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Far from predictions that COVID-19 would be the “great exposer,” the pandemic is something of a “great equalizer,” 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 era, as well as identify opportunities and challenges for these modes of research going forward.

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...
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] | ● Combines synchronous group social support with asynchronous discussion board social support  
● Provides detailed feedback on dietary and physical activity self-monitoring and online records from a counselor  
● Captures weight via a Bluetooth-enabled “smart scale” with no person contact |
| Anti-Obesity Phenetermine-Topiramate Extended Release Pharmacotherapy vs Placebo Among Patients Using a Wearable Activity Tracker (Remote) [6] | ● Leverages VitalCare, a digital health platform that allows remote collection of data from the wearable tracker and digital wellness devices used in the study  
● Allows subjects to document study medication compliance  
● Facilitates remote visits through a video conference between subjects and appropriate study team members |
| Feasibility of a Telematics Pre-operative Assessment in a Bariatric Surgery During Covid-19 (Remote) [7] | ● 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  
● Measures changes in the default mode network, changes in executive functioning, quality of life, mood, and salivary markers-in-person |
| Evaluation of Brain Activity Changes After a Behavior Change Weight Loss Intervention (Hybrid) [20] | ● Compares brain changes in individuals with overweight or obesity enrolled in either the Noom Healthy Weight mobile health program or a matched control  
● Develops customized preoperative food plan/diet  
● Employs remote psychological sessions to discuss psychopathological symptoms, life history, compliance to prior treatments, and compliance to preoperative nutritional recommendations |
| Adding Financial Incentives to Online Group-Based Behavioral Weight Control: An RCT (Remote) [12] | ● 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  
● Incorporates remote pleasant activity monitoring |
| Promoting Lifestyle Change Via Tailored mHealth Feedback to Improve Health (SMARTER) (Remote) [13] | ● 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  
● Utilizes smartphone app to self-monitor diet, Fitbit tracker to monitor physical activity, and Wi-Fi-enabled digital scale for daily self-weighing |
| Sustaining the Reach of a Scalable Weight Loss Intervention Through Financial Incentives (Hybrid) [21] | ● Provides digital feedback messages based on self-monitoring data  
● Provides financial incentives for utilizing the incentiveHEALTH weight loss program, a technology-supported multi-component coaching intervention for weight loss  
● Includes a website, objective weight assessment using HIPAA-compliant kits, daily social cognitive theory-based email and text message support, and online access to health coaches  
● Focuses on closing attrition gap in a primary care clinic predominantly serving African American patients through an innovative research-practice partnership involving primary care, research expertise, and a small business |

Table 1 (continued)

| Study                                                                 | Digital Approaches                                                                 |
|----------------------------------------------------------------------|-----------------------------------------------------------------------------------|
| Pilot Trial of a Telephone Weight Loss, Nutrition, Exercise Study (WelNES) (Remote) [22] | ● 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 |
| Evaluating a Remotely Delivered Plant-Based Behavioral Weight Loss Treatment (Remote) [23] | ● Tests the first remotely-delivered whole food plant-based diet (WFPBD) behavioral weight loss intervention for adults with obesity  
● Includes behavioral weight loss strategies and live coaching through an e-learning platform to provide positive reinforcement and problem-solving support |
| EMPOWER: Empowering the Management of Pain-Obesity-Weight Through Enhanced Reward (Hybrid) [24] | ● 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 |

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 tele-health 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, increased 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.

