**ANCILLARY REVIEWS**

**DO NOT DELETE. Submit the completed checklist below with your protocol.**

| **Which ancillary reviews do I need and when do I need them?** Refer to HRP-309 for more information about these ancillary reviews. | | | |
|---|---|---|---|
| **Select yes or no** | **Does your study…** | *If yes…* | **Impact on IRB Review** |
| ☐ **Yes** <br> **X No** | Include Gillette resources, staff or locations | *Gillette Scientific review and Gillette Research Administration approval is required. Contact:* <br> *research@gillettechildrens.com* | **Required prior to IRB submission** |
| **X Yes** <br> ☐ **No** | Involve Epic, or Fairview patients, staff, locations, or resources? | *The Fairview ancillary review will be assigned to your study by IRB staff* <br> *Contact:* ancillaryreview@Fairview.org | **Approval must be received prior to IRB committee/ designated review.** <br><br> **Consider seeking approval prior to IRB submission.** |
| ☐ **Yes** <br> **X No** | Include evaluation of drugs, devices, biologics, tobacco, or dietary supplements or data subject to FDA inspection? | *STOP – Complete the Medical Template Protocol (HRP-590)* <br><br> *The regulatory ancillary review will be assigned to your study by IRB staff* <br> *Contact: medreq@umn.edu* <br> *See https://policy.umn.edu/research/indide* | |
| | Require Scientific Review? Not sure? See guidance in the Investigator Manual (HRP-103). | *ONLY REQUIRED BIOMEDICAL RESEARCH REVIEWED BY FULL COMMITTEE* | |
| **X Yes** <br> ☐ **No** | Relate to cancer patients, cancer treatments, cancer screening/prevention, or tobacco? | *Complete the CPRC application process.* <br> *Contact: ccprc@umn.edu* | |

| | | | |
|---|---|---|---|
| ☐ **Yes**<br>**X No** | Include the use of radiation?<br>(x-ray imaging, radiopharmaceuticals, external beam or brachytherapy) | *Complete the AURPC Human Use Application and follow instructions on the form for submission to the AURPC committee.*<br>*Contact: barmstro@umn.edu* | **Approval from these committees must be received prior to IRB approval;**<br><br>**These groups each have their own application process.** |
| ☐ **Yes**<br>**X No** | Use the Center for Magnetic Resonance Research (CMRR) or MR at Masonic Institute for the Developing Brain (MIDB) as a study location? | *Complete the CMRR pre-IRB ancillary review*<br>*Contact: ande2445@umn.edu* | |
| ☐ **Yes**<br>**X No** | Include the use of recombinant or synthetic nucleic acids, toxins, or infectious agents? | *STOP – Complete the Medical Template Protocol (HRP-590)* | |
| ☐ **Yes**<br>**X No** | Include the use of human fetal tissue, human embryos, or embryonic stem cells? | *STOP – Complete the Medical Template Protocol (HRP-590)* | |
| **X Yes**<br>☐ **No** | Include PHI or are you requesting a HIPAA waiver? | *If yes, HIPCO will conduct a review of this protocol.*<br>*Contact: privacy@umn.edu* | |
| ☐ **Yes**<br>**X No** | Plan to use CTSI Monitoring services, and/or have an IND, IDE, or designated NSR-IDE by the UMN IRB? | *The CTSI monitoring ancillary review will be assigned to your study by IRB staff.*<br>*Please note eligibility criteria here.*<br>*Contact: fencl003@umn.edu* | **Approval must be received prior to IRB approval.**<br><br>**These groups do not have a separate application process but additional information from the** |
| ☐ **Yes**<br>**X No** | Use data from CTSI Best Practices Integrated Informatics Core (BPIC)<br>Formerly the AHC Information Exchange (AHC-IE)? | *The Information Exchange ancillary review will be assigned to your study by IRB staff*<br>*Contact: bpic@umn.edu* | |
| ☐ **Yes**<br>**X No** | Use the Biorepository and Laboratory Services to collect tissue for research? | *STOP – Complete the Medical Template Protocol (HRP-590)*<br><br>*The BLS ancillary review will be assigned to your study by IRB staff.* | |

| | | | |
|---|---|---|---|
| | | *Contact: Jenny Pham* *Pham0435@umn.edu* | **study team may be required.** |
| **X Yes** **☐ No** | Have a PI or study team member with a conflict of interest? | *The CoI ancillary review will be assigned to your study by IRB staff* *Contact: becca002@umn.edu* | |
| **X Yes** **☐ No** | Need to be registered on clinicaltrials.gov? | *If you select "No" in ETHOS, the clinicaltrials.gov ancillary review will be assigned to your study by IRB staff* *Contact:* fencl003@umn.edu | |
| **X Yes** **☐ No** | Require registration in OnCore? | *If you select "No" or "I Don't Know" in ETHOS, the OnCore ancillary review will be assigned to your study by IRB staff* *Contact: oncore@umn.edu* | **Does not affect IRB approval.** |

**PROTOCOL COVER PAGE**

| | |
|---|---|
| **Protocol Title** | Time toxicity of cancer: the time demands of cancer-related activities and their impact on well-being and quality of life |
| **Principal Investigator/Faculty Advisor** | Name: Rachel I. Vogel, PhD |
| | Department: Obstetrics, Gynecology, and Women's Health |
| | Telephone Number: 612-624-6928 |
| | Email Address: isak0023@umn.edu |
| **Student Investigator** | Name: |
| | Current Academic Status (Student, Fellow, Resident): |
| | Department: |
| | Telephone Number: |
| | Institutional Email Address: |
| **Scientific Assessment** | Nationally-based, federal funding organizations |
| **Version Number/Date:** | 4.0, 02/27/2024 |

**REVISION HISTORY**

| Revision # | Version Date | Summary of Changes | Consent Change? |
|---|---|---|---|
| 1 | 05/05/2023 | Named mobile app for use in the protocol as Daynamica and provide details for data security | No |
| 2 | 09/14/2023 | Added option to interact with participants via email regarding data collection, clarify consent procedure options (both electronic and paper, in-person or remote) | Yes |
| 3 | 02/27/2024 | Increase total number to be consented to account for drop out before mobile app data collection (replace individuals who consent but do not download/utilize the mobile app) | No |
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**ABBREVIATIONS/DEFINITIONS**

| | |
|---|---|
| AUC | Area under the curve |
| EHR | Electronic Health Record |
| CAB | Community Advisory Board |
| MARS | Mobility App Rating Scale |
| PETS | Patient Experience with Treatment and Self-Management |
| POI | Point of interest |
| QOL | Quality of Life |
| TBQ | Treatment Burden Questionnaire |

## 1.0 Objectives

1.0 Purpose: Our overall objectives are to 1) measure, describe, and quantify sources of cancer-related time toxicity among individuals treated for cancer, and their effect on QOL; and 2) create time toxicity scores which can be used in future studies to identify opportunities to minimize time toxicity. Our specific aims are:

Aim 1: Measure and describe components of objective time use associated with cancer-related healthcare interactions via a mobile health application.

Aim 2: Characterize associations between measures of cancer-related time use and self-reported well-being, and explore the role of context in modifying these associations.

Aim 3: Create a time toxicity summary score based on measures of cancer-related time use and assess its association with psychosocial outcomes.

## 2.0 Background

2.1 Significance of Research Question/Purpose: Cancer-related demands on patients' time and stress have multiple sources: time spent on care itself (appointments, taking medication), travel and wait times, and other activities such as scheduling, paperwork, dealing with bills and insurance, and organizing one's schedule in order to accommodate time for these activities. *The time spent on these activities competes with time patients would otherwise dedicate to loved ones, work, childcare, preventive care, caregiving, household activities, or leisure time***.** Leisure time serves as a buffer to cope with negative life events through distraction, adaptation, self-restoration, and stress compensation, enabling better coping with cancer.[1, 2] The burdens of care can only be fully understood in the context of and in interaction with other time and labor demands. *Accurately defining and measuring time toxicity as both the direct and indirect time burdens of cancer and related treatments is a necessary first step for identifying effective interventions to address them*.

