk factors, testing, isolation, seropositivity, symptoms, hospitalization, loss of family or friends, and loss of income.

Through questionnaire assess COVID-19 specific psychological distress (e.g., fear, anxiety and depressive symptoms), and health care, financial and social disruptions.

**Secondary Endpoints**

Through data pull report obtain age, race, ethnicity, language preference, household income, insurance status, date of diagnosis, date of primary treatment, date of last treatment, treatment types, cancer site, cancer stage, active disease vs. remission status and comorbidities.

**Exploratory Endpoints**

Through questionnaire assess Items also assess resiliency factors such as social support, perceived benefits under times of stress, and ability to manage stress.

Objectives	Endpoints
<b>Primary</b>	
Administer a brief, self-report, online-based questionnaire to assess experiences during the COVID-19 pandemic; COVID-19 specific psychological distress); health, financial and social disruptions; perceived benefits and social support; and HRQoL in a convenience sample of cancer patients and survivors at Sylvester.	Exposure, risk factors, testing, isolation, seropositivity, hospitalization, loss of family or friends; fear, anxiety and depressive symptoms
<b>Secondary</b>	
Evaluate the extent to which COVID-19 experiences are associated with COVID-19 specific psychological distress; health, financial and social disruptions; perceived benefits and social support; and HRQoL.	Age, race, ethnicity, language preference, insurance status, household income, date of diagnosis, date of primary treatment, date of last treatment, treatment types, cancer site, cancer stage, active disease vs. remission status and comorbidities
<b>Exploratory</b>	
Evaluate the extent to which resiliency factors such as social support and perceived benefits moderate the effects of COVID-19 experiences on COVID-19 specific psychological distress and HRQoL.	Resiliency factors such as social support, perceived benefits under times of stress, and ability to manage stress.

**4 STUDY DESIGN**

**4.0 Overall Design**

We have developed a 10-minute questionnaire that taps into how experiences during the COVID-19 pandemic (e.g., exposure, risk factors, testing, isolation, seropositivity, hospitalization, loss of family or friends, loss of income), may have impacted multiple domains

of health-related quality of life (HRQoL; physical, emotional and social well-being), and other areas such as COVID-19 specific psychological distress (e.g., fear, anxiety and depressive symptoms), and disruptions to health care, finances and social interactions. We also include a widely used and well-validated brief measure of HRQoL in cancer patients and survivors. The questionnaires will be administered online via email contact using a RedCap platform. Emails will be sent to Sylvester cancer patients and survivors who have consented to be contacted for research purposes and have an active email address. Data regarding clinical and sociodemographic characteristics of the respondents will be extracted from the electronic data warehouse (EDW) repository by linking the questionnaires to their medical record number (MRN).

Our Study Hypotheses are as follows:

**Hypothesis 1:** After adjusting for relevant clinical (e.g., cancer type, stage, treatment) and sociodemographic (e.g., age, race, ethnicity) factors, more adverse COVID-19 experiences will be significantly associated with poorer HRQoL.

**Hypothesis 2:** After adjusting for relevant factors, greater adverse COVID-19 experiences will be significantly associated with greater COVID-19 specific psychological distress and health, financial and social disruptions.

**Hypothesis 3:** After adjusting for relevant factors, (a) greater COVID-19 specific psychological distress and health, financial and social disruptions will be significantly associated with poorer HRQoL and (b) mediate the association between COVID-19 adverse experiences and HRQoL.

**Hypothesis 4:** Among participants with greater social support, greater perceived benefit, and greater ability to manage stress, the association between adverse COVID-19 experiences will not be significantly associated with COVID-19 specific psychological distress and HRQoL. Whereas COVID-19 experiences will be significantly associated with greater COVID-19 specific distress and poorer HRQoL in participants with lower social support and perceived benefit.

