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LETTER TO THE EDITOR

Investigator initiated research in times of COVID-19: Let's go digital!

The COVID-19 outbreak and subsequent worldwide lockdowns have led to a temporal suspension of elective clinical care and many types of (non-COVID-19-related) medical research in many countries. Clinical trials are deeply affected on different levels by this ongoing crisis; trials are put on hold by sponsors and responsible authorities, patients cannot attend study visits, and research staff have restricted access to the hospital and research facilities or are transferred to provide COVID-19 care. A balance between protecting patients, healthcare workers, and researchers from COVID-19 on the one hand and the importance of continuing medical research that will eventually lead to new insights and treatments for other diseases on the other hand is searched for. During planning and initializing one of our new trials, we realized that prevention of spread of SARS-CoV-2 and rapid execution of clinical trials are not always contradictory. We would like to share our experience on designing and conducting a fully remotely conducted randomized clinical trial.

We designed and are currently conducting a "COVID-19 proof" single-center, prospective, randomized, double-blind, sham-controlled trial for a non-CE marked medical device. Institutional review board (IRB) approval, patient recruitment, informed consent procedure, dispensing the medical device, and trial monitoring visits are all done remotely while being in compliance with Good Clinical Practice (GCP) standards, the current ethical and legal framework, and the institutional and national COVID-19 lockdown measures.

Our study population consists of 100 patients with moderately severe gastroesophageal reflux. It has been shown that body position during sleeping has an effect on nighttime gastroesophageal reflux.[1] When sleeping in the left lateral decubitus position, the stomach is positioned below the esophagus, resulting in less reflux episodes compared to the right lateral position. The investigational medical device will gently vibrate when the body is in the right lateral position, training patients to sleep more on their left lateral position and thereby reducing nighttime gastroesophageal reflux.

The intended study population for this trial typically uses self-care and over the counter products for their complaints and searches online for information. Therefore, we used the Google Ads platform to recruit study participants. If someone searches for one of the keywords in Google ("reflux during sleep," "how to prevent acid during the night"), a targeted advertisement containing information about our study is displayed within the results. If they click on the advertisement, they are redirected to our hospital webpage with information of the study and contact information for participation. Additional information about the study is provided by regular mail, e-mail, and/or by (video) call by the investigator, and written informed consent is obtained. Next, all trial visits are conducted "virtual." Daily questionnaires are automatically sent by e-mail to the participant, the medical device is delivered to the home address of the participants, and the investigator provides detailed study instructions by video call. Patients are regularly contacted by phone during the 5-week trial to ensure adherence to the trial protocol and respond to any questions.

The whole process of designing the study, writing the study protocol, obtaining IRB approval, and first patient inclusion was less than 3 months. In the next two months, which fell during the first COVID-19 wave, we were able to recruit over 150 interested study participants who are currently in screening or are already randomized and participating in the study. It is estimated that the whole study duration (including data analysis and manuscript submission) will be within 12 months.

Patient recruitment is essential for the successful completion of clinical trials and other forms of research involving human subjects. Twenty-five percent of the clinical trials are being stopped prematurely, with poor recruitment being the most frequently reported reason.[2] Up to 61% of clinical trials fail to recruit their original recruitment target.[3,4] Digital platforms, such as Google, Facebook, Twitter, and Instagram, can be attractive tools for recruitment in medical research and show promising efficacy, while they are relatively unknown by clinical scientists.[5,6] Researchers can target potential study participants based on their personal information or search keywords and thereby reach and recruit a wider population faster and more cost-effective. Alternatively, a rare disease patient organization group on social media can be approached.

The use of these platforms raises several ethical and privacy issues, that has been clustered in three sets of ethical challenges: (a) questions concerning the quality of research, (b) informed consent and privacy challenges, and (c) new power asymmetries based on access to data and control over technological infrastructures.[7] For example, one simple click on a recruitment advert generates traceable data to the advertisement platform, Google AdWords in our study.[8] While no unnecessary data are being collected by the investigator, the advertisement platform will learn that a specific individual has reflux complaints. This might be acceptable for the Google user, but when recruiting online for a clinical trial in a more stigmatizing disease, this could be otherwise. In addition, the reputation of social media platforms (such as Instagram, TikTok, and Facebook) regarding the respect for privacy has been widely discussed and thorough regulatory guidance and bioethical literature on the use of these social media platforms as recruitment tool for clinical trials is lacking.[9,10]

We acknowledge that our clinical trial is well suited to be performed remotely, and this may not be possible in other clinical trials due to specific sample collection or investigations. However, we believe that in many clinical trials (a part of) the study procedures can be performed digitally or remotely which will ultimately benefit the patient and the investigator. Due to this crisis, we were forced to design and conduct our clinical trial fully remotely. Interestingly, this led to a more "patient-centered" and more efficient clinical trial. By sharing our experience, we aim to motivate other researchers to rethink the design of current and new clinical trials.

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REFERENCES

1. Khoury RM, Camacho-Lobato L, Katz PO, Mohiuddin MA, Castell DO. Influence of spontaneous sleep positions on nighttime recumbent reflux in patients with gastroesophageal reflux disease. *Am J Gastroenterol*. 1999;94(8):2069–2073.
2. Kasenda B, von Elm E, You J, et al. Prevalence, characteristics, and publication of discontinued randomized trials. *JAMA*. 2014;311(10):1045–1052.
3. Walters SJ, Bonacho dos Anjos Henriques-Cadby I, Bortolami O, et al. Recruitment and retention of participants in randomised controlled trials: a review of trials funded and published by the United Kingdom Health Technology Assessment Programme. *BMJ Open*. 2017;7(3):e015276.
4. McDonald AM, Knight RC, Campbell MK, et al. What influences recruitment to randomised controlled trials? A review of trials funded by two UK funding agencies. *Trials*. 2006;7:9.
5. Whitaker C, Stevelink S, Fear N. The use of facebook in recruiting participants for health research purposes: a systematic review. *J Med Internet Res*. 2017;19(8):e290.
6. van Gelder M, van de Belt TH, Engelen L, Hooijer R, Bredie SJH, Roeleveld N. Google AdWords and facebook ads for recruitment of pregnant women into a prospective cohort study with long-term follow-up. *Matern Child Health J*. 2019;23(10):1285–1291.
7. Sharon T. The Googlization of health research: from disruptive innovation to disruptive ethics. *Per Med*. 2016;13(6):563–574.
8. Curtis BL. Social networking and online recruiting for HIV research: ethical challenges. *J Empir Res Hum Res Ethics*. 2014;9(1):58–70.
9. Gelinas L, Pierce R, Winkler S, Cohen IG, Lynch HF, Bierer BE. Using social media as a research recruitment tool: ethical issues and recommendations. *Am J Bioeth*. 2017;17(3):3–14.
10. Bhatia-Lin A, Boon-Dooley A, Roberts MK, et al. Ethical and regulatory considerations for using social media platforms to locate and track research participants. *Am J Bioeth*. 2019;19(6):47–61.