

Protocol

Digital Phenotyping for Monitoring and Disease Trajectory Prediction of Patients With Cancer: Protocol for a Prospective Observational Cohort Study

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Abstract

Background: Timely recognition of cancer progression and treatment complications is important for treatment guidance. Digital phenotyping is a promising method for precise and remote monitoring of patients in their natural environments by using passively generated data from sensors of personal wearable devices. Further studies are needed to better understand the potential clinical benefits of digital phenotyping approaches to optimize care of patients with cancer.

Objective: We aim to evaluate whether passively generated data from smartphone sensors are feasible for remote monitoring of patients with cancer to predict their disease trajectories and patient-centered health outcomes.

Methods: We will recruit 200 patients undergoing treatment for cancer. Patients will be followed up for 6 months. Passively generated data by sensors of personal smartphone devices (eg, accelerometer, gyroscope, GPS) will be continuously collected using the developed LAIMA smartphone app during follow-up. We will evaluate (1) mobility data by using an accelerometer (mean time of active period, mean time of exertional physical activity, distance covered per day, duration of inactive period), GPS (places of interest visited daily, hospital visits), and gyroscope sensors and (2) sociability indices (frequency of duration of phone calls, frequency and length of text messages, and internet browsing time). Every 2 weeks, patients will be asked to complete questionnaires pertaining to quality of life (European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire [EORTC QLQ-C30]), depression symptoms (Patient Health Questionnaire-9 [PHQ-9]), and anxiety symptoms (General Anxiety Disorder-7 [GAD-7]) that will be deployed via the LAIMA app. Clinic visits will take place at 1-3 months and 3-6 months of the study. Patients will be evaluated for disease progression, cancer and treatment complications, and functional status (Eastern Cooperative Oncology Group) by the study oncologist and will complete the questionnaire for evaluating quality of life (EORTC QLQ-C30), depression symptoms (PHQ-9), and anxiety symptoms (GAD-7). We will examine the associations among digital, clinical, and patient-reported health outcomes to develop prediction models with clinically meaningful outcomes.

Results: As of July 2023, we have reached the planned recruitment target, and patients are undergoing follow-up. Data collection is expected to be completed by September 2023. The final results should be available within 6 months after study completion.

Conclusions: This study will provide in-depth insight into temporally and spatially precise trajectories of patients with cancer that will provide a novel digital health approach and will inform the design of future interventional clinical trials in oncology. Our findings will allow a better understanding of the potential clinical value of passively generated smartphone sensor data (digital

phenotyping) for continuous and real-time monitoring of patients with cancer for treatment side effects, cancer complications, functional status, and patient-reported outcomes as well as prediction of disease progression or trajectories.

International Registered Report Identifier (IRRID): PRR1-10.2196/49096

(*JMIR Res Protoc* 2023;12:e49096) doi: [10.2196/49096](https://doi.org/10.2196/49096)

KEYWORDS

cancer; digital phenotyping; biomarkers; oncology; digital phenotype; biomarker; data collection; data generation; monitor; monitoring; data collection; predict; prediction; model; models; mobile phone

Introduction

Cancer continues to be the leading cause of morbidity and mortality worldwide and a serious public health challenge [1-3]. Early cancer detection as well as increased effectiveness and availability of novel treatment approaches such as immunotherapy and targeted therapies have resulted in a steadily growing number of cancer survivors [4-7]. Continuous monitoring of patients undergoing treatment for cancer and cancer survivors is important for timely identification of cancer treatment complications and cancer progression that is important for optimized long-term prognosis [8]. Therefore, there is an urgent need for developing widely available, automated, and evidence-based monitoring systems of patients with cancer [9].

The COVID-19 pandemic continues to be a serious public health challenge [10]. Patients with cancer are vulnerable to SARS-CoV-2 infection due to immunosuppression, frequent hospital visits [11,12], and lower efficacy of the COVID-19 vaccines [13]. The mortality risk of patients with cancer infected with SARS-CoV-2 was greater than that of the general population and was shown to exceed by 33% among patients with thoracic and hematologic malignancies [14-16]. A meta-analysis of 52 studies and 18,650 patients estimated the probability of death at 25.6% in patients with cancer infected with COVID-19 [17]. Furthermore, the COVID-19 pandemic caused major delays and interruptions in cancer treatments [18,19], and they are estimated to have caused over 15% increase in additional cancer deaths [20]. Finally, patients with cancer were vulnerable to adverse mental health and quality of life sequelae during the COVID-19 pandemic [21,22].

Although there is no standardized definition for mobile health (mHealth), the World Health Organization defines mHealth as “medical or public health practice that is delivered with the support of mobile phones, patient monitoring devices, and other wireless devices.” mHealth encompasses the use of mobile phones and other wireless technologies for health care and is a promising approach for improving health monitoring and delivery of health interventions [23-25]. The adoption of telehealth and mHealth solutions is growing [26]. The number of digital health apps currently exceeds 300,000, with hundreds of apps being introduced every day [27]. The market size of digital health apps will grow exponentially in the coming decade [27]. However, the adoption of digital health apps in clinical practice is limited due to numerous obstacles such as unclear clinical value because they are often not developed by health care professionals and not tested in clinical environments [28]. Thus, there is an urgent need to develop evidence-based personalized telehealth or mHealth solutions and test them in

real-world clinical environments that would allow evidence-based monitoring of vulnerable patients with cancer and would ideally consider the clinical, functional, and patient-reported health outcomes [29-31].