**Assessment Measures:** Our team, in collaboration with investigators from the MD Anderson Cancer Center and UCLA, has developed a comprehensive assessment of COVID-19 experiences that includes 15 objective items that assess exposure, risk factors, testing, isolation, seropositivity, symptoms, hospitalization, loss of family or friends, and loss of income. Drawing from published measures that have assessed the impact of pandemics and other major national stressors such as 9/11, a 37-item measure was developed to assess COVID-19 specific psychological distress (e.g., fear, anxiety and depressive symptoms), and health care, financial and social disruptions. Items also assess resiliency factors such as social support, perceived benefits under times of stress, and ability to manage stress. Responses are provided in a Likert like scale (from 0 to 4) where participants are asked to rank statements from “strongly disagree” to “strongly agree.” The measure provides a total score summary that indicates the degree to which the COVID-19 pandemic has negatively impacted the participant. Items that tap into resiliency are reverse scored. In addition to the summary score, based on psychometric analyses upon collection of the data, the scale is expected to yield 7 subscale scores: COVID-19 Specific Distress; Health Care Disruptions and Concerns; Disruption to Daily Activities and Social Interactions; Financial Hardship; Perceived Benefits; Functional Social Support; and Perceived Stress Management Skills. The assessment will also include the Functional Assessment of Cancer Therapy-7 (FACT-G7) which is a well-validated and commonly used measure of HRQoL in oncology. A total score provides an index of HRQoL.

The questionnaire consists of three sections: (A) Questions specific to the COVID-19 pandemic such as testing, serostatus, risk factors, loss of family or friends, risk factors, isolation; (b) Thoughts, experiences and emotions regarding the COVID-19 pandemic; and (c) health-related quality of life. Questions on race, ethnicity, household income, and employment will be confirmed to be asked to confirm some of the data variables that will be extracted. We expect that the average participant will take about 10 minutes to review the e-ICF and complete the questionnaire.

**Electronic Health Record (EHR) Data Variables:** As described below, we will extract the following variables for consented participants from the electronic data warehouse (EDW) which serves as a repository of the EHR:

Age, race, ethnicity, language preference, insurance status, household income, date of diagnosis, date of primary treatment, date of last treatment, treatment types, cancer site, cancer stage, active disease vs. remission status and comorbidities.

#### 4.1 Definition

A participant is considered to have completed the study if he or she has completed the questionnaire.

The end of the study is defined as completion of data analyses after the data pull.

## 5 STUDY POPULATION

### Recruitment Procedures:

A pre-screening process will be used to determine whether potential participants are eligible to participate. The pre-screening process will take place electronically by querying the Consent to Contact Registry (after undergoing their review process and obtaining approval) based on the inclusion parameters stated above: visit at Sylvester within the past 5 years, signed Consent to Contact form, ICD-10 cancer diagnosis, English, Spanish or no language preference (in which case an option to English or Spanish links will be available), email address on record.

Eligible participants will be identified by accessing data in the University of Miami Miller School of Medicine (UM/MSOM) Electronic Data Warehouse (EDW) via the Consent to Contact Registry. The EDW serves as a repository of all UM/MSOM electronic health records and contains information pertinent to the proposed inclusion and exclusion criteria. We will identify patients who had a least one visit at the UM/MOSM Sylvester Comprehensive Cancer Center (Sylvester) within the past 5 years and have signed a "Consent to Contact" form. For participants that meet these two criteria (i.e., visit during the past 5 years and signed consent to contact), we will then ascertain a cancer diagnosis within that period via a recorded ICD-10 code. Any patient from this sample with an ICD-10 confirmed cancer diagnosis will then move to the next stage of recruitment which will involve determining whether the patient has (a) an email address on record with permission to contact via email; and (b) a stated language preference of English or Spanish, or no preference (in which case we will assume the patient is likely to be an English or Spanish speaker). Upon identification of a potential pool of participants based on these parameters, we will use the RedCap platform to push an email invitation describing the nature of the study, why they are being invited to participate and procedures should they agree to participate.

