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Adaptation of Metabolomics and Microbiomic Research Protocols During the COVID-19 Pandemic

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Abstract

Background: When the COVID-19 pandemic hit in 2020, researchers in the P30 Center for the Study of Symptom Science, Metabolomics, and Multiple Chronic Conditions at Emory University's Nell Hodgson Woodruff School of Nursing faced major challenges in recruitment and data collection due to limited access to the clinic and community facilities and the risk of COVID-19 exposure associated with in-person study contact.

Objectives: The purpose of this paper is to (a) describe how a cadre of pilot/supplement principal investigators adapted their studies to allow for safe and trustworthy data collection during the COVID-19 pandemic (March 2020 through date of publication), and (b) discuss steps that facilitated the technical aspects of remote data collection, especially involving biological specimens.

Results: Four pilot studies and two administrative supplements within the center—all at different stages of execution—adopted various alternative remote recruitment, enrollment, and data and specimen collection approaches to continue their research endeavors in a way that maximized the safety of both the research participants and the research teams.

Discussion: The paper concludes with a discussion on the importance of a participant-centered approach when using remote methods, actions, or steps initiated to facilitate the technical aspects

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of remote data collection and reflections on the continued use of remote research strategies beyond the COVID-19 pandemic.

Keywords

data collection; pandemics; research design; specimen handling

The P30 Center for the Study of Symptom Science, Metabolomics, and Multiple Chronic Conditions was established at Emory University Nell Hodgson Woodruff School of Nursing in 2018 to strengthen the capacities of a diverse faculty of nurse scientists to conduct innovative translational research using metabolomics and microbiomic technologies to better understand symptoms in individuals with multiple chronic conditions (Corwin et al., 2021). The COVID-19 pandemic (March 2020 through date of publication) presented major challenges to in-person study visits and data collection for the Center's six research studies, leading nurse scientists to develop alternative protocols to minimize COVID-19 exposure risk for both participants and team members. Challenges also arose because of limited access to the clinic and community facilities early in the pandemic (March–September 2020).

The six Center studies include four pilot studies and two supplement studies that were at different stages at the start of the pandemic (Table 1). Two pilot studies were nearing the end of the data collection phase. Two pilot studies and one supplement had not enrolled any participants before the pandemic hit, and one supplement was in the middle of data collection.

The purpose of this paper is to describe how the pilot principal investigators (PIs) modified their studies to allow for safe and trustworthy data collection during the pandemic, discuss lessons learned, and provide steps initiated to facilitate technical aspects in remote data collection.

Methods: Challenges and Adaptations

Screening and Recruitment

Prior to the onset of the COVID-19 pandemic, screening and recruitment activities for all Center studies relied mostly on face-to-face interactions with potential participants. Studies with a defined clinic population prescreened and recruited eligible individuals at the clinic visit. Other strategies included use of clinic spaces to post flyers and/or clinical partners to distribute flyers for referral and attendance at community events and participant-related support groups. As patient recruitment and enrollment were dependent on the clinic or community setting for all studies, significant changes needed to be made to all study protocols. Alterations to screening and recruitment protocols were determined by each PI with input from the institutional review board (IRB) and P30 Center leadership. Studies that underwent significant changes to their protocol received approval from the program officer at the National Institute of Nursing Research (NINR). Considerations in developing remote recruitment or enhanced safety protocols included stage/enrollment of the study, clinic status, and type of data being collected.

Screening methods that worked well within remote study protocols included the use of clinic calendars to screen patients with clinic appointments or telehealth visits (Pilot 3) and the use of a clinical data warehouse affiliated with the university health care system to identify those who met eligibility criteria (Pilot 4). Eligible individuals were contacted via email or letter which described the purpose of the study, study timeline, and remote visit procedures. A follow-up phone call was made 1 week after sending the email or letter to gauge interest in the study.