Digital phenotyping allows continuous and spatially and temporally precise quantification of individual's phenotype in his or her natural environment by using passively harnessed data from personal digital devices, including smartphone sensors [32,33]. Digital phenotyping approaches have been increasingly tested across mental health and somatic conditions [34], including amyotrophic lateral sclerosis [35], multiple sclerosis [36], posttraumatic stress disorder [37], depression [38], schizophrenia [39], sleep disorders [40], and spine disorders [41]. There is a growing body of evidence that passively generated data can allow identification of treatment complications and disease trajectories of patients with cancer. For example, the Helping Our Patients Excel study of 10 patients (mean age 60 [SD 11] years and mean Eastern Cooperative Oncology Group performance status of 1 [SD 0.66]) with gynecological cancer undergoing palliative chemotherapy found that passively acquired accelerometer data using wearable devices enabled the identification of high-risk patients and complications [42]. In another prospective observational study, 62 individuals undergoing elective cancer surgery were followed up using a smartphone app for a median of 147 (IQR 77-179) days after the surgery [43]. They found that exertional physical activity in patients who experienced postoperative events (27%) was lower than that in those who did not experience postoperative events, suggesting that this approach can allow to quantify recovery after cancer surgery [43]. However, these studies are limited by small to moderate sample sizes and consideration of a snapshot of cancer journey. Numerous barriers remain for implementing mobile-sensing data into the care of patients with cancer due to ongoing challenges related to raw data analysis and interpretation as well as integration of results in the clinical workflow [44]. Interpretation of passively collected data within clinical contexts requires multidisciplinary collaboration to identify potential clinical values of the mobile-sensing data. The analysis of passively harnessed sensing data is another important challenge, and it has been shown that deep learning approaches can be used to anticipate complications of patients undergoing treatment for hematologic malignancies [45]. Therefore, future studies are warranted to better understand the potential clinical values of mobile sensing data in oncology.

The aim of our study is to evaluate the usefulness of passively generated smartphone sensor data streams (as in digital phenotyping) for monitoring patients with cancer. We will evaluate if novel cancer trajectory biomarkers that integrate

high-resolution passively acquired data streams from smartphone sensors with actively collected data can enable real-time data analytics and monitoring of patients with cancer in their natural environment. We will (1) develop and adapt a monitoring system tailored for patients with cancer that integrates passively and actively acquired data streams, (2) investigate if continuous monitoring of patients with cancer using passively collected data acquired through personal smartphones correlates with objective and patient-reported health status and therefore can be used as actionable digital phenotype, and (3) develop prediction models anticipating disease trajectories as well as functional and reported outcomes of patients with cancer. This study will allow to better understand the potential clinical value of passively generated smartphone sensor data (digital phenotyping) for continuous and real-time monitoring of patients with cancer for treatment side effects, cancer complications, functional status, and patient-reported outcomes, as well as prediction of disease progression or trajectories.

Methods

Study Design

This is a prospective observational cohort study with a 6-month follow-up of patients diagnosed with cancer who will use a smartphone app to acquire continuously generated data from smartphone sensors (passively generated data) and deploy questionnaires (actively generated data). This study is conducted at the Department of Oncology, Hospital of Lithuanian University of Health Sciences, Kaunas, Lithuania, in collaboration with Vytautas Magnus University, Kaunas, Lithuania, and ProIT, Vilnius, Lithuania.

Patient and Public Involvement

Patient involvement in this study will last for the duration of the study and will include continuous collection of smartphone sensor data, actively collected questionnaire data via LAIMA app, and 3 in-person visits. The patients and the public were not involved in the design of this study.

Recruitment

The study inclusion criteria are (1) diagnosis of cancer, (2) current active treatment (radiation therapy, chemotherapy) for cancer or surveillance, (3) ability to comprehend Lithuanian, (4) ownership of a smartphone device (Android or iOS platform) that can support the smartphone apps, (5) age of 18 years or older, and (6) ability to provide informed consent. Patients will be excluded if they have cognitive, visual, or functional impairment or any other clinically significant medical condition that in the opinion of the study investigators could affect participant safety, preclude evaluation of responses, or interfere with the ability to comply with the study procedures.

Ethics Approval

Ethics approval was obtained from the Kaunas Regional Bioethics Committee on April 14, 2022 (protocol BE-2-31). All participants will provide informed consent before inclusion in this study. Identifying data will be available for the study oncologists and will be deidentified for other members of the

research team. Patients will not receive compensation for participating in this study.

Sample Size

The sample size was calculated using the Digital Phenotyping Power Calculator tool [46]. We plan to recruit 200 patients diagnosed with cancer undergoing active treatment and actively follow-up with them for at least 3 months, with expected missing data of <50% that will allow to achieve power (type 1 error .05) of .971 at effect size (β_1) of .03 and power of 1 and effect sizes (β_1) of .05 and .07.

Primary Outcome

We will examine changes in each of the collected digital biomarker data streams during the 6-month follow-up period in relation to progression-free survival. Cancer progression will be defined based on clinical, laboratory, and radiological data in accordance with guidelines and criteria for the specific cancer type. Cancer progression will be determined by the treating oncologist according to relevant clinical guidelines.

Secondary Outcome

We will examine temporal changes in questionnaire data trajectories collected using the LAIMA app and will examine the association of passively harnessed digital biomarkers with actively collected questionnaire data. We will also examine the association of passively acquired digital biomarker data with clinically relevant outcomes of patients with cancer, such as overall survival, cancer-related complications (type of complication, unexpected presentation to emergency department or hospital admission), and cancer treatment-related adverse events. The precision of digital biomarker data to identify and predict clinically relevant outcomes of patients with cancer will be examined.

Digital Data

Data will be collected using the LAIMA app that was developed by the researchers based on the open-source Beiwe platform [47]. The LAIMA app is supported by iOS and Android operating systems. We also developed a corresponding digital platform that is linked with the smartphone app and will be used for patient registration and remote monitoring by the study investigators.

