Commentary

Impact of the COVID-19 Pandemic on Telehealth Research in Cancer Prevention and Care: A Call to Sustain Telehealth Advances

Elyse R. Park, PhD, MPH [1,2]; Caroline Chiles, MD[3]; Paul M. Cinciripini, PhD[4]; Kristie L. Foley, PhD[3]; Lisa M. Fucito, PhD[5,6]; Jennifer S. Haas, MD[1,2]; Anne M. Joseph, MD[7]; Jamie S. Ostroff, PhD[8]; Nancy A. Rigotti, MD[1,2]; Donna R. Shelley, MD[9]; Kathryn L. Taylor, PhD[10]; Steven B. Zeliadt, PhD, MPH[11,12]; Benjamin A. Toll, PhD[13,14]; and On behalf of the Smoking Cessation at Lung Examination (SCALE) Research Group

History of Telehealth and Barriers to the Use of Telehealth in Clinical Research

History has taught us to adapt and learn from crises to improve how we deliver care and conduct research to improve clinical outcomes. The coronavirus disease 2019 (COVID-19) pandemic is a modern public health crisis that is an opportunity for us to evaluate how to protect and expand our clinical care and research mission to improve the physical and mental health of patients when engaged in cancer prevention, early detection, and treatment research.

The remote delivery of clinical services started in the 1960s with the National Aeronautics and Space Administration (NASA) establishing the modality to treat astronauts.[1] Twenty years ago, the Centers for Medicare and Medicaid Services began reimbursing remote services in rural and underserved areas.[2] To our knowledge, the widespread adoption of telehealth (the remote delivery of clinical and educational activities, services, and research) for the delivery of clinical care has been very limited for a multitude of reasons, including concerns regarding its efficacy compared with traditional encounters, the cost, adequate health insurance reimbursement, and privacy concerns. However, at the onset of the COVID-19 pandemic, clinical practices quickly converted to the telehealth delivery of care while appropriately maintaining and abiding by privacy laws and, for many, hoping that reimbursement would catch up to practice. Thus, COVID-19 catapulted telehealth to become a reality for many patients and providers.

There are many opportunities to use remote technologies to tackle long-standing inequities in clinical trial research. Over 25 years ago, the National Institutes of Health Revitalization Act of 1993 publicized the critical need to expand access to clinical trials to include women and racial and/or ethnic minorities.[3] Racial and ethnic inequities in cancer clinical trial participation are well established, with access barriers including competing demands (time and financial burden) and mistrust (fears of mistreatment, unknown research procedures, and unintended consequences).[4-6] Telehealth can ameliorate these long-standing access issues by reducing the burden of travel to cancer centers for trial visits or relocation, and thus the associated costs of trial participation (eg, time off of work, childcare responsibilities). Furthermore, telehealth can facilitate the presence of family members at visits as an opportunity for in-depth dialogue regarding patients' fears and underlying mistrust concerning participation in cancer clinical trials. One of the great benefits of telehealth is its ability to combat disparities in cancer care and trial accessibility, thereby improving access to care and opportunities to enroll in therapeutic and nontherapeutic trials for all patients. We currently have an opportunity to improve equity in trial participation because telehealth circumvents many barriers to participation among patients of lower socioeconomic status and/or those who are vulnerable by eliminating travel logistics, decreasing the amount of time lost from work, and providing greater language and/or literacy options for delivery. As of 2019, approximately 81% of adults in the United States own smartphones, many of whom are of low socioeconomic status,[7] and 90% use the internet,[8] representing an extraordinary and continually expanding opportunity to interface with patients who are engaged in research. However, to ensure that existing disparities do not widen, it will be

Corresponding Author: Elyse R. Park, PhD, MPH, Mass General Hospital/Harvard Medical School, Departments of Psychiatry and Medicine, Health Policy Research Center, 100 Cambridge Street, 16th fl, Boston, MA 02114 (epark@mgh.harvard.edu).

[1]Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; [2]Dana Farber/Harvard Cancer Center, Boston, Massachusetts; [3]Wake Forest School of Medicine, Winston-Salem, North Carolina; [4]The University of Texas MD Anderson Cancer Center, Houston, Texas; [5]Yale Cancer Center, New Haven, Connecticut; [6]Yale School of Medicine, Yale University, New Haven, Connecticut; [7]University of Minnesota Medical School, Minneapolis, Minnesota; [8]Memorial Sloan Kettering Cancer Center, New York, New York; [9]New York University School of Global Public Health, New York, New York; [10]Georgetown Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC; [11]University of Washington School of Public Health, Seattle, Washington; [12]Veterans Affairs Puget Sound Health Care System, Seattle, Washington; [13]Hollings Cancer Center, Charleston, South Carolina; [14]Medical University of South Carolina, Charleston, South Carolina

DOI: 10.1002/cncr.33227, **Received:** June 8, 2020; **Revised:** August 23, 2020; **Accepted:** August 28, 2020, **Published online** Month 00, 2020 in Wiley Online Library (wileyonlinelibrary.com)

critical to engage in problem-solving (eg, the provision of iPads or webcams) to ensure that technology access does not impede trial participation.