Whether cancer-related tasks and time use become a toxic burden depends on unique patient situations. Disadvantaged patient populations and those with multiple other responsibilities are likely to be most affected, and some of these populations bear a disproportionate cancer burden.[3, 4] For example, low-income patients and some ethno-racial minority groups experience more pain and symptom burden, more financial distress, lower survival rates, and poorer QOL.[5-7] Other vulnerable groups include: women who, despite shifts in traditional family roles, often still carry significant household and family responsibilities in addition to contributing to family incomes; populations with limited geographic access to cancer care [8] such as rural populations with long travel distances to clinics; and those with

reduced transportation access who need to rely on public transit and other means of travel.[9, 10]

2.2 Preliminary Data: The concept of time toxicity in cancer care expands the concept of treatment burden in chronic disease management. Theories such as the Burden of Treatment Theory [11] and Cumulative Complexity Model [12] have highlighted the complexity of treatment burden. Instruments such as the Treatment Burden Questionnaire (TBQ) [13] and the Patient Experience with Treatment and Self-management survey (PETS) [14] collect recall-based data on various aspects of treatment burden including patient workload and its impact on patient well-being. Our proposal will add to the field by creating measures that capture time spent on specific cancer-related tasks (e.g. time in clinics, traveling time), and by exploring how sources of treatment burden interact with specific individual (clinical, demographic, life stage) situations that may or may not make the same cancer-related task burdensome.

In work by our group, we have estimated cancer-related time uses among patients with metastatic breast cancer during initial treatment [15] and among patients with cancer receiving chemotherapy [16]. We have also examined self-reported cancer-related workload among patients with breast cancer and found those with stage III and IV cancer reported disproportionate cancer-related time and workload burdens and found these burdens were associated with worse psychosocial outcomes and lower QOL (*in preparation*). In a study of adolescents and young adults with cancer, we found that those with the most intensive cancer treatments more often believed that cancer would negatively impact their plans for work and/or school.[17] In that study, we also found that only a fraction of patients' time is spent interacting with healthcare providers, with substantial time spent traveling to and waiting for care services. The work proposed here will help identify areas to improve time efficiency of care.[15, 16] One of our conclusions was that total time spent on care should not only be reduced, but also distributed more efficiently to allow for more health-care free days.[18] For example, splitting 10 hours of cancer care over two instead of five days gives patients three days that are uninterrupted by care.

We will build on our prior work and comprehensively measure cancer-related time burdens. For this, we will use a customized version of the Daynamica mobile application, created by Co-PI Wolfson and Co-I Fan, which is an established, easy-to-use sensor-based tool to collect data automatically on daily activities and time use requiring minimal user input. More details on the app are provided below. Between 2016 and 2020, the Daynamica app has been deployed in multiple research studies [19-23], collecting information from over 2,000 individuals with >20,000 days of time use and well-being data.

2.3 Existing Literature: The relevant literature is cited in sections 2.1 and 2.2 above. There is an urgent need for a tool that generates accurate, comprehensive, and timely measures of logistic toxicity.

## 3.0 Study Endpoints/Events/Outcomes

3.1 Primary Endpoint/Event/Outcome:

Aim 1: Summary measures of time use by activity and trip type; for each activity/trip type, the number of minutes per day spent on that activity, the number of separate episodes, and the number of days per week on which that activity occurs
Aim 2: Daily well-being, as measured by the American Time Use Survey
Aim 3: Time toxicity score

3.2 Secondary Endpoint(s)/Event(s)/Outcome(s): overall quality of life, emotional health, symptoms, financial toxicity

## 4.0 Study Intervention(s)/Interaction(s)

4.0 Description: A total of 80 individuals receiving treatment for metastatic breast or advanced stage ovarian cancer will be asked to 1) complete a baseline survey and install the Daynamica mobile app on their smartphone; 2) carry the smartphone for 28 consecutive days while outside the home; 3) keep smartphone location and motion services active; 4) confirm and correct (if needed) smartphone-detected activities and trips; 5) use the app interface to provide additional information on activities and trips related to cancer treatment tasks; 6) complete daily surveys regarding well-being; and 7) at the end of the 28 day period, complete an online survey. Individuals who do not install and use the Daynamica mobile app after completing the consent process and baseline survey will be replaced and not count toward the goal sample size of 80 participants.

## 5.0 Procedures Involved

5.1 Study Design: Observational cohort study

5.2 Study Procedures: All participant interactions fall under Aim 1. Aims 2 and 3 involve analysis of data collected under Aim 1.

A total of up to 100 individuals currently undergoing treatment for metastatic breast or advanced stage ovarian cancer (frontline, maintenance or for recurrence) will be invited to participate in the study. Participation in the study will not affect clinical treatment decisions. Enrolled participants will be asked to:

1) Complete a baseline survey (paper or online per personal preference).
2) Install the Daynamica app from the Google Play or Apple App Store on their smartphone (we will provide a smartphone with the app pre-installed to participants who do not own one).

3) Carry the smartphone for 28 consecutive days while outside the home.
4) Keep smartphone location and motion services active.
5) Confirm and correct (if needed) smartphone-detected activities and trips.
6) Use the Daynamica app interface to provide additional information on activities and trips related to cancer treatment tasks and complete daily well-being surveys
7) Complete a follow-up survey at 28 days (paper or online per personal preference).

Data collection will include a combination of daily activity data (objective and self-report) and well-being data (self-report) obtained through the mobile app for 28 days, along with baseline and follow-up surveys following completion of the daily data collection (**Table 1**). Details on each measure are provided below.

**Table 1. Patient-Report Data Collection Timing and Measures**

| **Timing** | **Day 0** | **--- Daily Mobile App---** | | **Day 28** |
|---|---|---|---|---|
| **Data Tool** | **Survey** | **Sensor data** | **Survey** | **Survey** |
| *Time Use Measures* | | | | |
| Daily time and cancer-related activity type | | X | X | |
| Opportunity time costs | X | | X | X |
| Typical (non-cancer) time demands | X | | | X |
| *Outcome and Covariate Measures* | | | | |
| Daily well-being, burden | | | X | |
| Quality of Life | X | | | X |
| Demographics | X | | | X |

Mobile application data. Once installed on a participant's phone, the Daynamica app will capture location information and automatically infers time, type, and location of activities and trips, providing a "calendar view" of each day (see **Figure 1**). Participants can edit and provide additional details about each activity or trip, allowing them to break them into smaller episodes (e.g., time traveling to/from, waiting for, and receiving treatment) and provide self-reported information on subjective well-being. The datasets produced by the app are summarized at the episode level, with detailed data including type, start time, end time, location (or route for trips), and any additional information solicited from participants.