Studies recruiting at community events and clinic spaces pivoted to contactless recruitment methods including the creation of a Facebook group, use of Facebook ads, partnering with relevant community organizations to disseminate study flyers electronically, and virtual presentations. Recruitment methods, such as Craigslist and ResearchMatch, which had been planned even prior to COVID-19, became even more critical.

For Supplement 1, recruiting patients during a clinic visit was critical for study success, as clinical data needed to be correlated with study data. The investigator worked with clinic partners to develop enhanced safety protocols, including personal protective equipment (PPE), to continue in-person recruitment once nonessential research was permitted to resume. Despite recruitment challenges posed by clinic de-densification efforts and increased use of telehealth, the researcher successfully resumed in-person recruitment. With a resurgence of COVID-19 in late December 2020, the investigator chose to cease clinic visits until she was fully vaccinated.

Informed Consent

Prior to COVID-19, all studies collected informed consent in person. For Supplement 1 that resumed in-person clinic visits, participants completed paper consent forms with the investigator in full PPE and social distancing. All other studies developed remote electronic consent protocols via Research Electronic Data Capture (REDCap), with the informed consent reviewed by the coordinator and the participant over the phone. Pilots 3 and 4 included an additional option for telephone informed consent.

Biological Specimens

Pre-COVID protocols for pilot studies included collection of blood via venipuncture, rectal swabs or subgingival microbiome specimens, and saliva for local inflammatory markers. With the move to remote data collection, two studies (Pilots 1 and 2) suspended collection of biological specimens for newly enrolled participants and 3-month follow-up visits. Supplement 1, which continued with in-person clinic visits using enhanced safety protocols, made minor modifications to pre-COVID biologic specimen collection. Wearing PPE and maintaining social distancing whenever possible, the researcher accompanied the participant to an outpatient laboratory where a phlebotomist collected tubes of blood for research purposes. After receiving instructions, participants self-collected the rectal swab in a private restroom in the clinic.

Semi-remote Specimen Collection Protocol—One study (Supplement 2) developed a semi-remote specimen data collection protocol in which participants self-collected samples

with pick-up of biospecimens by the research coordinator from participants' homes. The in-person protocol for this study included collection of blood for metabolomics and systemic inflammatory markers, subgingival plaque for subgingival microbiome, and saliva for oral inflammatory markers. Several protocol adaptations were required to maximize safety and allow participants to self-collect specimens from home. First, as this study was focused on oral health and the oral microbiome, it was decided that saliva would be collected for metabolomics instead of blood. This matrix is closer to the microbiome of interest and more adequately reflects oral microbiome metabolites and related pathways. Second, saliva was determined to be the most appropriate matrix to replace the collection of subgingival plaque for microbiome analysis. Subgingival plaque would not have been feasible for participants to collect independently, whereas saliva is easily self-collected; its microbiome is shed from various oral habitats and is representative of the overall oral microbiome (Yamashita & Takeshita, 2017). For measurement of systemic inflammatory markers, self-collected dried blood spots (DBS) replaced venipuncture (Mirowsky et al., 2015; Sakhi et al., 2015).

Participants received all necessary self-collection supplies (Table 3) along with a detailed instruction packet via United States Postal Service Priority Mail, a trackable service. For salivary microbiome, participants drooled 1 cc of saliva into a collection device (OMNIgene Oral 501, DNA Genotek). Saliva for both local inflammatory markers and metabolomics were collected by passive drool into a separate clean container. Whatman® 903 protein saver cards were used by participants to self-collect five DBS. Timing of specimen collection was an important consideration for this protocol design. While the salivary microbiome specimen can be kept at ambient temperatures for up to one year, saliva for metabolomics and oral inflammatory markers must be refrigerated immediately after collection and picked up within several hours for storage at −80°C. DBS must be air dried for at least 4 hr at room temperature prior to freezer storage. Detailed instructions, communication with the research coordinator, and in-person pick-up of the biospecimens from the participants' homes ensure fidelity to the specimen collection protocol.