Virtual technologies have been in existence for a significant amount of time (ie, digital data collection has existed for >20 years) and are transformative for clinical research, but their uptake has been slow. Barriers to the uptake of telehealth include providers and/or staff (lack of technological training, resistance to change, perception of impersonal care), organizational (cost, lack of reimbursement, liability and privacy concerns), and patient (access to devices and internet, digital literacy, familiarity and/or comfort with technology) barriers.[9,10] However, in response to the COVID-19 pandemic, institutions are expediting and expanding their existing remote research infrastructure to preserve ongoing research. This expansion includes transitions to remote laboratories for biospecimen processing; shipping research investigational products; remuneration changes to reloadable debit cards, e-checks, or gift codes; and modifications to electronic consent (eg, e-signature, e-consent) and study visits (with electronic health record [EHR] documentation required). To facilitate the ability of investigators and research staff to work remotely, institutional encrypted equipment was loaned (eg, laptops, webcams) or purchased (eg, printers), programs for source document changes (eg, editable PDFs) were made available, Health Insurance Portability and Accountability Act (HIPAA)–compliant software programs (eg, Zoom accounts, Microsoft teams) were provided, and HIPAA-compliant shared drives were established.

Impact of the COVID-19 Pandemic on the Use of Telehealth for Clinical Research

In advancing the use of virtual methods to conduct clinical research, it is integral to follow the international standards set by the International Conference on Harmonization Good Clinical Practice guidelines to protect the rights and confidentiality of study participants. In this article, we have discussed infrastructure changes to institutions, institutional review board (IRB) criteria for the review of remote research, and privacy guidelines intended to facilitate compliance with the spirt of the 13 core principles of the International Conference on Harmonization Good Clinical Practice guidelines.

In response to COVID-19, institutions made policies regarding permitted research; some existing research and new research was halted. The continuation of existing studies was contingent on institutional approval, which required design modifications to eliminate in-person contact, including recruitment, delivery, and data collection activities (surveys and biospecimens). Institutions made modifications to their IRB procedures. Some IRB reviews were halted (eg, new protocols, amendments to existing protocols) and some IRBs changed their procedures. Examples of changes included: 1) IRB approval being waived for study procedures that were modified from in-person to telehealth (minor deviation); 2) expedited IRB procedures were developed for protocol amendments needed to maintain research; and 3) IRB-specific review panels were established for COVID-19–specific studies.

This public health crisis has highlighted the importance of using both traditional in-person as well as decentralized or virtual modalities: in other words, "blended designs" with which to conduct clinical research. These virtual research strategies include leveraging electronic research tools: 1) querying EHRs to automate recruitment; 2) conducting virtual outreach (eg, sending HIPAA-compliant clinician videos that describe a trial, thereby removing the need for patients to come into the hospital and/or clinic to interface with a clinician for trial access); 3) conducting remote informed consent (waiving the requirement for written informed consent); 4) telephone-based and video-based intervention delivery; and 5) using remote collection methods for data collection (eg, via virtual and/or electronic telemetry), including biological tests. These virtual research strategies, particularly the waiving of written informed consent and permitting e-consenting, have been allowed by the Office for Human Research Protections since July 2018 when the Common Rule was revised.[11] However, COVID-19 has catalyzed institutions to fast-track IRB amendments to allow for virtual consent, intervention delivery, and data collection to preserve the scientific integrity of clinical research.

In response to the pandemic, the National Cancer Institute (NCI) central IRB released policies to support remote consent and, with these policies, the NCI is leading the charge to accommodate patients and research participants during this critical time. For example, the NCI central IRB provided guidelines specifying that the investigator or designee and the potential participant can conduct remote consent. These guidelines stipulate that the informed consent must be sent to the participant prior to this conversation and that a witness must listen to the investigator and/or designee and participant. After the informed consent, documentation stating the witness's name and presence for the informed consent process must be included. However, the requirement for the witness's signature is determined by local institutional policy.

Smoking Cessation at Lung Examination Collaboration as a Case Study for the Use of Telehealth in Clinical Research

The Smoking Cessation at Lung Examination (SCALE) collaboration is an initiative sponsored by the NCI to conduct research on tobacco treatment within a specific group, namely long-term smokers (≥30 pack-years) who are screened for lung cancer using low-dose computed tomography (LDCT).[12] The pairing of tobacco treatment and LDCT screening has the potential to generate a large pool of data regarding screening and tobacco cessation outcomes. These data will be valuable to researchers studying issues such as the incorporation of tobacco treatment into the LDCT screening visit or how to provide these services most effectively in a variety of lung cancer screening clinical settings. The purpose of the SCALE collaboration is to share data and methods from NCI-funded and Veterans Administration–funded research projects to enable cross-project research on smoking cessation interventions within the setting of LDCT screening for lung cancer.