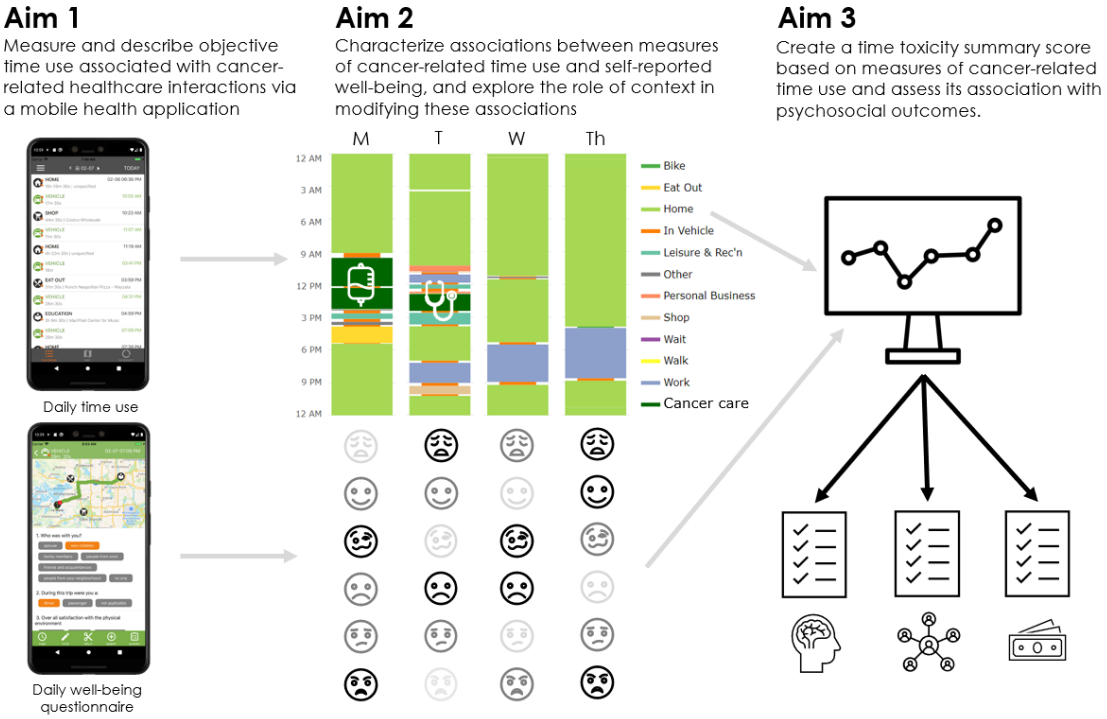


**Figure 1. Smartphone app measurements and aims.**

For this study, participants will install an app on their personal smartphones for a 28-day period. The app, currently designed to capture common activities, e.g. home, work, shopping, education, eating out, leisure/recreation, car, bike, bus, will be modified to allow users to indicate and annotate cancer care-related activities. When a cancer care-related activity is reported, participants will be prompted to provide additional information on three items: wait time, time with the provider, and time spent receiving treatment or imaging. If participants repeatedly visit the same care location, these episodes will be automatically recognized such that participants need only provide the additional information. At the end of each day, participants will be asked to complete a short (<5 minute) 8-item survey, including questions regarding any phone calls or other activities that day related to cancer that were not otherwise reported, and time spent on those activities. The survey will also include questions on well-being based on the American Time Use Survey: two positive emotion questions (happy and meaningful) and four negative emotion questions (sad, painful, stressful, and tired). These questions will generate episode-level well-being measures, and will be used to generate outcome variables of daily emotional well-being: (1) U-Index at the person-day level: the proportion of time an individual spends in an unpleasant state during the 24-hour period, with an unpleasant state defined as the individual having a negative emotion more intense than any positive emotions; (2) Duration-weighted sum of average happiness,

meaningfulness, sadness, pain, stress, and tiredness scores during a 24-hour period at the person-day level.

Survey data. Additional patient-reported outcomes will be collected at baseline and 28 days (following completion of mobile app data). Measures will be collected on paper or via online surveys in REDCap per participant preference. Study outcomes include reliable and validated measures used previously by the study team and will be scored following standard procedures.

*Demographics:* Demographic characteristics collected will include age, sex, race/ethnicity, household income, education, insurance status, relationship status, parenting and caregiver status, employment status, and zip code to assess rurality and distance from clinic.

*General Quality of Life:* QOL is a multi-dimensional concept including domains of physical, psychological, social health, and overall life satisfaction.[27] We will measure QOL using the Functional Assessment of Cancer Therapy - General (FACT-G) questionnaire (39 items).[31]

*Depression and Anxiety:* Symptoms of anxiety and depression will be measured using the Hospital Anxiety-Depression Scale (HADS). This measure consists of 14 items rated on a 4-point scale and provides separate scores for anxiety and depression, including cut-offs for potentially clinically relevant anxiety and depression.

*Distress:* We will measure cancer-related distress using the National Comprehensive Cancer Network Distress Thermometer, a single-item tool measuring distress on a scale from 0-10 with an accompanying problem list of potential contributing issues, including practical, physical, family, emotional, and spiritual concerns.[33, 34]

*Symptom Management:* Breast and ovarian cancers and their treatments can result in significant side effects and symptom burden for patients and these symptoms can increase healthcare utilization while decreasing QOL. The MD Anderson Symptom Inventory (MDASI) is a multi-symptom patient-reported measure of 13 core symptoms that are common and often severe, with impacts on functioning, in patients with cancer.[35]

*Opportunity Costs:* The Oncology Opportunity Cost Assessment Tool (OOCAT) evaluates opportunity costs - including time spent seeking care, lost wages, lost leisure time, and other indirect costs associated with seeking cancer care.[36] The 18–item instrument includes six domains: travel, appointments, work and school, home, health system, and caregiver burden.

*Work, Insurance and Financials:* We will measure financial toxicity using the Comprehensive Score for Financial Toxicity (COST) instrument, an 11-item questionnaire validated in individuals with cancer.[37] We will also measure current employment status, days missed due to illness, and health insurance coverage using

validated measures derived from the American Cancer Society Study of Cancer Survivors II [38] and National Health Interview [39] surveys.

*Patient-reported time burden*: We will ask respondents to add free-text comments, for example to describe circumstances in their life that may have amplified or reduced the cancer-related time burdens.

Medical record data. Participant medical data, including diagnosis, treatments received and dosage, adverse events, comorbidities and healthcare encounters, will be abstracted from the medical records at each site and entered into REDCap.

5.3 Follow-Up: Survey data will be collected before the study and immediately after participants finish using the app for 28 days.

Individually Identifiable Health Information: We will obtain written HIPAA agreement from participants. Daynamica uses GPS location data to infer activity type and trip mode; such detailed location data constitute Protected Health Information (PHI).

## 6.0 Storing Data for Future Use

6.1 Storage and Access:

Daynamica user data on the device is saved only on internal smartphone storage, which is encrypted, inaccessible to other applications on the device and is deleted when the Daynamica app is uninstalled. Study participants are instructed to use a passcode to secure their device while engaged in data collection. In the case of unauthorized device access, the location data visible in the Daynamica app is the same as would be readily available by viewing an individual's Google or Apple Maps location history. When notified that a device has been lost or stolen, the Daynamica team will terminate data collection, which prevents device users from viewing participant location data from within the app.

The Daynamica app transfers data to a server for additional processing and secure storage. For this project, the upload and processing server will be operated entirely by UMN Health Sciences Technology (HST). Daynamica will coordinate with HST to install necessary software on secure, HIPAA-compliant HST servers. Prior to the start of data collection, Daynamica will be provided with access to an HST server to install the software needed to receive uploads from the Daynamica smartphone app. Once data collection begins, Daynamica staff will no longer have access to HST servers. The HST server will be configured to receive uploads and transfer the PHI location data to a separate server that does not accept external connections. Non-PHI data will be made available via a secure API so that study managers can access information about data completeness. The setup of the UMN HST server will be

similar to that used for previous projects, specifically DashPAD (UMN IRB Study #00006570), in collaboration with Chris Dinger and HST.