Fully Remote Specimen Collection Protocol—Two studies (Pilots 3 and 4) that had not begun data collection before cessation of research developed fully remote protocols. Participants received all necessary self-collection supplies (Table 3), a detailed instruction packet, and prepaid return FedEx packaging. The fully remote protocols used Whatman® 903 protein saver cards for metabolomics, Mitra® volumetric absorptive microsampling (VAMS) devices (Neoteryx) for cytokines and other ELISA measures, and Omnigene•GUT for microbiome (DNA Genotek).

MITRA® VAMS devices overcome some challenges for quantitative bioanalysis. Using traditional DBS cards present challenges resulting in assay bias, particularly the hematocrit effect (a higher hematocrit value yields a smaller DBS; a lower hematocrit value yields a larger DBS) and lack of homogeneity (Harahap et al., 2020). VAMS provides an easy way to obtain, transport, and analyze remote collection blood source. The MITRA® device contains a porous tip for accurate and reproducible collection of a fixed volume of blood through the principle of wicking (Harahap et al., 2020). No air drying is required, and samples remain stable at room temperature for weeks. This approach was used for systemic inflammatory markers and study-specific biomarkers as it allows for quantitative analyses of proteins. The

Whatman® 903 protein saver card was used for metabolomics as it is the method preferred by the metabolomics core.

For untargeted metabolomics, DBS samples collected using Whatman cards were recently shown to have similar performance to plasma samples, with strongly concordant metabolite profiles after standardization (interclass correlation 0.52) and comparable performance in distinguishing cases and controls in a sample of 79 women living with HIV (Tobin et al., 2021). However, there were differences in the ability to detect different classes of metabolites; DBS were better able to detect peptides, while plasma samples yielded better detection of lipid metabolites.

The previous microbiome collection protocol included a rectal swab, which must be placed on ice after collection until frozen at −80°C. By contrast, the Omnigene•GUT stool sample collection system allows participants to easily collect a high-quality stool sample from home. This collection system allows for rapid homogenization and stabilization at the point-of-collection as well as transport and storage of stabilized DNA at ambient temperature for 60 days, thus ensuring that microbiota profiles accurately represent the in vivo state (Doukhanine et al., 2014, 2016).

Surveys

The pilot studies and Supplement 1 collected common data elements (Table 2) and study-specific questionnaires. Supplement 2 had different aims and only collected study-specific questionnaires. Prior to COVID-19, questionnaires were completed at the study visit on paper or electronically via Research Electronic Data Capture (REDCap) using a tablet or computer. The COVID-19 transition incorporated virtual survey completion via REDCap for most studies. Online links for REDCap surveys were sent once informed consent was complete; participants completed surveys using their smartphones, tablets, or computers. A few variations to this virtual survey completion method were adopted. Pilot 2 collected questionnaire data via phone or virtual (Zoom) interviews, and Pilot 3 provided participants a paper option for all questionnaires. Because paper copies of the Food Frequency Questionnaire (FFQ) had already been purchased, both Supplements 1 and 2 used paper FFQ forms. Pilots 3 and 4 allowed participants to choose paper or online FFQ forms.

Clinical Measurements and Cognitive Testing

Prior to COVID-19, clinical measures were collected for all studies at in-person study visits and included height, weight, waist circumference, blood pressure, and hemoglobin via point-of-care testing. Two studies (Pilot 1 and Supplement 2) included cognitive testing. With the onset of the pandemic, each study made adaptations to these protocols according to where they were in terms of recruitment and data collection, research question, and original design. For example, Supplement 2 transitioned cognitive testing to a virtual (Zoom) interface. Pilots 1 and 2, which were close to completing recruitment and data collection, ceased collection of clinical measures for remaining study visits. The semi-remote and fully remote studies adopted various strategies for clinical measurement including electronic medical record review for hemoglobin, self-collection of blood pressure, weight, and waist circumference, and self-report of height. A tape measure for collection of waist

circumference was provided for each participant. A blood pressure monitor (Omron 7 Series® Upper Arm) and/or digital scale were provided for any participant who did not have their own to self-collect these measures during their virtual study visit. All studies and protocol changes received IRB approval.