The LAIMA app and digital platform will be used to collect and integrate (1) passively generated data streams from smartphone sensors that will be uploaded to the LAIMA platform and integrated with questionnaires and clinical data, (2) actively collected questionnaire data that study participants will be prompted to answer in predefined days at 2-week intervals after inclusion in this study, and (3) sociodemographic and clinical data that will be entered by the study investigators at initial and follow-up study visits. In this study, we will include questionnaires that are commonly used for clinical and cancer research and were validated in Lithuanian as well as clinical data that are relevant for patients with cancer. The data will be uploaded to the server and aggregated. We utilize cloud services for secure data storage as well as data preparation and predictive modeling using generated data. The LAIMA platform has several data preparation methods such as classification,

clustering, regression, and ranking. The platform also has a built-in artificial intelligence algorithm function. The LAIMA app and platform are compliant with the European Union General Data Protection Regulation requirements [48]. Continuously and passively generated data from smartphone sensors will be collected during the course of this study that will take from 3 to 6 months for each patient included in this study. The following smartphone sensor data will be considered for this study:

1. Mobility data will include continuous collection and aggregation of passively generated data streams from the accelerometer (mean time of active period, mean time of exertional physical activity, distance covered per day, duration of inactive period), GPS (places of interest visited daily, hospital visits), and gyroscope.
2. Sociability indices will include continuous capture and aggregation of frequency of duration of phone calls, frequency and length of text messages, and internet browsing time.

Questionnaires

Eastern Cooperative Oncology Group Questionnaire

The Eastern Cooperative Oncology Group questionnaire will be used for the assessment of the functional status of patients with cancer during their clinic visits [49]. It is a widely used measure of the functional status of patients with cancer in clinical practice and in clinical trials.

European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire

The European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C30) will be used for the assessment of quality of life of the study participants [50,51]. The EORTC QLQ-C30 will be deployed during study visits and via the LAIMA app. The EORTC QLQ-C30 consists of 9 multi-item functional scales and 6 single-item symptom scales that evaluate global health status, functional status, role functioning, emotional functioning, cognitive functioning, social functioning, fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties. Scores are linearly transformed to a scale ranging from 0 to 100, with higher scores indicating better health-related quality of life on global health status and functional status scales and worse health-related quality of life on symptom scales.

Patient Health Questionnaire-9

The Patient Health Questionnaire-9 (PHQ-9) will be used for the assessment of depressive symptom severity during study visits and via the LAIMA app [52,53]. The PHQ-9 consists of 9 symptoms of depression that respondents rate based on their severity during the preceding 2 weeks, with a greater score indicating greater depressive symptom severity and with scores of 10 or greater indicating moderate to severe depressive symptoms.

General Anxiety Disorder-7 Questionnaire

The General Anxiety Disorder-7 (GAD-7) scale will be used for the assessment of anxiety symptom severity during the study visit and via the LAIMA app [54,55]. The GAD-7 includes 7 questions pertaining to generalized anxiety disorder, with higher scores indicating greater anxiety symptom severity.

COVID-19 Fears Questionnaire

The COVID-19 Fears Questionnaire for chronic medical conditions will be used for evaluating fears related to the COVID-19 pandemic [56,57]. This questionnaire includes 10 items. Respondents are asked to select the response that reflects how much each statement describes their experience on a typical day in the last week on a 5-point numerical scale ranging from 1 (not at all) to 5 (extremely). The total score is the sum of all items and ranges from 10 to 50, with higher scores reflecting greater COVID-19 fear. The questionnaire has been validated in Lithuania [56] and will be administered during the study visits.

Questionnaire Administration

The Eastern Cooperative Oncology Group questionnaire, EORTC QLQ-C30, PHQ-9, GAD-7, and the COVID-19 Fears Questionnaire for chronic medical conditions will be administered by trained clinicians. Deidentified data will be entered into a database, and hard copy documents are kept on-site under lock and key. EORTC QLQ-C30, PHQ-9, GAD-7 will also be deployed via the LAIMA app to study participants in predefined 2-week intervals via text messages and a secure link to the website. Participants will have 2 days to complete each questionnaire. The data will be uploaded to the LAIMA digital platform and integrated with other data sources for each patient.

Sociodemographic Data

We will consider patients' age at the time of cancer diagnosis and study inclusion, gender, education, job, and marital status. The type of smartphone device and operating system (Android, iOS or other) will be recorded.

Clinical Data

Information about cancer diagnosis, cancer location, presence of distant metastases, and tumor, node, metastasis stage at time of study inclusion, date of cancer diagnosis, and pathology results, including relevant molecular data, will be recorded at the initial study visit. We will record information regarding currently active cancer treatment(s), including radiation therapy (dose, target, and number of fractions) and chemotherapy (chemotherapeutic agent and dose and treatment start and finish dates). We will also gather information about all previous cancer treatments (surgery, radiation therapy, and chemotherapy), including their date, radiation dose, and chemotherapeutic agent(s). Information about comorbidities and currently used medication will be considered.

At 2 follow-up visits that will take place at 1-3 months and 3-6 months after patient inclusion in the study, we will record information pertaining to cancer treatment (chemotherapy, radiation therapy, and other) that is ongoing or that the patient has received during the follow-up period. Disease progression

and its date will be evaluated using standard clinical assessment studies and relevant criteria. Treatment complications (date and description) and unanticipated visits to the emergency department (date and description) will be recorded for all study patients. Disease progression and complications of patients who will not be able to attend the follow-up visit will be evaluated by reviewing medical records or via phone interviews. All clinical and sociodemographic data will be recorded and entered into the LAIMA platform by the study investigators who are board-certified oncologists.

Detailed Procedure

Baseline Visit

At the baseline visit, the study investigator will inform the patients about the study and procedures, and informed consent will be obtained. Participants will complete a battery of questionnaires that will be administered by the study investigators (Table 1). The LAIMA app will be installed into the participant's personal smartphone device, and an account will be created. Participants will be provided with a personal password and informed about the procedures in case he or she decides to withdraw from the study. The study investigators will ensure that the passively acquired data are being properly collected from a smartphone device by registering in the LAIMA platform.

Table 1. Study protocol.