The details of the data processing and storage plan are:

- All data collected by the Daynamica app will be linked to a randomly-generated, non-identifiable participant ID code. Only the principal investigator(s) and approved study managers will have access to the data file linking participant ID codes to participant contact information (e.g., phone number, email address), and this data file will be stored in a separate secured location (e.g., UMN Box).
- The identifiable (i.e., PHI) data collected by Daynamica consists of detailed location information in the form of the GPS coordinates of daily trips and activities. These data are stored in a separate table in the encrypted internal app database and are linked to (non-identifiable) time and type information about daily trips and activities via a numeric "calendar item" code. Only the principal investigator(s) will have permission to download the PHI data and link it to other participant information via the calendar item codes.
- Upon request, HST staff will be provided with access to relevant documentation and source code of both the Daynamica app and the server software to verify that the uploads are happening as described in this plan for the purpose of security review. Daynamica source code is proprietary, and hence access to source code by HST staff, if needed, will be subject to a Non-Disclosure Agreement between Daynamica, Inc. and the University of Minnesota.
- Study investigators and managers will access a dashboard to assist in study management. This dashboard will be based entirely on non-PHI data provided via a secure API managed by HST; the dashboard will not have any access to the PHI location data stored on HST servers.

De-identified data collected as part of the project will be available for sharing in raw or aggregate form. A long-term data sharing and preservation plan will be used to store and make publicly accessible the data beyond the life of the project. The data will be deposited into the Data Repository for the University of Minnesota (DRUM). This University Libraries' hosted institutional data repository is an open access platform for dissemination and archiving of university research data. Date files in DRUM are written to an Isilon storage system with two copies, one local to each of the two geographically separated University of Minnesota Data Centers. The local Isilon cluster stores the data in a way that the data can survive the loss of any two disks or any one node of the cluster. Within two hours of the initial write, data replication to the 2nd Isilon cluster commences. The 2nd cluster employs the same protections as the local cluster, and both verify with a checksum procedure that data has not altered on write. In addition, DRUM provides long-term preservation of digital data

files for at least 10 years using services such as migration (limited format types), secure backup, bit-level checksums, and maintains a persistent DOIs for data sets, facilitating data citations. In accordance to DRUM policies, the de-identified data will be accompanied by the appropriate documentation, metadata, and code to facilitate reuse and provide the potential for interoperability with similar data sets. The DRUM has data access policies and procedures consistent with NIH data sharing policies.

All identifiable data, including app data and data entered in REDCap along with paper documents, will be destroyed within 10 years of study completion.

6.2 Data: Survey data (baseline, day 28) and mobile application activity and well-being summary data will be stored and available for future use.

6.3 Release/Sharing: Survey data will be available as a .csv file that can be exported into MS Excel, SAS, SPSS, or ASCII files.

The final data file to be shared will include (a) raw item-level data (where applicable to recreate analyses; will not include location data) with appropriate variable and value labels and (b) computed variables created during analysis. These data will be the de-identified and individual- or aggregate-level data used for the final and published analyses.

Dataset documentation will consist of electronic codebooks documenting the following information: (a) a description of the research questions, methodology, and sample, (b) a description of each specific data source, and (c) a description of the raw data and derived variables, including variable lists and definitions (project codebook). To aid in final dataset documentation, throughout the project, we will maintain a log of when, where, and how data were collected, decisions related to methods, coding, and analysis, statistical analyses, software and instruments used, where data and corresponding documentation are stored, and future research ideas and plans.

The Principal Investigators will be the data stewards while the data are “active” (i.e., during data collection, coding, analysis, and publication phases of the project), and will be responsible for documenting and managing the data throughout this time. Additional project personnel (project coordinators and graduate research assistants) will also be responsible for adhering to the data management plan.

The PIs will develop study-specific protocols and will train all project staff who handle data to follow these protocols. Protocols will include guidelines for managing confidentiality of data, as well as protocols for naming, organizing, and sharing files and entering and downloading data.

At the end of the project, the data will be archived and shared and the University of Minnesota Libraries will serve as the steward of the de-identified, archived dataset

from that point forward. These de-identified data will be available to all interested parties. No specific data sharing agreement will be needed for DRUM; however, DRUM does have a general end-user access policy available online.

## 7.0 Sharing of Results with Participants

7.1 Participants will be able to view their own data on the mobile app, however, we will not otherwise share results with participants.

## 8.0 Study Duration

8.1 The duration an individual participant will be involved in the study is approximately 30 days. We plan to enroll all participants within 24 months and anticipate all study procedures and data analysis will be completed within 60 months.

## 9.0 Study Population

9.1 Inclusion Criteria:

- 18 years of age or older
- Diagnosed with advanced stage (III, IV) ovarian (ovarian, fallopian tube or prmary peritoneal) or metastatic breast cancer [do not need to be newly diagnosed]
- Currently receiving any type of therapy for their cancer [can be front-line, maintenance therapy, or treatment for recurrence]
- Able to complete study tasks in English
- Able to provide voluntary informed consent
- Own an Android or iOS smartphone on which the operating system is version 9.0 or higher for Android or 10.0 higher for iOS; or willing to use a researcher-provided smartphone

9.2 Exclusion Criteria:

- Those who are currently incarcerated
- Have opted out of research contact

9.3 Screening: Potentially eligible participants will be identified by a study coordinator. Those identified as potentially eligible will be called ahead of an upcoming clinical appointment or approached at the time of a scheduled visit by the clinic's research coordinator or study staff.

## 10.0 Vulnerable Populations

10.1 Vulnerable Populations:

| Population / Group | Identify whether any of the following populations will be primary focus of the research (targeted), included but not the focus of the research or excluded from participation in the study. |
|---|---|
| Children | Excluded |
| Pregnant women/fetuses/neonates | included but not the focus |
| Prisoners | Excluded |
| Adults lacking capacity to consent and/or adults with diminished capacity to consent, including, but not limited to, those with acute medical conditions, psychiatric disorders, neurologic disorders, developmental disorders, and behavioral disorders | Excluded |
| Non-English speakers | Excluded |
| Those unable to read (illiterate) | Excluded |
| Employees of the researcher | Excluded |
| Students of the researcher | Excluded |
| Undervalued or disenfranchised social group | included but not the focus |
| Active members of the military (service members), DoD personnel (including civilian employees) | included but not the focus |

| | |
|---|---|
| Individual or group that is approached for participation in research during a stressful situation such as emergency room setting, childbirth (labor), etc. | Excluded |
| Individual or group that is disadvantaged in the distribution of social goods and services such as income, housing, or healthcare. | included but not the focus |
| Individual or group with a serious health condition for which there are no satisfactory standard treatments. | included but not the focus |
| Individual or group with a fear of negative consequences for not participating in the research (e.g. institutionalization, deportation, disclosure of stigmatizing behavior). | included but not the focus |
| Any other circumstance/dynamic that could increase vulnerability to coercion or exploitation that might influence consent to research or decision to continue in research. | Excluded |

10.2 Additional Safeguards:

All participants will have a cancer diagnosis, which is a serious health condition. This study specifically aims to understand the time burdens of cancer care. Our study carries minimal risk for participants.

The proposed research will not specifically seek military members or DOD personnel, disadvantaged individuals or members of undervalued or disenfranchised social groups, however, if volunteers meets the inclusion criteria and also happen to be from one of the groups checked above, they will be eligible to participate in the study.

## 11.0 Number of Participants

11.1 Number of Participants to be Consented: Up to 100

## 12.0 Recruitment Methods

12.1 Recruitment Process:

Recruitment and initial patient contact will be made by the patient's healthcare team and/or clinic study coordinator. Potentially eligible patients will be approached at or near the time of any scheduled visit by the clinic's research coordinator or study staff.

The study coordinator will review medical records and upcoming provider and chemotherapy schedules for individuals who may be eligible for this study. They may contact the provider prior to the visit to confirm their eligibility if questions arise.

Individuals may be recruited in the following ways depending on visit type:

Standard of Care visit with oncologist/provider:

*Video visits*: For appointments that are conducted via virtual video, the provider will briefly describe the study at the end of the virtual visit and ask if the participant is interested in learning more about the study and how to participate. If they are interested and have time to meet with the study coordinator at that time, the study coordinator will then join the in-progress virtual visit to describe the study. If the participant is interested in participating, the study coordinator will provide them with the consent materials via mail or a link to the electronic consent in REDCap via email.