Those who agree to participate in the study will open the survey link from the study invitation where they can review and electronically sign the electronic informed consent form (e-ICF) through RedCap. The e-ICF describes the purpose of the study, potential benefits, potential risks, compensation or lack thereof, and access to clinical and demographic data in the patients' electronic health record (EHR) repository in the EDW.

If the patient has provided their consent and filled out the questionnaire then they will be assigned a unique identifier. The unique identifier will be linked to their medical record number (which is restricted view) and then as described above we will extract the following variables for consented participants from the electronic data warehouse (EDW) which serves as a repository of the EHR:

Age, race, ethnicity, language preference, insurance status, household income, date of diagnosis, date of primary treatment, date of last treatment, treatment types, cancer site, cancer stage, active disease vs. remission status and comorbidities.

Depending on the number of eligible participants, invitations will be staggered in a manner that is aligned with resources of our research lab to process data collected and address any study related matters. Survey responses will be tracked for completion. If a patient does not respond to the initial survey request no more than two additional subsequent reminders will be sent via RedCap to patient email. Patients will be given the option to opt-out of any subsequent emails as part of the e-consent process.

**Accrual Goals:** We estimate about 5,000 patients meeting eligibility criteria (e.g. consent to contact, ICD-10 cancer code, email address, active SCCC patients within the last 5 years, English or Spanish language preference). Of those 5,000 patients we estimate about 3,000 patients will consent to participate and fill out the measures.

**Study Timeline:** Study activities are estimated to be completed within one year. This is a onetime questionnaire request pushed via email to all eligible SCCC cancer patients and survivors. If a patient does not respond to the initial request then three subsequent attempts will be made unless the patient has opted not to receive such requests. The clinical data pull for consented patients will occur after questionnaire completion. Preliminary analysis will then be conducted and reported in aggregate form.

## 5.0 Inclusion Criteria

1. SCCC active patient (visit within past 5 years).
2. ICD-10 confirmed cancer diagnosis.
3. Consented to be contacted for research.
4. Has an active email address.
5. English or Spanish speaker.
6. Age 18 or older at time of cancer diagnosis.

## 5.1 Exclusion Criteria

1. Non-active patient (i.e., no visit within past 5 years).
2. Language other than English or Spanish.
3. No email address on record.
4. No consent to contact on record.

## 6 STUDY PROCEDURES

### 6.0 Duration of Intervention/Study Procedures

This is a one-time questionnaire administration.

## 7 INTERVENTION/EXPERIMENTAL MANIPULATION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

### 7.0 Participant Discontinuation/Withdrawal from the Study

Participants are free to withdraw from participation in the study at any time upon request.

An investigator may discontinue a participant from the study for the following reasons:

- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation

## 8 SCHEDULE OF ASSESSMENTS

### 8.1 Screening

The Consent to Contact Registry list will serve as the first screening for eligibility. At Screening, the following procedures/tests will be performed:

- Eligibility (Inclusion/Exclusion criteria)

### 8.2 On Study Evaluations

After consent by the participant the following assessments will occur once:

- COVID-19 HRQoL measures
- Electronic data pull containing clinical characteristics

### 8.3 STUDY CALENDAR

Study Procedures	Screening <sup>a</sup>	On Study
Inclusion/Exclusion Criteria	XX	
Informed consent	XX	
COVID-19 measures		XX
Clinical Characteristics Data Pull		XX

## 9 UNANTICIPATED PROBLEMS

### 9.1 Definition of Unanticipated Problems

The Office for Human Research Protections (OHRP) considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

### 9.2 Unanticipated Problem Reporting

The investigator will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB) as per institutional guidelines.

### 9.3 Reporting Unanticipated Problems to Participants

Not Applicable

## 10 DATA REPORTING

### 10.1 Data submission

Only investigators and assigned research staff will have access to study data. The electronic case report forms will be available to the sponsor, IRB or regulatory authorities in event of an audit.