	Visit 1 (month 0)	Data collected using smartphone app	Visit 2 (months 1-3)	Visit 3 (months 3-6)
Data collected only at initial visit				
Informed consent	✓			
Installation of mobile app	✓			
Demographic and sociodemographic data	✓			
Clinical data	✓		✓	✓
Treatment complications and adverse events	✓		✓	✓
Functional status (Eastern Cooperative Oncology Group)	✓		✓	✓
Health-related quality of life (EORTC QLQ-C30 ^a)	✓		✓	✓
Symptoms of depression (Patient Health Questionnaire-9)	✓		✓	✓
Symptoms of anxiety (General Anxiety Disorder-7)	✓		✓	✓
COVID-19 Fear (COVID-19 Fear Questionnaire)	✓		✓	✓
Questionnaire data collected using smartphone app (every 2 weeks)				
Health-related quality of life (EORTC QLQ-C30)		✓		
Symptoms of depression (Patient Health Questionnaire-9)		✓		
Symptoms of anxiety (General Anxiety Disorder-7)		✓		
Passively collected data using smartphone app (continuous)				
Accelerometer		✓		
Gyroscope		✓		
GPS		✓		
Phone on or off		✓		
Phone calls		✓		
Phone calls		✓		
Text messages		✓		
Internet browsing time		✓		

^aEORTC QLQ-C30: European Organization for Research and Treatment of Cancer Core Quality of Life questionnaire.

Follow-up Visits

All study patients will complete follow-up visits at months 1 to 3 and months 3 to 6 after the study inclusion. Follow-up visits will take place during routine clinical visits or via telephone encounter. We anticipate that most follow-up encounters will take place during in-person clinic visits. At follow-up visits, patients will complete the study questionnaires, and relevant clinical, laboratory, and imaging data will be reviewed for assessment of disease progression and treatment-related adverse events (Table 1). Given the observational nature of this study, patients will undergo clinical, laboratory, and imaging evaluation as clinically indicated and per appropriate guidelines because

we will include patients with different cancer diagnoses undergoing different treatments. At the end of month 6 of the study or in case of patient death, the app will be remotely uninstalled from the device. Monitoring of passively generated data via smartphone sensors and actively collected questionnaire data via LAIMA app collection and upload in the platform will be conducted daily. Patients without passively generated or uploaded data for 3 days or more will be contacted by the study investigators, and problems will be resolved.

Data Analysis

Data cleaning will be performed on both active and passive data. The main cleaning tasks will be removing errors,

identifying outliers, and filling the missing data. Moreover, data will be transformed using aggregation and normalization methods. Missing data from smartphone sensors will be restored using data recovery extension (Firebase Cloud Messaging). For small numbers of missing observations, the missing values will be inputted using linear or polynomial interpolation methods (data imputation will not be used for mixed effects regression models). Cases with more than half of the smartphone sensor data missing will be excluded from the analyses. Missing answers in a questionnaire will not be considered in the analyses, and data imputation will not be performed as it could skew the results of the analyses. A descriptive analysis (mean, SD, median, relative frequencies for qualitative variables) of all the variables will be performed. To investigate associations among digital, clinical, and patient-reported health outcomes, χ^2 test (qualitative characteristics) or 2-sided t test or Mann-Whitney (quantitative characteristics) U test will be conducted. To visualize data, boxplots, bar plots, and heatmaps will be used. In the initial exploratory analyses, we will analyze each digital biomarker separately that will be followed by their aggregation to identify the most informative biomarkers and their sets for different clinical and patient-reported outcome measures of patients with cancer. Mixed effects regression models will be used for the analysis of longitudinal data obtained from smartphone sensors. For all hypotheses, statistically significant differences will be evaluated at a significance level of .05, and multiple comparison adjustments will be performed. Statistical analysis will be employed using SPSS software (version 27; IBM Corp) and RStudio (version 2022.12.0+353; Posit, PBC).

Results

Patient recruitment and data collection are expected to be completed by September 2023. As of July 2023, we have reached the planned recruitment target, and patients are undergoing follow-up. The final results of this study should be available within 6 months after the study completion.

Discussion

In this prospective observational cohort study, 200 patients with cancer will be followed up for 6 months by using (1) continuously and passively generated data from sensors (accelerometer, gyroscope, GPS) of smartphone devices (digital phenotyping) and (2) actively collected data using questionnaires

for assessment of quality of life, symptoms, depression, anxiety, and COVID-19 fear. Disease progression and treatment complications will be evaluated during clinic visits. This study will allow to better understand the potential value of passively generated data from smartphone sensors for remote real-time monitoring of patients with cancer and anticipation of disease progression or trajectories, treatment complications, and unfavorable patient-reported outcomes.

Digital phenotyping is a promising approach in oncology that enables utilization of data that are passively generated by patients in their natural environments. It is a user-friendly approach because it uses personal digital devices, thus causing limited interruption of daily routine and device use habits. High and growing adoption of smartphones across age groups underscores the scalability of digital phenotyping approaches [58]. However, the barriers for deploying and integrating the digital phenotyping approach in oncology workflow should be considered and addressed, including data privacy and security concerns and participant willingness to share data. Caveats of analysis of passively generated data and its integration with routinely collected clinical and patient-reported data should be overcome to provide clinically meaningful digital biomarkers that can provide additional clinical value above and beyond the standard of care of patients with cancer. Emerging evidence suggests that this approach can be promising to predict the complications of cancer treatment [42,43]. However, it remains largely unclear if this approach can accurately prognosticate disease and treatment trajectories of patients with cancer. Our findings will allow us to better understand the potential clinical value of digital biomarkers for the prediction of clinical and patient-centered trajectories of patients with cancer.

The limitation of this study is the inclusion of patients with different cancer diagnoses and undergoing various treatments that can have a direct impact on the digital biomarkers included in this study. However, this will allow us to better understand which patients could potentially benefit the most from such a monitoring approach. The use of sensors of personal smartphone devices will provide real-world data with regard to patient behavior in their natural home environment but is subjected to individual differences of smartphone use habits. We hope that our study will provide further insights regarding the value of digital biomarkers and will be used to inform the planning and implementation of interventional clinical trials in oncology.