*Phone visits*: The provider will describe the study and if interested, give the patient contact information for the study coordinator. The patient will be instructed to contact the study coordinator for more information and to proceed with the consent process.

*In clinic*: The provider may introduce the study and the study coordinator will describe the study in detail. The coordinator can conduct in-person consent or provide information for the patient to complete the consent online in REDCap at a later time.

Chemotherapy administration or other in-person healthcare visit:

The study coordinator will describe the study. If the patient is interested in participating, the study coordinator will conduct in-person consent.

Eligible and interested patients will be asked to complete the consent form and HIPAA forms. Registration will occur after the subject consent is signed and eligibility is confirmed, but before any study data are collected.

Upon completion of the screening evaluation, eligibility confirmation and obtaining consent, the study staff will enroll the subject into REDCap.

12.2 Source of Participants: Patients receiving care at a participating clinic site.

12.3 Identification of Potential Participants: Potentially eligible participants will be identified by a clinic study coordinator by reviewing the clinic schedule and medical records. The study coordinators will confirm that the patient has not declined research (we will not approach patients with "Research Opt-out" status indicated their medical record, in order to comply with Minnesota Statute 144.651, subdivision 13).

12.4 Recruitment Materials: A study summary sheet is included.

12.5 Payment: Participants will receive $25 for completing the baseline survey and mobile app installation. Participants will receive an additional $125 for completing the 28-day mobile application data collection, and $25 following completion of the final survey for a total of up to $175.

## 13.0 Withdrawal of Participants

13.1 Withdrawal Circumstances: No participant will be withdrawn from the study against their will. Participants will only be withdrawn from the study if they ask to withdraw, become too ill or die prior to completing the study. If participants become too ill, they will not be withdrawn from the study until they have given their voluntary consent for study withdrawal.

13.2 Withdrawal Procedures: If a participant chooses to withdraw at any point, their decisions will be respected without repercussions. Data collected until the point of withdrawal will be used unless the participant specifies otherwise.

13.3 Termination Procedures: Participants will not be terminated from the study for any reason.

## 14.0 Risks to Participants

14.1 Foreseeable Risks: This study has few risks. We identified the following 2 possible risks to subjects:

Risk to confidentiality: Inadvertent breaches of confidentiality by investigators or their staff are unlikely but may occur. Identifying information will be kept private and all identifiers will be removed prior to any data being given to researchers. The records will be identified only with a unique ID number on an encrypted database. Data transfer will only occur with de-identified data with encrypted transfer of all information containing protected health information between participants and study databases.

The Daynamica app records information about daily activities, including relevant locations such as home and work. These data are potentially highly sensitive, and hence there is a non-trivial risk of loss of confidentiality and privacy if the data are accessed inappropriately. We have put multiple safeguards in place to ensure data security, including strict guidelines about which study team members have access to

which data, and how the data are to be used. In addition, the Daynamica app empowers users by providing an interface to review and edit all data collected (e.g., change start/end times, modify activity types and trip modes, etc.). Further, users are always free to turn off the app during time periods where they would prefer not to be tracked.

Discomfort while interacting with the app or answering survey questions: There is a possibility that some participants may feel uncomfortable interacting with the app or when answering survey questions which may remind them of their cancer diagnosis. They will be reminded that they can skip any questions or discontinue at any time.

The data from these studies will not be used to direct patient care. Therefore, participation in this study will have no influence on the care the patient receives nor will it influence treatment decisions.

*Adverse event reporting:* This study carries minimal risk and will comply with the University of Minnesota IRB reporting requirements. Events requiring prompt reporting include any adverse event that requires a change to the protocol or consent form, any unauthorized disclosure of confidential information, any unresolved subject complaint or any protocol deviation that resulting in harm or the unanticipated death of an enrolled subject. Deaths are not considered an adverse event for this protocol as this is not a treatment study, however, participants may die as a result of unexpected progression of the disease before completing research activities.

Refer to http://www.research.umn.edu/irb/guidance/ae.html#.VC7xraI0-sh for additional guidance.

Any event requiring prompt reporting to the IRB must also be reported to the Masonic Cancer Center's SAE Coordinator (email - mcc-saes@umn.edu).

14.2 Reproduction Risks: N/A

14.3 Risks to Others: N/A

## 15.0 Incomplete Disclosure or Deception

15.1 Incomplete Disclosure or Deception: N/A

## 16.0 Potential Benefits to Participants

16.1 Potential Benefits: We expect no immediate benefits for study participants. Some participants may appreciate contributing to a study that might benefit others diagnosed with cancer in the future.

## 17.0 Statistical Considerations

17.1 Data Analysis Plan:

Aim 1: For the time use component, we will focus on characterizing the distributions of summary measures of time use by activity and trip type. Similar to our previous work,[19] we will compute, for each activity/trip type, the number of minutes per day spent on that activity, the number of separate episodes, and the number of days per week on which that activity occurs. For common activities and trip types (home, work, driving), means and variances of these measures generally provide useful summaries of how individuals engage in these activities. For less common activities such as cancer care-related activities, total number of episodes, total time spent, and the mean/variance of episode duration may be more meaningful summary measures.

Aim 2: *Qualitative analysis component*. Some individual circumstances (for example, competing time demands, level of support, flexibility of employers) that either buffer against or aggravate the burden cannot be easily ascertained from our app- and survey-based measurements. Therefore, we will examine free-text responses to open-ended survey questions. All entries will be transcribed. We will examine themes and consistencies. Two coders will read the entries and apply the constant comparative method to analyze and code data. As themes are identified, coders will return to the transcripts to reread and recode excerpts, thus ensuring that themes are grounded in data. A computer-assisted qualitative data analysis system (NVivo) will be used to enhance these analyses.

Aim 3: *Generating a time toxicity score.* Using the Daynamica app-based spatiotemporal data collected in Aim 1, we will calculate time-based measures for each individual that characterize the degree of burden and disruption to daily life associated with receiving treatments for cancer. We propose to quantify four subtypes of time toxicity: episodic toxicity, travel toxicity, opportunity toxicity, and scheduling toxicity. Each of these subtypes is described by a different set of time-based measures. **Table 2** lists the four subtypes and describes the time-based measures that we will calculate to characterize each subtype.

We will compute an individual's score for each time toxicity subtype by calculating an average of z-scores for each of the time-based measures associated with that subtype. This z-score averaging approach is commonly applied in a wide variety of domains to generate a single summary metric from observations taken on different subscales.[40-43] For example, if there are five time-based measures associated with a subtype (for example, those associated with Episodic Toxicity listed in Table 2), then we will first compute a z-score for each measure by subtracting its average and dividing by its standard deviation across all individuals. All features will be transformed so that higher values correspond to higher time burdens. The summary score for the subtype will be computed by averaging the five z-scores, then converting the resulting average into a population percentile from a standard Normal random variable expressed as a number out of 100. For example, if the

average of the summary feature z-scores associated with travel toxicity is 1.05, then the travel toxicity score will be P(Z<1.05) x 100 = 85, while a z-score average of -0.42 would lead to a travel toxicity score of P(Z<-0.42) x 100 = 34.