## 11 STATISTICAL METHODS

### 11.1 Statistical Hypothesis

**Our Study Hypotheses are as follows:**

**Hypothesis 1:** After adjusting for relevant clinical (e.g., cancer type, stage, treatment) and sociodemographic (e.g., age, race, ethnicity) factors, more adverse COVID-19 experiences will be significantly associated with poorer HRQoL.

**Hypothesis 2:** After adjusting for relevant factors, greater adverse COVID-19 experiences will be significantly associated with greater COVID-19 specific psychological distress and health, financial and social disruptions.

**Hypothesis 3:** After adjusting for relevant factors, (a) greater COVID-19 specific psychological distress and health, financial and social disruptions will be significantly associated with poorer HRQoL and (b) mediate the association between COVID-19 adverse experiences and HRQoL.

**Hypothesis 4:** Among participants with greater social support, greater perceived benefit, and greater ability to manage stress, the association between adverse COVID-19 experiences will not be significantly associated with COVID-19 specific psychological distress and HRQoL.

Whereas COVID-19 experiences will be significantly associated with greater COVID-19 specific distress and poorer HRQoL in participants with lower social support and perceived benefit.

## 11.2 Statistical Analyses

### General Approach

Data will be inspected and subjected to quality control procedures. Descriptive analysis will be computed for all variables to ensure values are within expected ranges and errors are eliminated. Non-normally distributed variables will be transformed by proper functions (e.g., natural log) or will be analyzed with non-parametric tests. We will first examine the reliability of assessment instruments. Estimates of internal consistency reliability (Cronbach's  $\alpha$ ) of all scales (e.g., COVID-19 pandemic reactions subscales) and composite scales (e.g., COVID-19 pandemic total score, HRQoL) will be computed for the whole sample and across various grouping variables (e.g., early stage vs. late stage disease; race, ethnicity). If a large discrepancy in reliability between groups is found, we will conduct item analysis (e.g., exploratory and confirmatory factor analysis) to identify and eliminate items causing the decreased reliability. To control for confounds related to our outcomes, we will conduct preliminary analysis to identify potential confounds. We will evaluate possible confounding variables (e.g., age, cancer site) to predict the outcomes and potential mediators in univariate regression analyses. Using significance  $\alpha$  level of .10, we will identify potentially significant confounding variables that will be used as control variables in our subsequent analyses.

### Analysis of the Primary and Secondary Endpoint(s)

Hypotheses 1-3 will be tested using path analysis. Path analysis is an extension of multiple regression and provides estimates of the magnitude and significance of the hypothesized casual connections among sets of variables, as well as the variance accounted for in the model. It is a special case of structural equation modeling (SEM) in which only single indicators are employed to evaluate associations of each variable in the model. Path coefficients, which are standardized regression coefficients (or beta weights), represent the magnitude of the association across variables. Error terms represent unexplained variance. Path analyses also provides an opportunity to test direct and indirect or mediation effects. Significance and goodness of fit of the model will be interpreted using several indices. A Comparative Fit Index (CFI) value of 0.90 or greater and a Root Mean Square Error of Approximation (RMSEA) of 0.08 or less will be used to establish model fit. If model fit is acceptable, the parameter estimates are then examined. The ratio of each parameter estimate to its standard error is distributed as a z statistic and is significant at the 0.05 level if its value exceeds 1.96 and at the 0.01 level if its value exceeds 2.56. If an unacceptable model fit is found, the model will be revised when the modifications are meaningful. Model modification involves adjusting a specified and estimated model by either freeing parameters that were fixed or fixing parameters that were free. The Lagrange multiplier and the Wald tests will be used to guide model modifications. In hypotheses 4, we will use multigroup analyses by levels of the moderator to identify differences in the magnitude of the associations based on the level of the moderator. In the event that the model poorly fits the data and modification techniques do not improve model fit, we will conduct traditional hierarchical regression analyses adjusting for relevant covariates to assess the association among proposed study variables.

## **12 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS**

### **12.1 Informed Consent Process**

#### **Consent/Assent and other Informational Documents Provided to Participants**

Consent forms describing in detail the study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting intervention/administering study intervention.