References

[1] S.A. Sayeed, L. Taylor, A pandemic induced Reduction: Bioethics and Justice, Univ. Tor. Med. J. 98 (1) (2021) 13–16.
[2] K. Hajifathalian, S. Kumar, C. Newberry, et al., Obesity is associated with worse outcomes in COVID-19: analysis of early data from New York City, Obes. Silver Spring Md. 28 (9) (2020) 1606–1612, https://doi.org/10.1002/oby.22925.
[3] A. Sharma, A. Garg, A. Rout, C.J. Lavie, Association of obesity with more critical illness in COVID-19, Mayo Clin. Proc. 95 (9) (2020) 2040–2042, https://doi.org/10.1016/j.mayocp.2020.06.046.
[4] M.M. McDermott, A.B. Newman, Remote research and clinical trial integrity during and after the coronavirus pandemic, JAMA. 325 (19) (2021) 1935, https://doi.org/10.1001/jama.2021.4609.
[5] D.S. West, Exploring the Optimal Treatment Components for a Contactless Online Group-Based Behavioral Weight Loss Program for the COVID 19 Pandemic. clinictrials.gov, 2021.
[6] A. Acomo, Anti-Obesity Phentermine-Topiramate Extended Release Pharmacotherapy vs Placebo Among Patients Using a Wearable Activity Tracker. clinicaltrials.gov (web archive link, 25 November 2021). (Accessed 25 November 2021). https://clinicaltrials.gov/ct2/show/NCT04408586.
[7] G. Silecchia, Feasibility of a Telematics Pre-Operative Assessment in a Bariatric Center of Excellence During Covid-19 Phase 2: A Prospective Observational Study. clinicaltrials.gov, 2020. Accessed November 25, 2021, https://clinicaltrials.gov/ct2/show/NCT04486417.
[8] R. Alvarez, A.J. Bonham, C.M. Buda, A.M. Carlin, A.A. Ghaferi, O.A. Varban, Factors associated with long wait times for bariatric surgery, Ann. Surg. 270 (6) (2019) 1103–1109, https://doi.org/10.1097/SLA.0000000000002826.
[9] T.I. Michaud, P.A. Estabrooks, W. You, et al., Sustaining the reach of a scalable weight loss intervention through financial incentives: a pragmatic feasibility, online randomized trial protocol, Contemp. Clin. Trials. 98 (2020), 106142, https://doi.org/10.1016/j.cct.2020.106142.
[10] A.J. Littman, E.J. Boyko, M.B. McDonell, S.D. Fihn, Evaluation of a weight management program for veterans, Prev. Chronic Dis. 9 (12) (2012) E99, https://doi.org/10.5888/pcd9.110267.
[11] R.E. Glasgow, C.C. Nelson, K.A. Kearney, et al., Reach, engagement, and retention in an internet-based weight loss program in a multi-site randomized controlled trial, J. Med. Internet Res. 9 (2) (2007), e11, https://doi.org/10.2196/jmir.9.2.e11.
[12] D.S. West, R.A. Krukowski, E.A. Finkelstein, et al., Adding financial incentives to online group-based behavioral weight control: an RCT, Am. J. Prev. Med. 59 (2) (2020) 237–246, https://doi.org/10.1016/j.amepre.2020.03.015.

[13] L.E. Burke, S.M. Sereika, B. Parmanto, et al., Effect of tailored, daily feedback with lifestyle self-monitoring on weight loss: the SMARTER randomized clinical trial, Obes. Silver Spring Md. 30 (1) (2022) 75–84, https://doi.org/10.1002/oby.23321.

[14] M.M. Reeves, C.O. Terranova, E.A.H. Winkler, et al., Effect of a remotely delivered weight loss intervention in early-stage breast cancer: randomized controlled trial, Nutrients. 13 (11) (2021) 4091, https://doi.org/10.3390/nu13114091.

[15] R. Muirhead, N. Kizirian, R. Lal, et al., A pilot randomized controlled trial of a partial meal replacement preconception weight loss program for women with overweight and obesity, Nutrients. 13 (9) (2021) 3200, https://doi.org/10.3390/nu13093200.

[16] D.L. Rosenbaum, A.D. Piers, L.M. Schumacher, C.A. Kase, M.L. Butryn, Racial and ethnic minority enrollment in randomized clinical trials of behavioral weight loss utilizing technology: a systematic review, Obes. Rev. Off. J. Int. Assoc. Study Obes. 18 (7) (2017) 808–817, https://doi.org/10.1111/obr.12545.

[17] S.S. Bajaj, F.C. Stanford, Beyond Tuskegee — vaccine distrust and everyday racism, N. Engl. J. Med. 384 (5) (2021), e12, https://doi.org/10.1056/NEJMp2035827.

[18] Policy changes during COVID-19, Telehealth HHS, Accessed January 16, 2022, https://telehealth.hhs.gov/providers/policy-changes-during-the-covid-19-public-health-emergency/, 2022.

[19] B. Jain, S.S. Bajaj, F.C. Stanford, All infrastructure is health infrastructure, Am. J. Public Health 112 (1) (2022) 24–26, https://doi.org/10.2105/AJPH.2021.306595.

[20] D.A. Michaelides, Evaluation of Brain Activity Changes After a Behavior Change Weight Loss Intervention. clinicaltrials.gov, 2021.

[21] D. Su, Sustaining the Reach of a Scalable Weight Loss Intervention Through Financial Incentives: An Exploratory Randomized Controlled Trial. clinicaltrials.gov, 2020. Accessed November 25, 2021, https://clinicaltrials.gov/ct2/show/NCT04225234.

[22] Pilot Randomized Trial of a Telephone Weight Loss, Nutrition, Exercise Study (WeLNESS). clinicaltrials.gov, 2021. Accessed November 25, 2021, https://clinicaltrials.gov/ct2/show/NCT03738540.

[23] E. Forman, A Pilot Study of a Novel Ad Libitum Plant-Based Behavioral Weight Loss Treatment. clinicaltrials.gov, 2021. Accessed November 25, 2021, https://clinicaltrials.gov/ct2/show/NCT04892030.

[24] Empowering the Management of Pain-Obesity-Weight Through Enhanced Reward. clinicaltrials.gov, 2021. Accessed November 25, 2021, https://clinicaltrials.gov/ct2/show/NCT04851587.