**Table 2. Time use subtypes and measures**

| Toxicity Subtype | Spatiotemporal Measures |
|---|---|
| **1. Episodic Toxicity** Toxicity associated with activities directly related to care. | • Number of days with a medical appointment per week<br>• Number of days receiving treatment per week<br>• Hours per week spent in medical appointments<br>• Hours per week spent receiving treatment |
| **2. Travel / Wait Time Toxicity** Toxicity associated with traveling to/from and waiting for medical appointments | • Number of trips to/from appointments per week<br>• Hours per week spent traveling to/from appointments<br>• Hours per week spent waiting for appointments<br>• Average distance traveled to/from medical appointments |
| **3. Opportunity Toxicity** Toxicity associated with the opportunity cost of time spent on cancer treatment-related medical activities | • Time spent on medical appointments as a fraction of time spent at home, on work, leisure, education, childcare, caregiving, and household<br>• Proximity of medical appointment/treatment locations to individual points of interest (home, work, etc.)<br>• Variation of schedule between days with and without a medical appointment |
| **4. Scheduling / Administrative Toxicity** Toxicity associated with paperwork, scheduling appointments, dealing with bills and insurance, arrangement to accommodate cancer-related activities | • Number of different locations associated with cancer care<br>• Number of appointments per week<br>• Hours per week spent on scheduling and administrative cancer work<br>• Weekly variation in the duration of medical appointments and calls<br>• Variation in time between medical activities |

The overall time toxicity score will be a weighted average of the four subtype scores $S_1, S_2, S_3, S_4$:$T = w_1S_1 + w_2S_2 + w_3S_3 + w_4S_4$ where the weights are constrained to sum to one. We will consider several versions of the time toxicity score defined by the relative weights of the various subtypes. The simplest time toxicity score is one where each subtype is assigned equal weight, and therefore the overall score is a simple average of the population percentiles across the four subtypes. For example, if an individual has subtype scores of 55, 75, 60, and 90, then their time toxicity score will be (55 + 75 + 60 + 90)/4 = 70, which suggests that their time toxicity burden is higher than approximately 70% of the population. In some scenarios, it may be appropriate to pre-specify non-equal weights for the different

subtypes; for example, personalized time toxicity scores could be generated based on individuals' prior weightings of each subtype, which, for example, might give opportunity toxicity more weight than travel toxicity.

In addition to pre-specified (equal or unequal) weights, we will also use our daily burden and well-being measures to derive data-driven versions of the time toxicity score. Let $M_{ij}$ denote the daily well-being measure of person *i* on day *j*. We will fit the model $\mathrm{M_{ij}} = \beta_0 + \beta_2 X_{ij} + \theta_1 S_{1ij} + \theta_2 S_{2ij} + \theta_3 S_{3ij} + \theta_4 S_{4ij} + \epsilon_{\mathrm{ij}}$ where $X_{ij}$ represents a set of individual, and day-level covariates, and $S_{1ij}, S_{2ij}, S_{3ij}, S_{4ij}$ are the subtype scores computed for person *i* on day *j*. The coefficients $\theta_1, \theta_2, \theta_3, \theta_4$represent the relative weightings of the subtypes that best predict the mean of $M$ after adjusting for covariates. These coefficients will be standardized to yield weights using the formula $w_k = \theta_k / \sum \theta_k$.

Our proposed approach to deriving time toxicity scores was developed with a view towards how this score may be used in clinical practice going forward. First, computation of the score relies only on time use summary metrics, which could be collected in a variety of ways. While the collection of these metrics is made substantially easier by the app, the time toxicity score could also be applied to time use summary metrics obtained via traditional diary-based recall methods. Second, the four component scores provide easy to understand insights into which types of time use are driving the overall score, and may allow clinicians and patients to better identify interventions (e.g., increased use of telehealth) that could reduce time toxicity. Lastly, the score can be easily adapted to different populations (by re-weighting subtype scores), applied with incomplete data (by using either imputed or complete-case data to compute subtype scores), and computed across a range of time periods.

17.2 Power Analysis:

Aim 1: Our planned sample size of 80 participants strikes a balance between feasibility and statistical precision and power to estimate the quantities of interest. We will recruit 40 participants with breast and ovarian cancer undergoing treatment at each of the two sites over a two-year period. We do not anticipate any difficulties obtaining this sample size. The UMN and UAB sites combined treat approximately 80 patients with newly diagnosed ovarian cancer, 100 with recurrent ovarian cancer, and 300 patients with metastatic breast cancer annually; therefore we will need to recruit <10% of eligible patients into this study over two years.

For descriptive statistics of individual-level measures (e.g., mean number of minutes per week spent on cancer care related activities) on the entire sample, we will be able to estimate means of continuous measures with a margin of error of ±0.22 standard deviations. For example, if the average number of minutes per week spent on cancer care in the sample was 250 with a standard deviation of 80, then the 95%

confidence interval for the mean number of minutes would be (232, 268). For comparing means of individual-level measures between two equal-sized subgroups (e.g., those with breast and ovarian cancer), our sample size yields 80% power to detect a difference of 0.64 standard deviations, equivalent to approximately 50 minutes using the same standard deviation as above. Our power to detect associations and differences for day-level measures will be higher since we will have ~20-28 (correlated) observations per person.

Aim 2: Though we have a limited number of individuals in our study, we will have sufficient power to detect associations between daily time use and self-reported well-being as we will have 28 days of observations for each participant. To estimate power, we conducted a simulation study to estimate the effect size of a binary daily time use measure (e.g., whether or not a medical appointment occurred on a given day) and continuous well-being. We generated probabilities of having a medical appointment from a Beta(2,4) distribution and well-being measures from a linear mixed model calibrated to have a mean of 3, a (Normal) residual standard deviation of 1.5 units, and within-person correlation of approximately 0.4. With 28 days of observations on N=80 participants, we estimate that we will have approximately 90% power to detect a difference of 0.25 units between days within different characteristics. An effect of this magnitude (approximately 5% of the range of the 1-6 well-being scale) seems plausible and is at or below a threshold likely to be clinically meaningful. Power to detect associations between continuous time use measures (e.g., number of hours spent on medical appointments) and well-being will be higher than for the binary measures.

Aim 3: The main target of inference in this aim is the association between the time toxicity score and survey measures at 28 days. With our planned sample size of n=80, we will have >80% power to detect a 0.4 standard deviation effect on survey measures associated with a 1 SD difference in the time toxicity score. Previous studies from our team among this target population identified a standard deviation of 17 points for the FACT-G QOL instrument,[44] hence a 0.4 SD effect would correspond to a difference of 6.8 points. This effect size corresponds to a "medium" effect on the FACT-G as suggested by a meta-analysis of studies using FACT-G as an outcome [45] and is in line with the effects demonstrated by supportive activities for cancer treatment such as muscle relaxation [46] and associations with co-occurring conditions such as skeletal morbidities.[47] Further, it has been previously shown that effect sizes of 0.35-0.5 are expected to be clinically relevant for QOL measures.[48]

17.3 Statistical Analysis:

Aim 1: These per-activity summary measures will be used as outcomes in generalized linear regression models to quantify differences between relevant subgroups (e.g., those caring for dependents vs. not, those experiencing higher vs.

lower treatment burden) adjusting for individual demographic and clinical characteristics. For example, we will be able to compute covariate-adjusted differences in the total number of episodes and minutes spent on various cancer care-related activities between patients with and without dependents, which will provide insight into how family structure affects the time burden of care. Random effects models will be used to quantify associations between factors that vary day to day within individuals and time use outcomes, e.g., to understand whether completing a cancer care-related task on a given day affects the number of hours spent working or engaged in leisure activities. In addition, we will apply techniques developed by Dr. Wolfson and colleagues [49] to describe day-level activity patterns via sequence alignment (see **Figure 1**). These techniques will allow us to identify clusters of days with similar activity sequences, and quantify how individual participants' characteristics determine their likelihood of experiencing these different day archetypes.