#### **Consent Procedures and Documentation**

Once a participant is deemed eligible based on review of data extracted from the Consent to Contact, RedCap will send an email invitation describing the study along with the electronic ICF (e-ICF). Participants will electronically sign the e-ICF via RedCap for participation in this study. A copy of consent will be provided to participants where they can email to themselves or print. Only after the e-ICF is signed, will the study questionnaire be available to the participant and the medical variables will be extracted. Should the participant have any questions regarding the consent form or the study, the study coordinator will be available to answer any questions. A contact number with hours of operation will be provided, as well as an email address for the study that will be managed by the study coordinator. The consent process will be thorough to ensure that any questions participants may have will be fully considered and answered. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

### **12.2 Study Discontinuation and Closure**

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, and the Institutional Review Board (IRB), and will provide the reason(s) for the termination or suspension.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met
- Determination of futility

### **12.3 Confidentiality and Privacy**

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, the safety and oversight monitor(s), and the sponsor(s) and funding agency. This confidentiality is extended to the data being collected as part of this study. Data that could be used to identify a specific study participant will be held in strict confidence within the research

team. No personally-identifiable information from the study will be released to any unauthorized third party without prior written approval as per institutional policies.

All research activities will be conducted in as private a setting as possible.

Individual's responses/statements will not include any information that identifies the individual, but the responses/statements will be coded and linked to their identity on a separate document or in a separate database.

All identifiable electronic data will be maintained on an encrypted device requiring a password for access. Passwords will not be shared and will be protected from access.

Multiple steps will be taken to guarantee confidentiality. All electronic surveys and forms will be entered and uploaded using Research Electronic Data Capture (REDCap). All REDCap data is securely hosted by the University of Miami's IT Department. Research IT administers project creation, user account management, and movement of projects from development to production. Authentication is performed via CaneID Authentication Service (CAS), the same institution-wide system used for a variety of applications. Other electronic data will be stored in password-protected files that only the PI and study staff will be able to access.

A unique identifier will be assigned when the response data is stored and a consent is signed. The identifier is triggered upon consent and the medical record number will be entered in order to obtain the limited clinical data. To ensure confidentiality of the data, REDCap tracks responses by attributing it to an email address. Access to the association between the individual who took the survey and the survey responses is restricted in the database and can only be accessed by authorized privileged users (system engineers, database admins). When the clinical data is linked to the response data it will be through the unique study code assigned to ensure privacy.

There are multiple levels of security once placed on the local network. All study personnel will be certified to conduct human subjects' research by the University of Miami Institutional Review Board. All data will be inspected for quality assurance prior to analysis. Prior to performing statistical analyses on quantitative data, the data will be checked, screened and verified. Data checking is critical to ensure the integrity of the database. Range checks will be routinely performed, and random items from the raw data will be checked against the entered data so that mistakes can be identified.

## 12.4 Data Storage

Data will be stored for future use and the data will be identifiable. A separate link from data to identifiers will be maintained but the link to the individuals' identity will be made available to those requesting data from the data bank and will be maintained separately from the data bank.

Data will be stored in a secured data server housed at the UM/MSOM SCCC. All study data will be captured by REDCap (<http://project-redcap.org/>), which provides secure data capture for clinical research studies. The University desktop requires secure login credentials accessible only to the research team and the hard drive on the desktop has secure encryption technology to prevent identification. The computer is located in the research office accessible only to the research team by entering the office with University ID.

REDCap servers are all virtual machines that are backed up daily. The backup data is stored to a disk storage appliance located offsite in a secure datacenter outside of the UM campus and then a copy of the backup is replicated to the datacenter in the UM medical campus. The backup team uses a secure user domain administration account that also has backup admin role with permission to backup and recover the machine. The backup team is the only group with access rights to this.

The REDCap servers are managed by the UHIT server admins, and (major) windows and internet explorer updates are applied on a monthly basis. All other (server and application specific) updates are managed by the Research IT team.