Results

Progress for each study to date is described in Table 4. At the start of the pandemic, Pilot 1 was approximately halfway to enrollment goals, and Pilot 2 was close to enrollment goals. During the pandemic, both pilots continued to collect questionnaire data but suspended biologic data collection. Pilot 3 had started enrollment, with study visits scheduled late-March 2020. All scheduled visits were canceled; previously enrolled participants were contacted with the rollout of the remote data collection protocol. Pilot 4 was not funded until after the start of the pandemic. Supplement 1 was approximately halfway through enrollment goals at the start of the pandemic and continued recruitment and enrollment during the pandemic. Supplement 2 had begun recruitment but had not enrolled participants before the start of the pandemic. Recruitment and enrollment for Pilots 3 and 4 and Supplement 2 are ongoing.

As all three remote studies are ongoing, the outcomes of these adaptations remain unknown. As a preliminary assessment of DBS data collection, we measured total protein concentration (Pierce™ 660nm Protein Assay Kit, ThermoFisher Scientific) from MITRA® blood microsampling of the first 20 samples from Pilot 3. Total protein concentration ranged from 551.45 to 1368.08 μg/mL, with a mean of 917.9. ± 239.6 μg/mL.

Discussion

Participant-Centered Approach

Our center is focused on multiple chronic conditions among Black/African American adults. While a participant-centered approach was adopted pre-COVID due to the hesitancy of Black/African American people to participate in research, after the onset of COVID-19 our P30 Center recognized that the pandemic disproportionately affected our participants and their families, exacerbating existing social inequities and putting them at increased risk for infection and severe illness (Bibbins-Domingo, 2020) as well as mental health concerns (Purtle, 2020). This recognition drove us to go beyond the usual risk versus benefit calculus to ensure all decisions around the research protocol emerged from a place of prioritizing the participant, ensuring benefits outweighed the risk of participation, and minimizing the burden of participation as much as possible. Examples of how this was accomplished included utilizing multiple modes of virtual visit delivery, providing both online and paper survey formats to accommodate individual preference, allowing participants to complete study components according to their personal schedule, convenient options for specimen return, and accommodating communication preferences both in terms of time and mode (e.g., text, phone, email, evenings, weekend).

Of primary importance was our effort to engage sensitively with our participant community. Critical to our success has been the sensitivity that our research coordinators demonstrate

regarding research participation for Black/African American participants, and the empathy and interpersonal skills they exemplify as they engage with participants.

Having a dedicated research coordinator with the availability to fulfill the recruitment and coordination needs of the study, given its scope and timeline, has been critically important and is highly recommended for facilitating a participant-centered approach. The research coordinator serves as the participant's primary contact and is available for questions and willing to adapt to the participant's needs. For studies that incorporated remote methods, the coordinator has been essential for guiding participants through a multistep protocol. Not only do our coordinators prioritize being available to address questions, they also frequently find themselves lending a listening ear to participants who share their daily challenges/experiences. These conversations can become lengthy but are necessary to establish trust and rapport with the participant.

Flexibility and adaptability to the participant's schedule have been key to successfully transitioning to a remote platform during the pandemic. We have had to be flexible around days and times that work better for virtual visits and be prepared for last-minute changes in scheduled times for contact and/or specimen pick-up. Having the ability to engage with participants outside of the usual business hours has worked to our advantage, making it possible for participants to start and complete the study according to their schedule and desired pace. For example, blood collection for the completely remote protocols must be collected in a fasting state. Thus, all virtual study visits were scheduled in the mornings. However, some participants were not able to complete the virtual study visit before work. To better meet participants' needs, Saturday morning visits were offered twice a month. We were also flexible with our mode of communication. Because the remote nature of our study required multiple points of communication, we accommodated the participant's preference in terms of communication mode utilizing email, phone call, text, or a combination of all three.

