

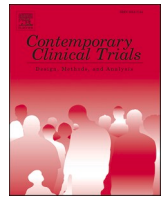


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# Contemporary Clinical Trials

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Short Communication

## Randomized clinical trials of weight loss: Pragmatic and digital strategies and innovations

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## ABSTRACT

During the COVID-19 pandemic, digital strategies and decentralized approaches allowed for the continuation of weight loss clinical trials despite in-person engagement coming to a halt. In particular, trials leveraged remote mediums to measure data in real-time across a broad array of metrics while testing novel strategies to streamline patient care. Such approaches may address longstanding challenges with traditional trials, including attrition and underrepresentation of racial and ethnic minorities. Ultimately, emerging data from trials utilizing both digital and in-person strategies may indicate the promise of a hybrid approach in incorporating a robust virtual component for continuous patient monitoring and an in-person component for patient adherence and data standardization. In this commentary, we provide an overview of the most innovative digital approaches in clinical trials of weight loss during the COVID-19 era, as well as identify opportunities and challenges for these modes of research going forward.

Far from predictions that COVID-19 would be the “great equalizer,” the pandemic is something of a “great exposé,” revealing institutional disparities in healthcare systems and eliciting a paradigm shift in how research is conducted [1]. Indeed, patients with obesity have more severe illness and worsened outcomes from COVID-19 [2,3], which has led to renewed public attention toward the concurrent obesity pandemic. Simultaneously, weight loss clinical trials, and clinical trials more generally, were largely suspended during the initial phases of the COVID-19 pandemic given safety concerns and practical obstacles in enrollment, data collection, and intervention delivery [4]. However, the ongoing pandemic also revealed the utility of alternative digital strategies that allow for continued RCT progress even as more infectious COVID-19 variants proliferated. Here, we describe some of the most innovative and pragmatic digital approaches undertaken by weight loss clinical trials during the COVID-19 pandemic and highlight innovations that should command continued utility during this pandemic and beyond.

The most successful weight loss clinical trials of the COVID-19 pandemic took advantage of decentralized, digital approaches to

continuously engage participants during social distancing and lockdowns. These trials delivered interventions such as counseling, exercise classes, diet regimens, and intensive behavioral therapy (IBT) through remote mediums including video conferencing, mobile apps, social media outlets, and phone calls (Table 1). While many trials focused on shifting existing interventions to virtual platforms, the most innovative trials experimented with novel digital pivots to tried-and-tested therapeutics. For example, the University of South Carolina-led study “Exploring Optimal Treatment Components for Contactless Online Group-based Behavioral Weight Loss Program (iREACH)” modified an intervention previously demonstrated as effective—combining synchronous group-based social support with asynchronous discussion board-based social support—by capturing body weight measurements electronically through a Bluetooth-enabled “smart scale.” [5] As a result, patients were independently and continuously able to track and share their outcomes over the course of the intervention, minimizing unnecessary trips to the doctor’s office. Likewise, the ongoing Mayo Clinic-led study “Anti-Obesity Phentermine-Topiramate Extended-Release Pharmacotherapy vs Placebo Among Patients Using a Wearable Activity

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**Table 1**  
Digital approaches employed by weight-loss RCTs during COVID-19.

Study	Digital Approaches
Exploring Optimal Treatment Components for Contactless Online Group-based Behavioral Weight Loss Program (iREACH) (Remote) [5]	<ul style="list-style-type: none"> <li>● Combines synchronous group social support with asynchronous discussion board social support</li> <li>● Provides detailed feedback on dietary and physical activity self-monitoring records from a counselor</li> <li>● Captures weight via a Bluetooth-enabled “smart scale” with no in-person contact</li> </ul>
Anti-Obesity Phentermine-Topiramate Extended Release Pharmacotherapy vs Placebo Among Patients Using a Wearable Activity Tracker (Remote) [6]	<ul style="list-style-type: none"> <li>● Leverages VitalCare, a digital health platform that allows remote collection of data from the wearable tracker and digital wellness devices used in the study</li> <li>● Allows subjects to document study medication compliance</li> <li>● Facilitates remote visits through a video conference between subjects and appropriate study team members</li> </ul>
Feasibility of a Telematics Pre-operative Assessment in a Bariatric Surgery During Covid-19 (Remote) [7]	<ul style="list-style-type: none"> <li>● Utilizes remote nutritional sessions to collect weight history, previous diets attempts, physical activity and lifestyle habits, food intake modality, water intake, and anthropometric measures</li> <li>● Develops customized preoperative food plan/diet</li> <li>● Employs remote psychological sessions to discuss psychopathological symptoms, life history, compliance to prior treatments, and compliance to preoperative nutritional recommendations</li> </ul>
Evaluation of Brain Activity Changes After a Behavior Change Weight Loss Intervention (Hybrid) [20]	<ul style="list-style-type: none"> <li>● Compares brain changes in individuals with overweight or obesity enrolled in either the Noom Healthy Weight mobile health program or a matched control</li> <li>● Measures changes in the default mode network, changes in executive functioning, quality of life, mood, and salivary markers in-person</li> </ul>
Adding Financial Incentives to Online Group-Based Behavioral Weight Control: An RCT (Remote) [12]	<ul style="list-style-type: none"> <li>● Utilizes online group-based behavioral weight control program with weekly synchronous chat sessions with or without weekly financial incentives for self-monitoring body weight and dietary intake</li> </ul>
Promoting Lifestyle Change Via Tailored mHealth Feedback to Improve Health (SMARTER) (Remote) [13]	<ul style="list-style-type: none"> <li>● Examines the effect of individualized real-time smartphone-based feedback of diet and physical activity self-monitoring on subsequent weight-control behaviors, weight loss outcomes, and sustainability of patient engagement</li> <li>● Utilizes smartphone app to self-monitor diet, Fitbit tracker to monitor physical activity, and Wi-Fi-enabled digital scale for daily self-weighing</li> <li>● Provides digital feedback messages based on self-monitoring data</li> </ul>
Sustaining the Reach of a Scalable Weight Loss Intervention Through Financial Incentives (Hybrid) [21]	<ul style="list-style-type: none"> <li>● Provides financial incentives for utilizing the incentaHEALTH weight loss program, a technology-supported multi-component coaching intervention for weight loss</li> <li>● Includes a website, objective weight assessment using HIPAA-compliant kiosks, daily social cognitive theory-based email and text message support, and online access to health coaches</li> <li>● Focuses on closing attrition gap in a primary care clinic predominantly serving African American patients through an innovative research-</li> </ul>