## 12.5 HIPAA Waiver

- I confirm that you will destroy or de-identify the information you collect at the earliest opportunity.
- I confirm that the information you collect will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study or for other research for which the use or disclosure of PHI is permissible.

## 12.6 Future Use of Stored Data

Data collected for this study will be analyzed and stored at the University of Miami on RedCap.

Data will be stored up to 10 years and only investigators on this application and future investigators who submit and obtain approval from the IRB.

The PI, Co-Is, and the UM IRB committee may provide release of the data in which case the protocol must meet the following:

- (a) Approval by the PI listed in this application;
- (b) A protocol approved by the UM IRB; and
- (c) A research focus that may provide knowledge to develop, enhance/or guide the psychosocial management of cancer patients and survivors during a pandemic, natural disaster or other chronic unforeseen naturalistic stressors.

## 12.7 Study Auditing and Monitoring

This study will be monitored (as applicable) and may be audited according to the University of Miami requirements. See also

<http://research.med.miami.edu/clinical-research/crors/monitoring>

Following the monitoring plan, the monitors will verify that the clinical trial is conducted and data are generated, documented (recorded), and reported in compliance with the protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), and applicable regulatory requirements.

## **Trial Monitoring, Auditing, and Inspecting**

The investigator will permit trial-related monitoring, quality audits, and inspections by, government regulatory authorities, of all trial-related documents (e.g., source documents, regulatory documents, data collection instruments, case report forms). The investigator will ensure the capability for inspections of applicable trial-related facilities. The investigator will ensure that the trial monitor or any other compliance or QA reviewer is given access to all trial-related documents and trial-related facilities.

### **12.8 Quality Assurance and Quality Control**

In addition to the Clinical Monitoring component of this protocol, Quality Assurance (QA) will be implemented to assess compliance with GCP and applicable regulatory requirements. Data or documentation audited shall be assessed for compliance to the protocol, accuracy in relation to source documents and compliance to applicable regulations.

### **12.9 Data Handling and Record Keeping**

#### **Data Collection and Management Responsibilities**

Data collection is the responsibility of the study staff at under the supervision of the principal investigator. The principal investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

Clinical data will be entered into RedCap. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate.

#### **Study Records Retention**

All records and documents relating to research studies and participants must be kept confidential to the extent permitted by law; however, records and documents shall be available in a timely manner to the University authorized employees or other agents authorized by the University including IRB members and HSRO staff and appropriate governmental agencies.

Although principal investigators are responsible for the creation and maintenance of research records and documents, such records and documents (including data collected pursuant to research) are the property of the University. Until the temporal requirements for record/document retention are met, investigators or others may not remove or destroy research records or documents (or copies of such records or documents) without written permission from the Vice Provost of Research. This permission requirement extends to investigators leaving the University even if they plan to continue the research at another institution.

### **12.10 Compliance with Protocol**

The investigator/institution should conduct the trial in compliance with the protocol agreed to by the regulatory authorities and which was given approval opinion by the IRB.

The investigator should not implement any deviation from, or changes of the protocol without a prior review and documented approval opinion from the IRB of an amendment, or when the changes involves only logistical or administrative aspects of the trial (e.g. change of telephone numbers).

The investigator, or designee, should document and explain any deviation from the approved protocol.

The investigator may implement a deviation from, or change of, the protocol to eliminate an immediate hazard to trial subjects without prior IRB approval opinion. As soon as possible, the implemented deviation or change, the reasons for it, and if appropriate, the proposed protocol amendments should be submitted:

- a. To the IRB for review and approval opinion;
- b. To the regulatory authorities

### **12.11 Publication and Data Sharing**

All information provided regarding the trial, as well as all information collected/documented during the course of the study will be regarded as confidential.

The financial disclosure information will be completed prior to trial participation from all PIs and Sub-Investigators who are involved in the trial.

Results will be published per agreements with institutional guidelines.

### **12.12 Conflict of Interest Policy**

The independence of this study from any actual or perceived influence is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The study leadership has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.