Clear and detailed communication tailored to the preferences of the participant is critical for participant-centered research studies using remote protocols. Virtual study visits via video or telephone may pose barriers that are not present with in-person interactions. However, these alternatives modes of communication are vital for maintaining open channels of communication. While clear communication between research team and participant is always important, we found it to be crucial during the pandemic when many of our participants—already vulnerable due to health or social circumstances—were facing additional stressors due to COVID-19. The mode of communication preferred by participants depended on the nature of the communication. Most participants responded well and appeared to prefer texting for brief reminders. For some hard-to-reach participants with whom ongoing communication was required, alternating between phone call, text, and email was effective. Videoconferencing was used for certain study components, such as education on specimen collection or cognitive testing. Ultimately, mode of communication depended on the purpose of the communication and participant preference.

Clear and precise instructions have a heightened importance when conducting research remotely. Lack of clarity frustrates the participant, slows their movement through the

protocol, and/or results in incomplete or inadequate data collection. Instruction packets were developed by respective study PIs and research coordinators after an informal trial of the specimen collection protocol by study PIs, research coordinators, and student volunteers to identify potential complications/challenges and time needed for specimen collection. Initial trials started with completing the data collection process (biological specimens and online surveys). This was followed by completely remote trials in which specimen kits were sent to volunteers, who completed the data collection process and returned the specimens using provided return packaging. Based on these informal trials, we found it was important to have a detailed step-by-step instruction packet accompanied by images/photos to ensure that the participant understood what, when, and how to collect and store each specimen (Supplementary Material 1). In addition to written and visual instructions, participants were provided with general instructions during enrollment and reminders about important protocol details, like the importance of fasting and hydration prior to the collection of certain specimens.

Remote Data Collection Considerations

We have discovered several key considerations for successful remote data collection; these considerations represent actions initiated to facilitate the technical aspects of remote data collection. First, due to varied timing in return of specimens resulting from shipping, a process was implemented in our fully remote studies to track time between specimen collection and specimen processing. The effects of return time on sample quality will be investigated using total protein for each blood sample, providing a method of standardization for quantitative analyses.

Second, it is important to optimize communication with the participant to determine their intentions surrounding when and how they will collect their specimens. Participants who display independence or confidence with specimen collection (e.g., diabetic history, nurses, researchers, or other health care professionals) can be offered the ability of independent specimen collection during their process, while less independent participants should be engaged in a virtual previsit to provide detailed instructions for specimen collection procedures. Family caregivers may also be helpful in taking blood pressure and completing specimen collection.

Third, the level of participant engagement required for a remote protocol can present a work–life balance challenge for the research team. Making full use of available technology can help. Pilots 3 and 4 utilized the Microsoft Bookings app, available through Microsoft 365, which has been useful in scheduling participants, sending emails and text messages, and providing links to access instructional videos for specimen collection. Pilots 3 and 4 also employed Avaya, a computer-based phone application available to all faculty and staff. This app allows calls to be made from, and received directly to, a laptop using an office phone number. Use of the app, instead of a personal phone, allows coordinators to be accessible while maintaining privacy and provides separation from work after normal operating hours. The Avaya app also ensures that people without the necessary technology to attend a virtual visit can participate in research by guiding participants through the specimen collection process over the phone. Some participants without computer access or had poor

internet connectivity, led to challenges with using video virtual visits. Telephone visits were utilized for individuals who were unable to participate in the virtual visits; with the aid of the participant instruction booklet, research coordinators could successfully talk participants through the process of self-collection of data over the telephone.

