Contemporary Clinical Trials 45 (2015) 41–54

Contents lists available at ScienceDirect

Contemporary Clinical Trials

journal homepage: www.elsevier.com/locate/conclintrial

Using e-technologies in clinical trials

Carmen Rosa [a,*], Aimee N.C. Campbell [b,c], Gloria M. Miele [d], Meg Brunner [e], Erin L. Winstanley [f]

[a] National Institutes of Health, National Institute on Drug Abuse, Bethesda, MD, USA
[b] New York State Psychiatric Institute, Department of Psychiatry, Columbia University Medical Center, New York, NY, USA
[c] Mount Sinai St. Luke's Hospital Department of Psychiatry and Behavioral Health, New York, NY, USA
[d] Columbia University College of Physicians and Surgeons, Department of Psychiatry, New York, NY, USA
[e] Alcohol and Drug Abuse Institute, University of Washington, Seattle, WA, USA
[f] The James L. Winkle College of Pharmacy, University of Cincinnati, Cincinnati, OH, USA

ARTICLE INFO

Article history:
Received 12 April 2015
Received in revised form 26 June 2015
Accepted 5 July 2015
Available online 12 July 2015

Keywords:
Clinical trials
E-technology
Social media
Apps
Smartphones
Internet

ABSTRACT

Clinical trials have been slow to incorporate e-technology (digital and electronic technology that utilizes mobile devices or the Internet) into the design and execution of studies. In the meantime, individuals and corporations are relying more on electronic platforms and most have incorporated such technology into their daily lives. This paper provides a general overview of the use of e-technologies in clinical trials research, specifically within the last decade, marked by rapid growth of mobile and Internet-based tools. Benefits of and challenges to the use of e-technologies in data collection, recruitment and retention, delivery of interventions, and dissemination are provided, as well as a description of the current status of regulatory oversight of e-technologies in clinical trials research. As an example of ways in which e-technologies can be used for intervention delivery, a summary of e-technologies for treatment of substance use disorders is presented. Using e-technologies to design and implement clinical trials has the potential to reach a wide audience, making trials more efficient while also reducing costs; however, researchers should be cautious when adopting these tools given the many challenges in using new technologies, as well as threats to participant privacy/confidentiality. Challenges of using e-technologies can be overcome with careful planning, useful partnerships, and forethought. The role of web- and smartphone-based applications is expanding, and the increasing use of those platforms by scientists and the public alike make them tools that cannot be ignored.

Published by Elsevier Inc.

1. Introduction

Historically, clinical trial activities, including recruitment, retention, delivery of interventions, and data collection, have been conducted using conventional "face-to-face" approaches. For example, newspaper or radio advertisements are used to recruit participants, mail or telephone calls are used to conduct follow-up assessments, interventions are delivered in person, and data are collected using paper-and-pencil instruments. Clinical trials have been slow to incorporate e-technology (i.e., digital and electronic technology that utilizes mobile devices or the Internet) into the design and execution of studies [6,110] and are challenged to keep pace with fast-moving developments in technology. For example, in the time it takes to design, implement, and publish findings from a research study (approximately 6 years), the world went from playing interactive video games (Wii) to using voice-activated personal assistants (Siri) [110]. Also, during this timeframe the Apple "App" store added approximately 1 million apps for the iPhone. Additional reasons for the sluggish adoption of e-technology include the limited empirical evidence on whether e-technologies improve or enhance the design of clinical trials and the paucity of regulatory guidance and policies, particularly when FDA-approval is required.

Study teams are, however, incorporating more e-technology into their study designs, perhaps most importantly because mobile technologies and Internet-based communication are becoming the new norm for patients. The culture of communication has changed as potential research participants integrate the Internet, smartphones, and social media into all aspects of their lives. According to recent surveys conducted by the Pew Research Center and summarized in Table 1, approximately 90% of all adults in the United States use the Internet and own a cell phone, and 74% are on a social network site, such as Facebook, Twitter, or Instagram [43]. While younger people are more likely to be using e-technology, older adults are increasingly adopting it into their lives as well. For example, the percentage of adults 65 years and older going online has increased from 14% in 2000 to 59% in 2013; 77% reported having a cell phone in 2013 [107]. Most people agree that the growth of the Internet, smartphones, and tablet devices could have widespread and beneficial health effects.

The purpose of this paper is to provide a general overview of the use of e-technologies in clinical trials research, specifically within the last

* Corresponding author at: Carmen Rosa, 6001 Executive Blvd, Bethesda, MD, USA.
E-mail addresses: crosa@nida.nih.gov (C. Rosa), anc2002@cumc.columbia.edu (A.N.C. Campbell), gmm23@columbia.edu (G.M. Miele), meganw@uw.edu (M. Brunner), erin.winstanley@uc.edu (E.L. Winstanley).

http://dx.doi.org/10.1016/j.cct.2015.07.007
1551-7144/Published by Elsevier Inc.

Table 1
Technology utilization by age of user.
Source: Pew Research Center, surveys conducted 2012–2014 http://www.pewresearch.org/.

	Internet use	Social media use	Own cell//smartphone
Teens (12–17)	95%	81%	88%//73%
Adults—all	87%	74%	90%//58%
Adults <30	97%	89%	98%//83%
Adults >65	59%	56%	77%//18%

decade. The objectives are to (1) present a summary of how e-technology is currently being integrated into clinical trial design, execution and dissemination; (2) illustrate how e-technology-based interventions are being used in the treatment of alcohol and drug abuse, as an example; (3) present the current status of regulatory guidelines for e-technology use, challenges and limitations; (4) summarize the advantages and limitations of e-technologies in clinical trials research; and (5) highlight future directions for the use of e-technologies in clinical research.