SCALE investigators have demonstrated a range of feasible virtual methods for screening, enrolling, delivering the intervention, and evaluating outcomes that offer lessons for sustaining research and engaging participants who otherwise may be excluded from research. Within the SCALE research collaborative, we have endeavored to leverage virtual research strategies and overcome regulatory challenges to help mitigate the disruption to our work. With remote outreach and delivery, our institutions are using novel ways to identify patients, such as using social media platforms (eg, Reddit, Facebook). SCALE institutions also are using novel ways to reach patients. For example, study recruitment is enhanced through brief clinician videos (of a primary care physician and radiologist), which can be accessed through institutional websites (eg YouTube, Vidscrip). Communication with study patients is being conducted through email (eg, MyChart messages), text (eg, Twilio), and video visits and calls (eg, Zoom, Doxy.me, and Cisco Jabber). We are using the EHR to screen for eligibility among patients undergoing lung cancer screening and for the provision of remote consent (via telephone, web, messaging, or mail).

At the onset of the pandemic, several SCALE studies increased their use of remote consent or transitioned from in-person to remote consent. At SCALE sites, lung cancer screening (LCS) shared decision-making visits, which are required prior to LCS, for the most part are conducted remotely (ie, through secure video visits or telephone calls); accordingly, SCALE studies have transitioned from in-person approaches at the LCS clinic (eg, a study flyer) to remote outreach and consent via telephone or video conferencing.

Our behavioral counseling interventions are conducted via telehealth (telephone or video). Remote data collection is used for both self-reported and biochemical validation of smoking status. Self-reported data are collected either by telephone, mail, or web-based platforms. To verify tobacco abstinence, sites use mailed saliva, nicotine strips, and in-person carbon monoxide (CO) collection. Because in-person data collection now is greatly limited, some sites have transitioned to remote expired CO collection through the use of an iCO Smokerlyzer (Bedfont Scientific Ltd, Kent, UK), which can be used with a smartphone. Patients use the device and either take a photo or conduct a live video stream to verify their identity for the specimen collection.

Patient and participant privacy issues must be attended to and therefore it is imperative that systems are in place to protect potential participants without representing a barrier to access. It is important to note that the COVID-19 pandemic has demonstrated that institutions can work swiftly to develop policies that enable remote access while establishing and maintaining protections for research participants. Specifically, SCALE institutions have established guidelines for conducting study or clinical visits virtually that emphasize privacy issues. For example, HIPAA-compliant videoconferencing software must be used, which can be integrated into the EHR. The EHR encounter note must specify that the visit was performed remotely and/or via telehealth using synchronous video. Communication between visits must be done via the EHR platform or encrypted institutional email. Institutional email and texting cannot be used without prior consent.

As part of their institutional review processes, many SCALE institutions have created criteria for the review of remote-facilitated research. An example is that some institutions now require an additional level of review, conducted by research information security or data security review, for new studies or procedures. An ancillary information security committee reviews any proposed remote technology, cloud-based computing, and/or wearable devices. The details regarding where data will be stored and the associated data flow are reviewed to ensure that the research data are secure before

the study is approved by the IRB. Institutions also are leveraging and expanding patient portals for communication, as well as finding novel ways to reach patients via telephone and text.

Future Directions and Areas for Improvement

The COVID-19 crisis is a call to action to accelerate how we can build on this experience to inform clinical research in the future, independent of a pandemic or other life-altering event. Not all clinical research can be conducted using remote methods. Many aspects of therapeutic trials must be delivered in person (eg, biospecimen collection, scans, or chemotherapy), but components of telehealth participation and evaluation must be explored. As a research community, it is essential that we continue to identify novel means with which to interface virtually with patients and research participants. During this pandemic, those trials that accommodate remote strategies are the ones that still are functioning, thereby sustaining our research and workforce. Indeed, the COVID-19 pandemic represents a watershed moment in clinical research, and it is critically important that we maintain these changes once the pandemic passes and capture this momentum to advance clinical research. Furthermore, as clinical trials that had been paused reopen, we can creatively leverage virtual modalities toward "blended" models of clinical research implementation.

There are limitations to a reliance on remote-only means for clinical delivery and research within the setting of lung cancer screening. To begin with, shared decision making, a requirement for initiating lung cancer screening, can be affected by communication barriers during remote visits such as connectivity issues, environmental distractions, and a restricted view of patients on screen. Patients need to come in for the actual lung scan, yet the time period for this in-person encounter currently is constricted, thereby eliminating the opportunity for in-person meetings with research staff to discuss study participation. In-person study eligibility screening and baseline data collection, which previously were conducted via an iPad while patients were in the lung cancer screening clinic waiting room, have been eliminated. Last, the use of a remote CO monitor for outcomes data is limited because of barriers to the supply, IRBs not approving its use, and a lack of smartphone access for some individuals.