Fourth, though it may seem that costs would decrease during a remote study, that is not necessarily true. Charges associated with remote studies include postage for mailing specimen collection kits and mileage for sample pick-up. Although not a frequent occurrence, resending specimen collection supplies incurs additional postage costs. There is a flat-rate contract with the mail carrier; however, the rate only applies within a specific radius. Since remote collection reaches people living in rural areas or neighboring states, there can be variations in shipping costs. An additional cost for one study was for the use of the clinical data warehouse for screening potential participants from the Emory Healthcare system. The study team received an Excel file with more than 1,100 prescreened individuals. The process was efficient and saved time by employing computer-based technology to identify potentially eligible individuals based on inclusion and exclusion criteria; however, the cost of this service must be included in the budget. Despite these additional costs, overall costs for remote collection may offset costs that would have been incurred for in-person visits. As some clinics do not have space available for collection of research data, other spaces must be used for collection of study data. Some studies had planned in-home data collection or other community locations that have costs related to mileage or gas. Other researchers had planned to utilize the research space at the clinical research centers, which at Emory charges $90 per hour.

Additional considerations for remote collection are unique to specific data types.

Surveys—Electronic surveys require follow-up and reminders sent via REDCap, direct email, and/or phone calls. Some participants complete all the questionnaires in one sitting. Others require text, email, or phone call reminders to start and/or complete the survey. Receipt of research compensation with a thank you card and reminder to complete surveys has been successful in prompting participants to complete electronic surveys.

Blood Collection—For participants unfamiliar with how to use a lancet, more than one stick can be necessary. Poor hydration or fast clotting time present a challenge for the dried blood spot card where blood must be carefully dropped onto the card. Participants in the semi-remote study who have fingerstick challenges may have a trained and appropriately garbed (PPE) research team member collect the blood spots at specimen pick-up. Studies using the MITRA® device find this collection method much easier to use since the finger can be placed against the device.

Other research studies have successfully incorporated components included in our remote protocols, including remote informed consent (De Sutter et al., 2020; Phillippi et al., 2018), electronic survey collection through REDCap (Tomko et al., 2019) and other platforms during COVID-19 (Hunersen et al., 2021), and biologic specimens (Feigelson et al., 2014). Studies including remote data collection methods have demonstrated these methods are feasible and promote participation of racially and geographically diverse individuals who

often do not participate in prospective research studies (Greenleaf et al., 2017; Phillippi et al., 2018). We found, in congruence with other remote studies, that approaches to communication and flexibility must be adjusted and tailored to participants' needs when implementing a remote protocol.

Reflections on Extending Remote Approaches Post-COVID

Remote collection can deepen the involvement of research participants in remote research projects. In many nonremote research projects, participants are minimally involved in the collection of their biosamples. In remote projects, by contrast, successful collection of biosamples requires that research participants understand not only what will be collected, but also how to collect it optimally to strengthen the findings of the study. This requires research staff to engage with participants at a deeper, more involved level, from informed consent onward, which may help participants feel more invested in the study and thereby perhaps be more likely to continue their participation over time.

Although in-person research was allowed to resume with enhanced safety protocols in place, the decision to move to completely remote protocols was made for some studies to protect high-risk study populations, such as persons with heart failure or HIV. This decision was influenced by vaccine availability at the time the protocols were developed, and the proportion of the community vaccinated with continuing recruitment and enrollment.

Protocols with remote strategies increase research participation accessibility for participants without transportation or those who live a significant distance from the city of Atlanta. Accessibility is also enhanced for research participants whose work or personal schedules make participation in an in-person study with fixed locations/times challenging. Caregivers in two of our center studies, for example, are often juggling full-time work in addition to their caregiver duties. The ability to complete all studies from home at the participant's own pace increases access to research participation.

Potential Pitfalls and Benefits of Remote Data Collection

One advantage of being part of an integrated center, such as the P30 Center, is the ability to combine common data elements to answer research questions across populations. Pre-pandemic protocols were standardized across all P30 pilot studies related to collection and processing of common data elements (Table 2). This approach allowed for the pooling of metabolomics and symptoms data to test hypotheses related to the primary aims of the P30 Center across pilot studies. Changes in data collection protocols during the pandemic, therefore, had important implications for the Center's original intentions to harmonize its data.