Aim 2: *Relating cancer-related time use measures to self-reported well-being.* Associations between time use and daily well-being measures will be quantified via longitudinal regression modeling. We will use generalized linear mixed models to describe the longitudinal relationship between daily time use summary measures (calculated in Aim 1) and self-reported daily well-being. Separate models will be fitted for each of the six daily well-being measures along with an overall well-being score, the U-index.[50, 51] Models will be of the form $g([E({W_{ij}}^{(r)})]) = \beta_0 + \beta_1 T_{ij} + \beta_2 X_{ij} + b_i + \epsilon_{ij}$ where ${W_{ij}}^{(r)}$ is the *r*th well-being measure (e.g., Happy, Sad, Stress) reported by person *i* on day *j*; *g* is a function depending on the regression model type; $b_i$ is a person-specific random effect, and $\epsilon_{ij}$ is the residual. The predictors of interest $T_{ij}$ are a vector of daily time use measures (time spent on medical appointments, number of medical-related phone calls, etc.). $X_{ij}$is a vector of covariates for adjustment including both individual-level (age, race, cancer type, etc.) and day-level (day of the week, time of year, time since initiation of the current round of treatment, etc.) factors. Mixed models are chosen to account for correlation of repeated measurements over the course of the 28-day mobile data collection period. The main output from these analyses will be inference about the coefficients in $\beta_1$, which summarize the association between time use measures and self-reported well-being. In addition to models of the type presented above, which correlate well-being with time use on the same day, we will also fit models using time use summary measures that aggregate time use longitudinally. These models will allow us, for instance, to assess whether aggregated cancer-related time use over the past week is a stronger predictor of daily well-being than time use on the current day only.

*Defining and exploring the role of context as an effect modifier.* We will use quantitative and qualitative approaches to understand the role of context in

modifying the association between cancer-related time use and well-being. Given limited sample size, we view the results from this part of the analysis as primarily hypothesis generating to guide future work. For the ***quantitative component*** of this analysis, we will follow two approaches. First, we will identify time use measures that appear moderately or strongly associated with self-reported well-being and run exploratory analyses to assess whether there is preliminary evidence that these associations are modified by well-established individual predictors of time use, in particular age, employment status, and family structure, as well as day- and individual-level contextual time use. To maximize statistical power, we will consider each candidate pair of measures of time use and well-being separately, by fitting models with main effects for the time use measure and potential moderator as well as an interaction term between them. Given limited sample size, we expect confidence intervals for moderation effects to be wide, and hence will focus primarily on their estimated magnitude. Second, we will derive covariates that define day-level time use patterns. For example, we will apply unsupervised clustering methods to identify common day structures (e.g., workday, stay at home, multiple errands). We will evaluate these derived day structures as potential modifiers of the association between time use and well-being; for example, to assess whether medical appointments on a workday lead to higher levels of stress than those that occur on a day mostly spent at home. To identify clusters of days with similar time use patterns, we will use standard k-means clustering [52] applied directly to time use measures as well as a novel sequence alignment-based approaches for identifying daily activity patterns recently co-developed by co-PI Wolfson.[49] For the k-means clustering, measures will be normalized so that distances between all measures are on the same scale. As the number of study participants is limited, we will constrain our clustering methods to generate a small number of clusters (3-5) so that each cluster contains a sufficient number of days to allow us to assess its effect on well-being.

Aim 3: To assess the association between time toxicity scores and survey-based measures (e.g. QOL), we will calculate individual time toxicity scores over the data collection period and fit linear regression models of the form $M_e = \gamma_0 + \gamma_1 S + \gamma_2 M_b + \gamma_3 X + \epsilon$ where $M_e$ and $M_b$ are survey measures taken at the beginning and end of the data collection period, $S$ is the time toxicity score, and $X$ is a set of individual-level covariates for adjustment. Separate models will be fit for each survey instrument used (e.g., FACT-G for QOL, HADS for depression and anxiety). Initially, we will fit unadjusted versions of these models (with $\gamma_3 = 0$) to assess whether the time toxicity score is associated with the final survey measurement, controlling only for the baseline survey measurement. Then, we will fit covariate-adjusted models to see whether associations between the time toxicity score and survey measures remain after controlling for individual characteristics. In exploratory analyses, we will investigate whether the associations between the time

toxicity score and survey measures are modified by individual-level covariates by including $S \times X$ interaction terms in the above regression model. Finally, we will investigate whether specific subtype scores are more strongly associated with survey measures by replacing the overall time toxicity score in the above model by the four subtype scores.

17.4 Data Integrity: Data integrity and completeness will be monitored on an ongoing basis by the study coordinator and statistician, using both the reporting tools provided by REDCap and the study/data management dashboard associated with the app.

## 18.0 Health Information and Privacy Compliance

18.1 Select which of the following is applicable to your research:

☐ My research does not require access to individual health information and therefore assert HIPAA does not apply. If this option is selected, please skip to Section 19.

X I am requesting that all research participants sign a HIPCO approved HIPAA Disclosure Authorization to participate in the research (either the standalone form or the combined consent and HIPAA Authorization).

☐ I am requesting the IRB to approve a Waiver or an alteration of research participant authorization to participate in the research.

Appropriate Use for Research:

☐ An external IRB (e.g. Advarra) is reviewing and we are requesting use of the authorization language embedded in the template consent form in lieu of the U of M stand-alone HIPAA Authorization. Note: External IRB must be serving as the privacy board for this option.

18.2 Identify the source of Private Health Information you will be using for your research (Check all that apply)

☐ I will use the Informatics Consulting Services (ICS) available through CTSI (also referred to as the University's Information Exchange (IE) or data shelter) to pull records for me

X I will collect information directly from research participants.

☐ I will use University services to access and retrieve records from the Bone Marrow Transplant (BMPT) database, also known as the HSCT (Hematopoietic Stem Cell Transplant) database.

X I will pull records directly from EPIC.

☐ I will retrieve record directly from axiUm / MiPACS

☐ I will receive data from the Center for Medicare/Medicaid Services

X I will receive a limited data set from another institution

Study coordinators at outside participating sites (e.g. University of Alabama Birmingham) will be reviewing the medical records of their participants at their site and entering the appropriate data in REDCap. This will include details regarding cancer diagnosis, stage, treatments received, hospitalizations and other medical encounters related to cancer diagnosis and treatment.

☐ Other. Describe:

18.3 Explain how you will ensure that only records of patients who have agreed to have their information used for research will be reviewed.

The study coordinators will confirm that the patient has not declined research (we will not approach patients with "Research Opt-out" status indicated their medical record, in order to comply with Minnesota Statute 144.651, subdivision 13).

18.4 Approximate number of records required for review: N/A

18.5 Please describe how you will communicate with research participants during the course of this research. Check all applicable boxes

☐ This research involves record review only. There will be no communication with research participants.

☐ Communication with research participants will take place in the course of treatment, through MyChart, or other similar forms of communication used with patients receiving treatment.

X Communication with research participants will take place outside of treatment settings. If this box is selected, please describe the type of communication and how it will be received by participants.

Communication with potential and consented participants will occur in-person during other scheduled clinic visits and by phone. Individuals interested in electronic consent will be emailed those materials directly from REDCap. Surveys will be mailed or emailed directly from REDCap. Enrolled and consented participants who complete an email authorization form may be contacted about the app use and data collection via email during the study period.

18.6 Access to participants

Participants will complete consent and HIPAA forms prior to any data collection. After they agree to participate, all data will be provided by the participants and from review of their medical records.

18.7 Location(s) of storage, sharing and analysis of research data, including any links to research data (check all that apply).

☐ In the data shelter of the Information Exchange (IE)

☐ Store ☐ Analyze ☐ Share

☐ In the Bone Marrow Transplant (BMT) database, also known as the HSCT (Hematopoietic Stem Cell Transplant) Database

☐ Store ☐ Analyze ☐ Share

X In REDCap (recap.ahc.umn.edu)

X Store X Analyze X Share

☐ In Qualtrics (qualtrics.umn.edu)

☐ Store ☐ Analyze ☐ Share

☐ In OnCore (oncore.umn.edu)

☐ Store ☐ Analyze ☐ Share

X In the University's Box Secure Storage (box.umn.edu)

X Store X Analyze X Share

X In an AHC-IS supported server. Provide folder path, location of server and IT Support Contact:

IT Support Contact:
IT Contact: Mike Doherty
\\cancer.ahc.umn.edu\cancer\CancerCenter\CCSG\Vogel, RI\time_toxicity

X Store X Analyze ☐ Share

☐ In an AHC-IS supported desktop or laptop.