Acknowledgments

This work was supported by the Research Council of Lithuania grant 01.2.2-LMT-K-718-05-0085.

Data Availability

Data will be available 6 months after study completion.

Conflicts of Interest

None declared.

References

1. Hastings K, Boothroyd D, Kapphahn K, Hu J, Rehkopf D, Cullen M, et al. Socioeconomic differences in the epidemiologic transition from heart disease to cancer as the leading cause of death in the United States, 2003 to 2015. *Ann Intern Med* 2018 Nov 13;169(12):836 [doi: [10.7326/m17-0796](https://doi.org/10.7326/m17-0796)]
2. Dagenais G, Leong DP, Rangarajan S, Lanan F, Lopez-Jaramillo P, Gupta R, et al. Variations in common diseases, hospital admissions, and deaths in middle-aged adults in 21 countries from five continents (PURE): a prospective cohort study. *Lancet* 2020 Mar 07;395(10226):785-794 [doi: [10.1016/S0140-6736\(19\)32007-0](https://doi.org/10.1016/S0140-6736(19)32007-0)] [Medline: [31492501](https://pubmed.ncbi.nlm.nih.gov/31492501/)]
3. OECD, European Observatory on Health Systems and Policies. Lithuania: country health profile. OECD iLibrary. URL: https://www.oecd-ilibrary.org/social-issues-migration-health/lithuania-country-health-profile-2017_9789264283473-en [accessed 2023-03-06]
4. Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Nikšić M, CONCORD Working Group. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet* 2018 Mar 17;391(10125):1023-1075 [FREE Full text] [doi: [10.1016/S0140-6736\(17\)33326-3](https://doi.org/10.1016/S0140-6736(17)33326-3)] [Medline: [29395269](https://pubmed.ncbi.nlm.nih.gov/29395269/)]
5. Coleman MP, Quaresma M, Berrino F, Lutz J, De Angelis R, Capocaccia R, et al. Cancer survival in five continents: a worldwide population-based study (CONCORD). *The Lancet Oncology* 2008 Aug;9(8):730-756 [doi: [10.1016/s1470-2045\(08\)70179-7](https://doi.org/10.1016/s1470-2045(08)70179-7)]
6. Weir HK, Thompson TD, Soman A, Møller B, Leadbetter S. The past, present, and future of cancer incidence in the United States: 1975 through 2020. *Cancer* 2015 Jun 01;121(11):1827-1837 [FREE Full text] [doi: [10.1002/cncr.29258](https://doi.org/10.1002/cncr.29258)] [Medline: [25649671](https://pubmed.ncbi.nlm.nih.gov/25649671/)]
7. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA Cancer J Clin* 2018 Jan;68(1):7-30 [FREE Full text] [doi: [10.3322/caac.21442](https://doi.org/10.3322/caac.21442)] [Medline: [29313949](https://pubmed.ncbi.nlm.nih.gov/29313949/)]
8. Hanna TP, King WD, Thibodeau S, Jalink M, Paulin GA, Harvey-Jones E, et al. Mortality due to cancer treatment delay: systematic review and meta-analysis. *BMJ* 2020 Nov 04;371:m4087 [FREE Full text] [doi: [10.1136/bmj.m4087](https://doi.org/10.1136/bmj.m4087)] [Medline: [33148535](https://pubmed.ncbi.nlm.nih.gov/33148535/)]
9. Rowland SP, Fitzgerald JE, Holme T, Powell J, McGregor A. What is the clinical value of mHealth for patients? *NPJ Digit Med* 2020;3:4 [FREE Full text] [doi: [10.1038/s41746-019-0206-x](https://doi.org/10.1038/s41746-019-0206-x)] [Medline: [31970289](https://pubmed.ncbi.nlm.nih.gov/31970289/)]
10. Johns Hopkins Coronavirus Resource Center. URL: <https://coronavirus.jhu.edu/> [accessed 2023-01-23]
11. Liang W, Guan W, Chen R, Wang W, Li J, Xu K, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *The Lancet Oncology* 2020 Mar;21(3):335-337 [doi: [10.1016/s1470-2045\(20\)30096-6](https://doi.org/10.1016/s1470-2045(20)30096-6)]
12. Rogado J, Obispo B, Pangua C, Serrano-Montero G, Martín Marino A, Pérez-Pérez M, et al. COVID-19 transmission, outcome and associated risk factors in cancer patients at the first month of the pandemic in a Spanish hospital in Madrid. *Clin Transl Oncol* 2020 Dec;22(12):2364-2368 [FREE Full text] [doi: [10.1007/s12094-020-02381-z](https://doi.org/10.1007/s12094-020-02381-z)] [Medline: [32449128](https://pubmed.ncbi.nlm.nih.gov/32449128/)]
13. Monin L, Laing A, Muñoz-Ruiz M, McKenzie D, del Molino del Barrio I, Alaguthurai T, et al. Safety and immunogenicity of one versus two doses of the COVID-19 vaccine BNT162b2 for patients with cancer: interim analysis of a prospective observational study. *The Lancet Oncology* 2021 Jun;22(6):765-778 [FREE Full text] [doi: [10.1016/S1470-2045\(21\)00213-8](https://doi.org/10.1016/S1470-2045(21)00213-8)]
14. Kuderer NM, Choueiri TK, Shah DP, Shyr Y, Rubinstein SM, Rivera DR, COVID-19 Cancer Consortium. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet* 2020 Jun 20;395(10241):1907-1918 [FREE Full text] [doi: [10.1016/S0140-6736\(20\)31187-9](https://doi.org/10.1016/S0140-6736(20)31187-9)] [Medline: [32473681](https://pubmed.ncbi.nlm.nih.gov/32473681/)]
15. Garassino MC, Whisenant JG, Huang L, Trama A, Torri V, Agustoni F, TERAVOLT investigators. COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study. *Lancet Oncol* 2020 Jul;21(7):914-922 [FREE Full text] [doi: [10.1016/S1470-2045\(20\)30314-4](https://doi.org/10.1016/S1470-2045(20)30314-4)] [Medline: [32539942](https://pubmed.ncbi.nlm.nih.gov/32539942/)]
16. Vijenthira A, Gong IY, Fox TA, Booth S, Cook G, Fattizzo B, et al. Outcomes of patients with hematologic malignancies and COVID-19: a systematic review and meta-analysis of 3377 patients. *Blood* 2020 Dec 17;136(25):2881-2892 [FREE Full text] [doi: [10.1182/blood.2020008824](https://doi.org/10.1182/blood.2020008824)] [Medline: [33113551](https://pubmed.ncbi.nlm.nih.gov/33113551/)]
17. Saini KS, Tagliamento M, Lambertini M, McNally R, Romano M, Leone M, et al. Mortality in patients with cancer and coronavirus disease 2019: A systematic review and pooled analysis of 52 studies. *Eur J Cancer* 2020 Nov;139:43-50 [FREE Full text] [doi: [10.1016/j.ejca.2020.08.011](https://doi.org/10.1016/j.ejca.2020.08.011)] [Medline: [32971510](https://pubmed.ncbi.nlm.nih.gov/32971510/)]
18. Riera R, Bagattini, Pacheco RL, Pachito DV, Roitberg F, Ilbawi A. Delays and disruptions in cancer health care due to COVID-19 pandemic: systematic review. *JCO Glob Oncol* 2021 Feb;7:311-323 [FREE Full text] [doi: [10.1200/GO.20.00639](https://doi.org/10.1200/GO.20.00639)] [Medline: [33617304](https://pubmed.ncbi.nlm.nih.gov/33617304/)]
19. Editorial. COVID-19 and cancer: 1 year on. *The Lancet Oncology* 2021 Apr;22(4):411 [doi: [10.1016/s1470-2045\(21\)00148-0](https://doi.org/10.1016/s1470-2045(21)00148-0)]
20. Maringe C, Spicer J, Morris M, Purushotham A, Nolte E, Sullivan R, et al. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study. *Lancet Oncol* 2020 Aug;21(8):1023-1034 [FREE Full text] [doi: [10.1016/S1470-2045\(20\)30388-0](https://doi.org/10.1016/S1470-2045(20)30388-0)] [Medline: [32702310](https://pubmed.ncbi.nlm.nih.gov/32702310/)]
21. Yu H, Zhou Z, Mo Q, et al. Prevalence of anxiety and depression among cancer patients during the COVID-19 pandemic: a systematic review and meta-analysis. *Research Square*. :1-16 Preprint posted online on December 28, 2020. [doi: [10.21203/rs.3.rs-133466/v1](https://doi.org/10.21203/rs.3.rs-133466/v1)]