As some studies were already in progress at the start of the pandemic, not all studies were able to pivot to a remote protocol. Pilots 1 and 2 had made significant progress in data collection, and Supplement 1 was more than halfway through data collection. Changing biological sample collection protocols at this point in these three studies would have introduced a significant covariate. Thus, Pilots 1 and 2 discontinued all biologic data collection. Supplement 1 worked with clinic partners to develop an enhanced safety protocol

to continue recruitment, enrollment, and study visits in-person at the clinics, although there were further delays due to the dramatic increases in COVID-19 cases.

Pilot studies 3 and 4 had not collected data from participants at the onset of the cessation in research in March 2020. The study PIs worked together to create a completely remote protocol for collection of all study data. This shared approach allowed for the pooling of data across the two studies. As the remote protocols were virtually the same, one clinical research coordinator was hired to work on both studies. This resulted in a team of study PIs, a clinical research coordinator, and student research assistants who worked together to test and refine a new and innovative remote approach to data collection. This transition to remote collection of biologic samples for some of our center studies does mean, however, that our original plan to pool data across all studies will no longer be possible given known differences by collection method in detected metabolite classes (Tobin et al., 2021), as well as differences in microbiome.

Unlike in-person biologic data collection, remote protocols may involve delayed receipt or processing of biologic samples and survey data. The semi-remote protocol addressed this by picking up samples the day of collection. This step was necessary, as the saliva samples must be stored at cold temperatures after collection. The fully remote protocols chose blood and stool sample collection methods that keep specimens stable at room temperature for weeks or months.

Conclusion

Adapting research protocols to maximize safety of participants and the research team during a pandemic required critical examination of research aims and goals, study progress, and target population characteristics for each study. The P30 investigators and research team members found creative and innovative ways to meet study goals using novel technology, remote methods, and a participant-centered approach. These protocols increase flexibility and access to research participation and will continued to be used in future research endeavors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Characteristics of Pilot Studies and Supplements

	Data Collection Site before COVID	Status at the Start of COVID	Adaptations During COVID
Pilot 1	On campus, Clinical Research Center	Actively enrolling participants	Moved data collection to online: completed study visits for T1 (n = 4) and T2 participants fully online then suspended enrollment.
Pilot 2	Clinic	Actively enrollment patients	Suspended enrollment for new patients. Completed T2 visit with online questionnaires only.
Pilot 3	Clinical Research Center	Beginning enrollment: 3 study visits scheduled starting March 24, 2020; all were canceled	Completely remote protocol.
Pilot 4	N/A	No enrollment	Completely remote protocol.
Supplement 1	Clinic	Middle of recruitment	Returned to study visits in the clinic with enhanced safety protocols.
Supplement 2	N/A	Beginning recruitment, no enrollment	Semi-remote protocol.

Table 2

Center for Study of Symptom Science, Metabolomics, and Multiple Chronic Conditions Common Data Elements