2. Integrating e-technologies into clinical trial design, implementation, and dissemination

Some clinical trial researchers have been early adopters of e-technology, using the Internet to recruit study participants [48] and creating computer- or Internet-based interventions [31,63]. Researchers have been using electronic tools for the last two decades to develop protocols, communicate with study personnel, randomize participants, collect data, and analyze results [86,103,115]. Early on, communication with participants was limited to directing individuals to a website for information about the study and providing specific contact information for recruitment and retention purposes [118]. Later, websites were used to distribute and collect data from online questionnaires for eligibility and consent purposes. More recently, clinical trials have started using social media (e.g., Facebook, Twitter), text messaging, and blogs to recruit and enhance retention of participants [61] and to meet regulatory requirements of community consultation [57,124], as well as mobile technologies (tablets, smartphones) to collect data (surveys, patient reported outcomes) and assess or monitor study compliance [134]. Investigators are also starting to integrate other innovative data collection approaches, such as using apps [17], GPS (global positioning system) [47], and wearable devices [68].

Electronic systems have been used for clinical trial implementation procedures, such as randomization and data entry, for the last two decades [106,115]. However, overall technological advances since then have been astronomical [6]. On March 9, 2015, Apple introduced its ResearchKit software, designed for medical and health research. As of March 30, 2015, several iPhone apps have been developed for use in large-scale studies on asthma, breast cancer, cardiovascular disease, diabetes, and Parkinson's Disease (http://www.apple.com/pr/library/2015/03/09Apple-Introduces-ResearchKit-Giving-Medical-Researchers-the-Tools-to-Revolutionize-Medical-Studies.html). Also, Google, Inc.'s has developed a tool intended as a medical device that could be used for clinical trials in the near future (http://hitconsultant.net/2015/06/24/google-developing-wearable-for-clinical-trial-research/). Below is an overview of how researchers are using technology to assist with various aspects of clinical trials, such as recruitment, retention, data collection, and dissemination of results.

2.1. Recruitment

Recruitment of participants into clinical trials is crucial to ensure the generalizability and validity of the study; however this is often one of the more challenging aspects of clinical research. Many clinical trials fail to meet initial participant recruitment goals as outlined in the study protocol [9,19,41]. In the last few years, Internet-based approaches have been increasingly used to supplement traditional recruitment strategies, and such approaches appear to be effective [55,60,81,140]. For example, Yuan et al. [140] used various web-based and social media strategies (Facebook, Twitter, LinkedIn, Craigslist, and Tumblr) to recruit individuals living with HIV, a challenging population to recruit in clinical trials, in part due to the stigma associated with HIV. The study successfully recruited, primarily through Facebook, 1404 adults who had diverse socio-demographic characteristics and represented a broad range of ages. Another study compared participant recruitment for a smoking cessation program using Facebook advertisements vs. traditional strategies (flyers, newspaper advertisements) [55]. The investigators found that approximately half (51.9%, n = 138) of the total sample (n = 266) were recruited via Facebook, with the only statistically significant difference between the two recruitment groups being age; subjects recruited using Facebook were approximately seven years younger compared to subjects recruited using print media. No between-group differences were observed for education, ethnicity, income, gender, or smoking characteristics.

Patients' preferences for e-technologies may influence the extent to which these tools can be effective strategies. Internet-based personal registry tools are used for screening and recruitment ("23andMe", "PatientsLikeMe") [26,64]. Also numerous apps are being developed by sponsors and academic institutions to help patients find relevant clinical trials, such as the National Library of Medicine Pharmaceutical Product Development's Clinical Trials app (http://www.clinicaltrials.com/industry/clinicaltrials_mobile.htm). Additional research is needed to elucidate how social media and other e-technologies are effective for recruitment based on specific content, specific disease types, when and how to target specific demographic subgroups, and other participant variables.

2.2. Engagement and retention

Another area that commonly challenges researchers is the retention of participants in studies, especially during long follow-up periods after the conclusion of active intervention. Prior to the advancement of mobile and Internet technologies, maintaining contact with participants over months or years of research took extensive staff effort and often resulted in less than ideal retention rates. The ability to maintain contact with subjects using mobile phones (e.g., calls, voicemail, texting), social media (e.g., Facebook), and websites has altered traditional retention strategies. The results of recent studies, however, again suggest that participant preference for e-technologies may influence how successful different engagement and retention strategies might be. For example, Rooke et al. [111] compared two studies that used telephone vs. Internet-based delivery of a treatment for cannabis use disorder and found that the telephone intervention had a significantly lower dropout rate compared with the web-based study (38% vs. 46% respectively, $p < 0.01$). Age may be a factor in participant preference for retention strategies and modality of intervention deployment, although other factors such as type and length of intervention and burden of disease cannot be ignored.

A study of African American breast cancer survivors' preferences for physical activity interventions found that there were no age differences in whether the physical activity intervention was administered via email/Internet, an in-person group, or the telephone [104]. Duncan et al. [44] studied a physical activity/healthy eating intervention using IT- and print-based delivery modes and reported no significant differences in outcomes among middle-aged males. Two additional studies with younger participants also found preferences for e-technologies. In a study of youth with Type 2 diabetes, Nguyen et al. [97] found that monetary incentives and technological approaches (mobile phones and websites) were the most effective strategies to engage and retain participants. In contrast, patients with rheumatoid arthritis, with a mean age of 61 years, preferred to complete research surveys via regular