To our knowledge, it is unknown whether the changes made to sustain research during this public health crisis will have a true lasting impact, but it appears improbable that the sweeping changes made to allow for telehealth modalities will be rolled back entirely after the pandemic passes. It is imperative that the lessons learned from this crisis, and the plurality of remote strategies that have enabled our research during it, continue to sustain our patient access and clinical research in the future. Indeed, the COVID-19 pandemic has advanced telehealth research. This crisis has catalyzed a call for "blended" model trials such that both traditional in-person and virtual modalities are possible to facilitate and sustain cancer prevention, screening, and treatment research.

FUNDING SUPPORT

Supported by the following grants: R01CA207078, R01CA207158, R01CA196873, R01CA207442, R01CA166147, R01CA207228, R01CA207229, and VA HSR&D IIR-16-071.

CONFLICT OF INTEREST DISCLOSURES

Elyse R. Park has received grants from the National Cancer Institute for work performed as part of the current study and has received royalties for chapters on smoking cessation from UpToDate. Caroline Chiles has received a grant from the National Institutes of Health for work performed as part of the current study and serves on a Multidisciplinary Expert Advisory Panel for AstraZeneca for work performed outside of the current study. Paul M. Cinciripini has received a grant from Pfizer for work performed outside of the current study. Jennifer S. Haas has received a grant from the National Cancer Institute for work performed as part of the current study. Jamie S. Ostroff has received royalties from UpToDate for work performed outside of the current study. Nancy A. Rigotti has received a grant from the National Cancer Institute for work performed as part of the current study and has received royalties for chapters on smoking cessation from UpToDate for work performed outside of the current study and previously consulted for Achieve Life Sciences, the manufacturer of an investigational smoking cessation medication. Benjamin A. Toll has received grants from the National Cancer Institute, participated in an advisory group regarding e-cigarettes for Pfizer, and has testified on behalf of plaintiffs who have filed litigation against tobacco companies as part of work performed outside of the current study. The other authors made no disclosures.

REFERENCES

1. LeRouge C, Garfield MJ. Crossing the telemedicine chasm: have the U.S. barriers to widespread adoption of telemedicine been significantly reduced? *Int J Environ Res Public Health*. 2013;10:6472-6484.
2. Centers for Medicare and Medicaid Services, US Department of Health and Human Services. Telehealth services. Accessed April 9, 2020. http://go.cms.gov/mln-telehealth-services-icn901705
3. National Institutes of Health Revitalization Act of 1993, HR 4, 103rd Cong (1993).
4. Hamel LM, Penner LA, Albrecht TL, Heath E, Gwede CK, Eggly S. Barriers to clinical trial enrollment in racial and ethnic minority patients with cancer. *Cancer Control*. 2016;23:327-337.
5. Duma N, Vera Aguilera J, Paludo J, et al. Representation of minorities and women in oncology clinical trials: review of the past 14 years. *J Oncol Pract*. 2018;14:e1-e10.
6. George S, Duran N, Norris K. A systematic review of barriers and facilitators to minority research participation among African Americans, Latinos, Asian Americans, and Pacific Islanders. *Am J Public Health*. 2014;104:e16-e31.
7. Pew Research Center. Mobile fact sheet. Published 2019. Accessed September 24, 2020. https://www.pewresearch.org/internet/fact-sheet/mobile/
8. Pew Research Center. Internet/broadband fact sheet. Published 2019. Accessed September 24, 2020. https://www.pewresearch.org/internet/fact-sheet/internet-broadband/#who-uses-the-internet
9. Scott Kruse C, Karem P, Shifflett K, Vegi L, Ravi K, Brooks M. Evaluating barriers to adopting telemedicine worldwide: a systematic review. *J Telemed Telecare*. 2018;24:4-12.

10. Almathami HKY, Win KT, Vlahu-Gjorgievska E. Barriers and facilitators that influence telemedicine-based, real-time, online consultation at patients' homes: systematic literature review. *J Med Internet Res*. 2020;22:e16407. doi:10.2196/16407
11. Office for Human Research Protections, US Department of Health and Human Services. Revised Common Rule. Accessed April 13, 2020. https://www.hhs.gov/ohrp/regulations-and-policy/regulations/finalized-revisions-common-rule/index.html
12. Division of Cancer Control and Population Sciences, National Cancer Institute. Smoking cessation at lung examination: the SCALE collaboration. Published 2020. Accessed September 24, 2020. https://cancercontrol.cancer.gov/brp/tcrb/scale-collaboration.html