Variable	Measurement
Demographic Factors	National Institutes for Nursing Research Common Data Elements
Age	BRICS forms (National Library of Medicine, 2016)
Race	
Ethnicity	Exact questions and responses shared for each pilot study
Gender	
Employment	
Education level	
Marital status	
Health insurance	
Household number	
Caregiver primary type	
Personal Health History	
Smoking status	Self-report (never, former, current)
Comorbidities	Charlson Comorbidity Index (Charlson et al., 1987)
Global Health	Patient-Reported Outcomes Measurement Information System (PROMIS) Global Health Scale (National Institutes of Health, 2014)
Stress	Perceived Stress Scale SF (PSS–4; Cohen et al., 1983)
Stool	Bristol Stool Chart (Lewis & Heaton, 1997)
Medical Record Data	
Blood pressure	Average of three readings taken 5 min apart after sitting for 5 min or per medical record for visit with study's biologic measure collection
Height	Standard stadiometer or per medical record for visit with study's biologic measure collection
Weight	Calibrated scale, or per medical record for visit with study's biologic measure collection
Hemoglobin	Point-of-care test or per medical record for recent visit
Self-Management Behaviors	
Dietary intake	Block-Bednar semiquantitative Food Frequency Questionnaire (modified to quantify probiotic intake; Block et al., 1990)
Medication intake	Self-report
Sleep	PROMIS Sleep Disturbance short form (National Institutes of Health, 2014)
Patient-Reported Symptoms and Outcomes	
Fatigue	Multidimensional Fatigue Inventory(MFI–20 ; Lin et al., 2009) PROMIS Short Form Fatigue 6a (National Institutes of Health, 2014)
Depression	Center for Epidemiological Studies Depression Scale (CES–D 10; Irwin et al., 1999; Radloff, 1977) PROMIS Short Form Depression 6a (National Institutes of Health, 2014)
Anxiety	State-Trait Anxiety Inventory (STAI; Spielberger, 1983) PROMIS Short Form Anxiety 6a (National Institutes of Health, 2014)
Pain	PROMIS Pain Intensity (National Institutes of Health, 2014)
Health-Related Quality of Life	NINR Common Data Elements BRICS Short Form 36 (National Library of Medicine, 2016) PROMIS Global Health Short Form 10 (National Institutes of Health, 2014)
Race-Related Stress	Index of Race-Related Stress ([IRRS], brief version; Utsey & Poterrotto, 1996)
Biologic Measures	

Variable	Measurement
Metabolites	Blood sample[a]
Gut microbiome	Rectal swab[a]
Hemoglobin	Point-of-care test (if not collected per medical record)
Cytokines	Blood sample

Note.

[a]One of the supplement studies has a focus on oral health and is collecting saliva for microbiome and metabolomics analysis.

Table 3

Semi-Remote and Remote Biological Data Collection

Source	Supply	Assay
Semi-Remote Protocol (Supplement 2)		
Saliva	OMNIgene Oral 501	Salivary microbiome
Saliva	Clean vial	Inflammatory cytokines, metabolomics
Dried blood spots	Whatman® 903 protein saver cards	Systemic inflammatory cytokines
Finger stick supply	Lancet, 1-in gauze sponge, adhesive bandage	N/A
Fully Remote Protocol (Pilots 3 and 4)		
Dried blood spots	Mitra® volumetric absorptive microsampling collection kit	Inflammatory cytokines
Dried blood spots	Whatman® 903 protein saver cards	Metabolomics
Finger stick supply	Lancets (2), 1-in gauze sponge, adhesive bandage	N/A
Stool	Omnigene•GUT collection kit	Gut microbiome

Table 4

Screening, Enrollment, and Study Completion Pre-COVID and During COVID

Study	Pre-Pandemic						Pandemic					
	Screened	Eligible	Contacted	Enrolled	Completed[a]	Withdrawn	Screened	Eligible	Contacted	Enrolled	Completed[a]	Withdrawn
Pilot 1	57	39	36	26	22	4	8	4	4	4	3	1
Pilot 2	44	44	39	39	23	0	0	0	0	0	3	0
Pilot 3	223	43	15	3	0	0	1249	162	123	33	8	6
Pilot 4	--	--	--	--	--	--	1198	91[b]	125	31	6	2
S1	468	32	28	24	14	0	85	14	11	10	6	0
S2	7	3	8	0	0	0	78	15	48	14	12	1

Note: Pilots 1 and 2 suspended biological data collection with the start of the pandemic. Study visits for Pilot 3 were scheduled for late-March 2020 and were canceled the week of March 16, 2020.

[a] Completed

[b] Full eligibility was determined after speaking with participant; recruitment is ongoing.