Provide UMN device numbers of all devices:

☐ Store ☐ Analyze ☐ Share

☐ Other.

Indicate if data will be collected, downloaded, accessed, shared or stored using a server, desktop, laptop, external drive or mobile device (including a tablet computer such as an iPad or a smartform (iPhone or Android devices) that you have not already identified in the preceding questions

☐I will use a server not previously listed to collect/download research data

☐I will use a desktop or laptop not previously listed

☐I will use an external hard drive or USB drive ("flash" or "thumb" drives) not previously listed

☐I will use a mobile device such as an tablet or smartphone not previously listed

18.8 Consultants. Vendors. Third Parties.

Participants will use a modified version of a mobile application provided by Daynamica, Inc. to collect data on their daily activities. Details of the application and storage process are provided in detail in Section 6.1 and will be controlled by UMN HST.

18.9 Links to identifiable data: When patients agreed to participate, they will be given a study ID which will be used for the remainder of the study. The identifying information will be stored in REDCap (survey data collection) with the study ID and all other data will be stored using this ID alone.

18.10 Sharing of Data with Research Team Members. Data will be shared using Box and REDCap.

18.11 Storage of Documents: All consent, HIPAA, email authorization, and survey paper forms will be stored in locked cabinets within locked offices/spaces. Electronic copies will be stored within REDCap, Box and on the AHC server space described above.

18.12 Disposal of Documents: Following publication and dissemination (up to 10 years post study initiation), all paper documents will be shredded and all identifying information in REDCap will be removed.

## 19.0 Confidentiality

19.1 Data Security: All study investigators and staff will be fully trained on data safety and participant confidentiality. An electronic copy of the signed consent form will be stored on an AHC-IS supported server. Participants' research data will not be placed in the participants' medical record.

Medical record data will be entered by the study coordinator and will be stored on the secure REDCap database. Study data will be de-identified before data analysis. Only the researchers directly involved with the study will have access to the data. Identifying data will be stored until completion of the study and manuscript submission.

Data collected by the Daynamica app will be uploaded to and stored on a secure HST server on a daily basis. As noted previously, all data will be referenced with study code numbers; the master file linking these codes to participant contact information will be stored separately.

Study staff involved in data collection will only have access to Daynamica data via the data quality dashboard described in the previous section. The dashboard provides data quality summary statistics such as the number of trips and activities that have been recorded by the app for each individual. It does not provide any access to individual-level demographic or location information. Only the study investigators will have access to both the full suite of uploaded data and the master file linking participant identifiers to contact information. After completion of the study, the master link file will be destroyed, so that all remaining data will not be connected to individual participant contact information.

19.2 Data Sharing: See Section 6.1. The University of Minnesota Libraries / DRUM will work with the investigative team to ensure the data are de-identified before they are made available to others.

## 20.0 Provisions to Monitor the Data to Ensure the Safety of Participants

20.1 Data Integrity Monitoring. The PI will review all signed consent forms for completeness at the time of participant entry into the study. The integrity of the data collected via the mobile app will be monitored by the PI and study staff using a password-protected, web-based study manager application.

20.2 Data Safety Monitoring. This study carries minimal risk and therefore the PI will assume responsibility for monitoring and reporting safety concerns/events to the University of Minnesota IRB. Events requiring prompt reporting include any adverse event that requires a change to the protocol or consent form, any unauthorized disclosure of confidential information, any unresolved subject complaint or any protocol deviation that resulting in harm or the unanticipated death of an enrolled subject. Compensation for Research-Related Injury

## 21.0 Compensation for Research-Related Injury

21.0 Compensation for Research-Related Injury: N/A

21.1 Contract Language: N/A

## 22.0 Consent Process

22.0 Consent Process (when consent will be obtained): All potential study participants will be provided a paper or electronic copy of the IRB-approved consent to review at a scheduled clinic visit at the oncology clinic or from home. Regardless of method, potential participants will be encouraged to ask for more information before deciding whether or not they would like to participate in the study.

In-person consent: In an area of the clinic where the conversation cannot be overheard, the PI or study coordinator will explain all aspects of the study in lay language and answer all questions regarding the study. If the participant decides to participate in the study, they will be asked to sign and date the consent and HIPAA documents (paper or electronic using the e-consent functionality in REDCap). The study coordinator/person obtaining written consent will also sign and date the consent document (paper or electronically). Participants will also receive a signed and dated copy of the consent and HIPAA forms (paper copy or emailed PDFs).

Remote consent: Individuals approached in the clinic may review the documents and consent at a later time online. Online consents and HIPAA forms will obtain signatures captured electronically via the e-consent functionality in REDCap. Individuals interested in this option will be emailed a link specifically for them to invite them to review and complete the documents. The recruiting coordinator will electronically sign and date the documents following completion by the participant.

Electronic signatures will be stored within REDCap as well as a copy on the Academic Health Center (AHC) secure servers. Access to these records will be limited to the study team as needed or required.

Patients who refuse to participate or who withdraw from the study will be treated without prejudice.

22.1 Waiver or Alteration of Consent Process (when consent will not be obtained, required information will not be disclosed, or the research involves deception): N/A

22.2 Waiver of Written/Signed Documentation of Consent (when written/signed consent will not be obtained): N/A

22.3 Non-English Speaking Participants: N/A

22.4 Participants Who Are Not Yet Adults (infants, children, teenagers under 18 years of age): N/A

22.5 Cognitively Impaired Adults, or adults with fluctuating or diminished capacity to consent: N/A

22.6 Adults Unable to Consent: N/A

## 23.0 Setting

23.0 Research Sites: Participants will be recruited through the University of Minnesota/MHealth Fairview network and through the University of Alabama Birmingham. All study procedures will be conducted at cancer clinics within these networks or remotely.

23.1 International Research: N/A

23.2 Community Based Participatory Research: N/A

## 24.0 Multi-Site Research

24.0 Study-Wide Number of Participants: Up to 100

24.1 Study-Wide Recruitment Methods: Participants will be recruited by site-specific staff following the procedures described in section 12.0 (Local Recruitment methods).

24.2 Study-Wide Recruitment Materials: Example study summary sheets and mail recruitment letter are included.

24.3 Communication Among Sites: Communication between sites be managed by the PI and UMN project manager. Both sites will have the most current version of the protocol, consent documents, and, HIPAA authorization. All modifications will be communicated to sites, and approved by the University of Minnesota IRB before the modification is implemented. All non-compliance with the study protocol or applicable requirements will be reported in accordance with university or local policy.

24.4 Communication to Sites: Regular teleconferences to facilitate communication between participating sites regarding the study's progress, patient updates, data completion, and other issues for discussion. The PI and University of Minnesota project manager will communicate more frequently as the study nears closure to ensure we do not over-enroll.

## 25.0 Coordinating Center Research N/A

## 26.0 Resources Available

26.1 Resources Available:

All investigators are committed to this project and will provide appropriate effort as needed. This study will be supported by an NIH R01 to Drs. Vogel and Wolfson with a subaward to Dr. Roque at UAB. Drs. Vogel and Wolfson will have appropriate dedicated time to oversee and conduct the research described.

All members of the study team have reviewed and approved the protocol and study procedures. They have understood their duties and study roles, and provide the

skills needed to conduct the study and study analyses. All members of the research team have relevant publication records. They have also completed appropriate trainings and these trainings will be revisited as appropriate, particularly for those involved directly with participants in the consent process and/or data collection.

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