22. Islam JY, Vidot DC, Camacho-Rivera M. Evaluating mental health-related symptoms among cancer survivors during the COVID-19 pandemic: an analysis of the COVID impact survey. *JCO Oncology Practice* 2021 Sep;17(9):e1258-e1269 [doi: [10.1200/op.20.00752](https://doi.org/10.1200/op.20.00752)]
23. Mao Y, Lin W, Wen J, Chen G. Impact and efficacy of mobile health intervention in the management of diabetes and hypertension: a systematic review and meta-analysis. *BMJ Open Diabetes Res Care* 2020 Sep;8(1):e001225 [FREE Full text] [doi: [10.1136/bmjdr-2020-001225](https://doi.org/10.1136/bmjdr-2020-001225)] [Medline: [32988849](https://pubmed.ncbi.nlm.nih.gov/32988849/)]
24. Marcolino MS, Oliveira JAQ, D'Agostino M, Ribeiro AL, Alkmim MBM, Novillo-Ortiz D. The impact of mHealth interventions: systematic review of systematic reviews. *JMIR Mhealth Uhealth* 2018 Jan 17;6(1):e23 [FREE Full text] [doi: [10.2196/mhealth.8873](https://doi.org/10.2196/mhealth.8873)] [Medline: [29343463](https://pubmed.ncbi.nlm.nih.gov/29343463/)]
25. mHealth: new horizons for health through mobile technologies. In: WHO Global Observatory for eHealth. Geneva: World Health Organization; 2011.
26. mHealth: new horizons for health through mobile technologies: second global survey on eHealth. World Health Organization. 2011. URL: <https://www.afro.who.int/publications/mhealth-new-horizons-health-through-mobile-technologie> [accessed 2022-09-22]
27. Grand View Research. URL: <https://www.grandviewresearch.com/industry-analysis/mhealth-app-market> [accessed 2023-01-20]
28. Kumar N, Khunger M, Gupta A, Garg N. A content analysis of smartphone-based applications for hypertension management. *J Am Soc Hypertens* 2015 Feb;9(2):130-136 [doi: [10.1016/j.jash.2014.12.001](https://doi.org/10.1016/j.jash.2014.12.001)] [Medline: [25660364](https://pubmed.ncbi.nlm.nih.gov/25660364/)]
29. Royce TJ, Sanoff HK, Rewari A. Telemedicine for cancer care in the time of COVID-19. *JAMA Oncol* 2020 Nov 01;6(11):1698-1699 [doi: [10.1001/jamaoncol.2020.2684](https://doi.org/10.1001/jamaoncol.2020.2684)] [Medline: [32672821](https://pubmed.ncbi.nlm.nih.gov/32672821/)]
30. McCall B. Could telemedicine solve the cancer backlog? *The Lancet Digital Health* 2020 Sep;2(9):e456-e457 [doi: [10.1016/s2589-7500\(20\)30194-1](https://doi.org/10.1016/s2589-7500(20)30194-1)]
31. Bakouny Z, Hawley JE, Choueiri TK, Peters S, Rini BI, Warner JL, et al. COVID-19 and cancer: Current challenges and perspectives. *Cancer Cell* 2020 Nov 09;38(5):629-646 [FREE Full text] [doi: [10.1016/j.ccell.2020.09.018](https://doi.org/10.1016/j.ccell.2020.09.018)] [Medline: [33049215](https://pubmed.ncbi.nlm.nih.gov/33049215/)]
32. Onnela J, Rauch SL. Harnessing smartphone-based digital phenotyping to enhance behavioral and mental health. *Neuropsychopharmacology* 2016 Jun;41(7):1691-1696 [FREE Full text] [doi: [10.1038/npp.2016.7](https://doi.org/10.1038/npp.2016.7)] [Medline: [26818126](https://pubmed.ncbi.nlm.nih.gov/26818126/)]
33. Torous J, Kiang MV, Lorme J, Onnela J. New tools for new research in psychiatry: a scalable and customizable platform to empower data driven smartphone research. *JMIR Ment Health* 2016 May 05;3(2):e16 [FREE Full text] [doi: [10.2196/mental.5165](https://doi.org/10.2196/mental.5165)] [Medline: [27150677](https://pubmed.ncbi.nlm.nih.gov/27150677/)]
34. Ebner-Priemer U, Santangelo P. Digital phenotyping: hype or hope? *The Lancet Psychiatry* 2020 Apr;7(4):297-299 [FREE Full text] [doi: [10.1016/s2215-0366\(19\)30380-3](https://doi.org/10.1016/s2215-0366(19)30380-3)]