**Table 1 (continued)**

Study	Digital Approaches
Pilot Trial of a Telephone Weight Loss, Nutrition, Exercise Study (WeLNES) (Remote) [22]	<ul style="list-style-type: none"> <li>● practice partnership involving primary care, research expertise, and a small business</li> <li>● Utilizes a novel telephone-delivered version of Acceptance and Commitment Therapy (ACT) behavioral weight loss intervention, based on prior success using ACT telephone counseling intervention for smoking cessation</li> </ul>
Evaluating a Remotely Delivered Plant-Based Behavioral Weight Loss Treatment (Remote) [23]	<ul style="list-style-type: none"> <li>● Tests the first remotely-delivered whole food plant-based diet (WFPBD) behavioral weight loss intervention for adults with obesity</li> <li>● Includes behavioral weight loss strategies and live coaching through an e-learning platform to provide positive reinforcement and problem-solving support</li> </ul>
EMPOWER: Empowering the Management of Pain-Obesity-Weight Through Enhanced Reward (Hybrid) [24]	<ul style="list-style-type: none"> <li>● Utilizes a group- and telephone-based program featuring integrated behavioral weight loss treatment and cognitive-behavioral pain coping therapy for adults with comorbid moderate-to-high impact low back pain and obesity</li> <li>● Incorporates remote pleasant activity scheduling, values clarification, mindfulness practice, goal setting, standard pain coping skills, and weight management including nutrition education and physical activity monitoring</li> </ul>

Tracker” utilizes classic weight loss medications in conjunction with VitalCare, a digital health platform and wearable tracker that allows investigators to remotely collect weight, exercise, and calories data and allows subjects to correspondingly document medication compliance [6]. These digital approaches extend traditional research methodologies of measuring discrete, well-defined outcomes at key moments to truly measuring data in real-time across a broader range of metrics and encouraging bidirectional, instantaneous communication between patients and investigators.

Remote weight loss clinical trials can also directly provide novel approaches to streamline patient care. For instance, take the “Feasibility of a Telematics Pre-operative Assessment in a Bariatric Surgery During Covid-19” trial conducted at the Sapienza University of Rome, in which researchers assess the efficacy of a telemedicine-based protocol to deliver the preoperative work-up for bariatric surgery [7]. The protocol involves telehealth visits to a nutritionist to collect anthropometric measures and assess weight history, previous diet attempts, physical activity, and lifestyle habits while preoperative diet plans are developed for the patient to follow in the weeks preceding the surgery. Subsequently, the patient remotely consults with a psychiatrist to discuss psychopathological symptoms, family history, compliance to previous treatment, and adherence to those preoperative diet plans. As waiting times for bariatric surgeries have nearly doubled from 86 to 159 days between 2006 and 2016 [8], largely driven by insurers who mandate prior attempted weight-loss documentation, incorporating such a telehealth preoperative component can facilitate quicker time-to-treatment periods for patients while reducing unnecessary in-person visits to providers.

Such emerging innovations and digital strategies may offer great promise to weight loss clinical trials through attenuated attrition and more representative research enrollment. Indeed, attrition has been identified as a significant issue with conventional, in-person weight loss clinical trials [9]: in a study by Littman and colleagues, only 50.4% of participants engaged in more than one encounter of the MOVE! Weight Management Program [10]. In another study by Glasgow and

colleagues, ongoing engagement with the experimental weight loss program ranged from 49% for the control group to 5.7% for one of the other groups [11]. Although evidence is currently limited, recent digital weight loss clinical trials have demonstrated retention rates exceeding 80–90% across a variety of populations, including breast cancer survivors, women planning pregnancy, and participants identifying with racial or ethnic minority groups [12–15]. Through reducing the time commitment, inconvenience, and cost needed for patients to fully participate, digital strategies can effectively improve adherence and reduce barriers to entry for clinical trials, such as transportation difficulties and caregiving responsibilities. Of note, these two are especially cited barriers to underrepresented minority participation in weight loss clinical trials [16]. Through videoconferencing appointments, data collection embedded into people's daily lives, and other digital strategies, researchers may be able to offer a less demanding avenue for individuals, especially from underrepresented minority populations, to contribute to research endeavors.

Certainly, given the tragic history of racial and ethnic minority involvement in medical research, most infamously with the Tuskegee Syphilis Study, trust toward the medical establishment has been shattered among certain populations [17]. However, paving opportunities for these communities to engage in weight loss trials and other research from the comfort of their homes may help to rebuild that trust. Efforts to ensure equitable trial enrollment are especially important given that racial and ethnic minorities are disproportionately impacted by obesity but are systematically underrepresented in weight loss clinical trials [16]. Indeed, weight loss trials, and clinical trials more generally, have long overrepresented white participants and thus resulted in therapies with questionable efficacy for racial and ethnic minorities. Encouragingly, the federal government has expanded the accessibility of telehealth through recent COVID-19 era policies that allow patients to receive care through standard video chat and text-based applications pursuant to HIPAA, as well as new waivers and regulatory changes that provide reimbursements to Medicare and Medicaid patients for telehealth services [18]. Such policies, if continued beyond the COVID-19 pandemic, may further promote digital approaches to weight loss trials and treatment while addressing related disparities. While we can celebrate the potential for digital strategies to increase representation, given this poor history, care must be taken to ensure that such strategies do not instead widen enrollment disparities because, for example, digital technologies and broadband connection may be more inaccessible to marginalized communities [19]. Much work, such as the 1993 National Institutes of Health Revitalization Act and other public policies that prioritize diversity, equity, and inclusion, has sought to increase the representativeness of clinical trials, but digital strategies offer an innovative way to expand enrollment into underrepresented communities with dignity, respect, and understanding.

To be sure, our enthusiasm with innovative digital strategies should not suggest that traditional clinical trials should be relegated to the past. For one, some interventions simply cannot be done virtually, such as bariatric surgery. Digital strategies are limited by what a reasonable patient can do within the confines of their home, whether that be consenting over video conference appointment, self-administering a therapy, or collecting data via a wearable device. Additionally, concerns of trial integrity inevitably persist—there might be poor patient understanding, adherence, or data standardization [4]. However, these considerations should not automatically disqualify digital strategies because the pandemic has shown how robust, controlled clinical trials can be conducted virtually with great benefit to patients. More focused patient education and greater technological assistance can extend contextual limitations and help allay integrity concerns. Ultimately, we see the future of weight loss clinical trials as a hybrid approach that benefits from the best of traditional and digital strategies. For instance, the clinical trial “Evaluation of Brain Activity Changes After a Behavior Change Weight Loss Intervention,” sponsored by Noom Inc., was completed entirely remotely, including weight monitoring, food

logging, and in-app chatting with a human coach, aside from electroencephalogram scans which had to occur in-person [20]. Similarly, the aforementioned “Feasibility of a Telematics Pre-operative Assessment in a Bariatric Surgery During Covid-19” trial demonstrates how surgical pre-assessments can be conducted almost entirely virtually with the surgical procedure itself performed in-person [7]. A hybrid approach may allow for greater convenience and participation through virtual components as well as the collection of vital data and mitigation of integrity concerns via in-person components, but emerging results from ongoing studies will be necessary to ascertain the promise of hybrid trials.

Researchers have embraced the use of mobile technology and digital tools in behavioral interventions for weight loss for nearly two decades, enabling a more seamless transition to remote clinical trials recently. Indeed, the COVID-19 pandemic has, by necessity, pushed clinical trials into the virtual world, leading to rapid innovation and revealing certain key benefits. Reduced costs, time commitments, and inconveniences to patients through digital strategies may, for instance, lead to lower clinical trial attrition and more representative enrollment, thereby creating therapies that are efficacious for all people rather than certain privileged cohorts. Additionally, the leveraging of increasingly prevalent technologies, such as wearable devices and home-use medical devices, to provide real-time physiological data will enable rich outcome tracking across a variety of indicators. Ultimately, all weight loss clinical trials may benefit from a hybrid approach that blends convenience, integrity, and practical concerns together.

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## Conflicts of interest

None.

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