35. Garcia-Gancedo L, Kelly ML, Lavrov A, Parr J, Hart R, Marsden R, et al. Objectively monitoring amyotrophic lateral sclerosis patient symptoms during clinical trials with sensors: observational study. *JMIR Mhealth Uhealth* 2019 Dec 20;7(12):e13433 [FREE Full text] [doi: [10.2196/13433](https://doi.org/10.2196/13433)] [Medline: [31859676](https://pubmed.ncbi.nlm.nih.gov/31859676/)]
36. Chitnis T, Glanz BI, Gonzalez C, Healy BC, Saraceno TJ, Sattarnezhad N, et al. Quantifying neurologic disease using biosensor measurements in-clinic and in free-living settings in multiple sclerosis. *NPJ Digit Med* 2019;2:123 [FREE Full text] [doi: [10.1038/s41746-019-0197-7](https://doi.org/10.1038/s41746-019-0197-7)] [Medline: [31840094](https://pubmed.ncbi.nlm.nih.gov/31840094/)]
37. McLean SA, Ressler K, Koenen KC, Neylan T, Germine L, Jovanovic T, et al. The AURORA Study: a longitudinal, multimodal library of brain biology and function after traumatic stress exposure. *Mol Psychiatry* 2020 Feb;25(2):283-296 [FREE Full text] [doi: [10.1038/s41380-019-0581-3](https://doi.org/10.1038/s41380-019-0581-3)] [Medline: [31745239](https://pubmed.ncbi.nlm.nih.gov/31745239/)]
38. Cormack F, McCue M, Taptiklis N, Skirrow C, Glazer E, Panagopoulos E, et al. Wearable technology for high-frequency cognitive and mood assessment in major depressive disorder: longitudinal observational study. *JMIR Ment Health* 2019 Nov 18;6(11):e12814 [FREE Full text] [doi: [10.2196/12814](https://doi.org/10.2196/12814)] [Medline: [31738172](https://pubmed.ncbi.nlm.nih.gov/31738172/)]
39. Barnett I, Torous J, Staples P, Sandoval L, Keshavan M, Onnela J. Relapse prediction in schizophrenia through digital phenotyping: a pilot study. *Neuropsychopharmacology* 2018 Jul;43(8):1660-1666 [FREE Full text] [doi: [10.1038/s41386-018-0030-z](https://doi.org/10.1038/s41386-018-0030-z)] [Medline: [29511333](https://pubmed.ncbi.nlm.nih.gov/29511333/)]
40. Teo JX, Davila S, Yang C, Hii AA, Pua CJ, Yap J, et al. Digital phenotyping by consumer wearables identifies sleep-associated markers of cardiovascular disease risk and biological aging. *Commun Biol* 2019;2:361 [FREE Full text] [doi: [10.1038/s42003-019-0605-1](https://doi.org/10.1038/s42003-019-0605-1)] [Medline: [31602410](https://pubmed.ncbi.nlm.nih.gov/31602410/)]
41. Cote DJ, Barnett I, Onnela J, Smith TR. Digital phenotyping in patients with spine disease: a novel approach to quantifying mobility and quality of life. *World Neurosurg* 2019 Jun;126:e241-e249 [FREE Full text] [doi: [10.1016/j.wneu.2019.01.297](https://doi.org/10.1016/j.wneu.2019.01.297)] [Medline: [30797933](https://pubmed.ncbi.nlm.nih.gov/30797933/)]
42. Wright AA, Raman N, Staples P, Schonholz S, Cronin A, Carlson K, et al. The HOPE pilot study: harnessing patient-reported outcomes and biometric data to enhance cancer care. *JCO Clin Cancer Inform* 2018 Dec;2:1-12 [FREE Full text] [doi: [10.1200/CCI.17.00149](https://doi.org/10.1200/CCI.17.00149)] [Medline: [30652585](https://pubmed.ncbi.nlm.nih.gov/30652585/)]
43. Panda N, Solsky I, Huang EJ, Lipsitz S, Pradarelli JC, Delisle M, et al. Using smartphones to capture novel recovery metrics after cancer surgery. *JAMA Surg* 2020 Feb 01;155(2):123-129 [FREE Full text] [doi: [10.1001/jamasurg.2019.4702](https://doi.org/10.1001/jamasurg.2019.4702)] [Medline: [31657854](https://pubmed.ncbi.nlm.nih.gov/31657854/)]

44. Low C. Harnessing consumer smartphone and wearable sensors for clinical cancer research. *NPJ Digit Med* 2020;3:140 [FREE Full text] [doi: [10.1038/s41746-020-00351-x](https://doi.org/10.1038/s41746-020-00351-x)] [Medline: [33134557](https://pubmed.ncbi.nlm.nih.gov/33134557/)]
45. Jacobsen M, Gholamipour R, Dembek TA, Rottmann P, Verket M, Brandts J, et al. Wearable based monitoring and self-supervised contrastive learning detect clinical complications during treatment of hematologic malignancies. *NPJ Digit Med* 2023 Jun 02;6(1):105 [FREE Full text] [doi: [10.1038/s41746-023-00847-2](https://doi.org/10.1038/s41746-023-00847-2)] [Medline: [37268734](https://pubmed.ncbi.nlm.nih.gov/37268734/)]
46. Barnett I, Torous J, Reeder H, Baker J, Onnela J. Determining sample size and length of follow-up for smartphone-based digital phenotyping studies. *J Am Med Inform Assoc* 2020 Dec 09;27(12):1844-1849 [FREE Full text] [doi: [10.1093/jamia/ocaa201](https://doi.org/10.1093/jamia/ocaa201)] [Medline: [33043370](https://pubmed.ncbi.nlm.nih.gov/33043370/)]
47. Beiwe. URL: <https://jponnela.com/bf20/technology/> [accessed 2023-09-11]
48. Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation) (Text with EEA relevance). *EUR-Lex*. 2016 Apr 27. URL: <https://eur-lex.europa.eu/eli/reg/2016/679/oj> [accessed 2023-01-30]
49. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *American Journal of Clinical Oncology* 1982;5(6):649-656 [doi: [10.1097/00000421-198212000-00014](https://doi.org/10.1097/00000421-198212000-00014)]
50. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993 Mar 03;85(5):365-376 [doi: [10.1093/jnci/85.5.365](https://doi.org/10.1093/jnci/85.5.365)] [Medline: [8433390](https://pubmed.ncbi.nlm.nih.gov/8433390/)]
51. Bunevičius A, Tamašauskas Š, Tamašauskas A, Deltuva V. Evaluation of health-related quality of life in Lithuanian brain tumor patients using the EORTC brain cancer module. *Medicina (Kaunas)* 2012;48(11):588-594 [FREE Full text] [Medline: [23455894](https://pubmed.ncbi.nlm.nih.gov/23455894/)]
52. Bunevicius A, Deltuva V, Tamasauskas S, Tamasauskas A, Bunevicius R. Screening for psychological distress in neurosurgical brain tumor patients using the Patient Health Questionnaire-2. *Psychooncology* 2013 Aug;22(8):1895-1900 [doi: [10.1002/pon.3237](https://doi.org/10.1002/pon.3237)] [Medline: [23233453](https://pubmed.ncbi.nlm.nih.gov/23233453/)]
53. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001 Sep;16(9):606-613 [FREE Full text] [doi: [10.1046/j.1525-1497.2001.016009606.x](https://doi.org/10.1046/j.1525-1497.2001.016009606.x)] [Medline: [11556941](https://pubmed.ncbi.nlm.nih.gov/11556941/)]
54. Pranckeviciene A, Saudargiene A, Gecaite-Stonciene J, Liaugaudaite V, Griskova-Bulanova I, Simkute D, et al. Validation of the patient health questionnaire-9 and the generalized anxiety disorder-7 in Lithuanian student sample. *PLoS One* 2022;17(1):e0263027 [FREE Full text] [doi: [10.1371/journal.pone.0263027](https://doi.org/10.1371/journal.pone.0263027)] [Medline: [35085349](https://pubmed.ncbi.nlm.nih.gov/35085349/)]
55. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med* 2006 May 22;166(10):1092-1097 [doi: [10.1001/archinte.166.10.1092](https://doi.org/10.1001/archinte.166.10.1092)] [Medline: [16717171](https://pubmed.ncbi.nlm.nih.gov/16717171/)]
56. Buneviciene I, Bunevicius R, Bagdonas S, Bunevicius A. Psychometric properties of the COVID-19 Fears questionnaire for chronic medical conditions in patients with pre-existing medical conditions. *Health Soc Care Community* 2022 Sep;30(5):e2866-e2873 [doi: [10.1111/hsc.13730](https://doi.org/10.1111/hsc.13730)] [Medline: [35088481](https://pubmed.ncbi.nlm.nih.gov/35088481/)]
57. Thombs B, Tao L, Wu Y, et al. Preliminary COVID-19 fears questionnaire: systemic sclerosis and chronic medical conditions versions. *OSF Preprints*. Preprint posted online on April 06, 2020. [doi: [10.31219/osf.io/m2ybt](https://doi.org/10.31219/osf.io/m2ybt)]
58. Share of adults in the United States who owned a smartphone from 2015 to 2021, by age group. *Statista*. URL: <https://www.statista.com/statistics/489255/percentage-of-us-smartphone-owners-by-age-group/> [accessed 2023-04-30]

Abbreviations

- EORTC QLQ-C30:** European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire
- GAD-7:** General Anxiety Disorder-7
- mHealth:** mobile health
- PHQ-9:** Patient Health Questionnaire-9
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Edited by A Mavragani; submitted 19.05.23; peer-reviewed by K Le Du, N Jacobson; comments to author 21.07.23; revised version received 24.07.23; accepted 31.07.23; published 10.10.23

Please cite as:

Jenciūtė G, Kasputytė G, Bunevičienė I, Korobeinikova E, Vaitiekus D, Inčiūra A, Jaruševičius L, Bunevičius R, Krikštolaitis R, Krilavičius T, Juozaitytė E, Bunevičius A

Digital Phenotyping for Monitoring and Disease Trajectory Prediction of Patients With Cancer: Protocol for a Prospective Observational Cohort Study

JMIR Res Protoc 2023;12:e49096

URL: <https://www.researchprotocols.org/2023/1/e49096>

doi: [10.2196/49096](https://doi.org/10.2196/49096)

PMID: [37815850](https://pubmed.ncbi.nlm.nih.gov/37815850/)

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