Addictive Behaviors 73 (2017) 204–208

Contents lists available at ScienceDirect

Addictive Behaviors

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

Short Communication

# Feasibility of biochemical verification in a web-based smoking cessation study

Sarah Cha[a,*], Ollie Ganz[a], Amy M. Cohn[a,b], Sarah J. Ehlke[a], Amanda L. Graham[a,b]

[a] Schroeder Institute for Tobacco Research & Policy Studies, Truth Initiative, Washington, DC, United States
[b] Department of Oncology, Georgetown University Medical Center, Washington, DC, United States

ARTICLE INFO

*Keywords:*
Smoking cessation
Biochemical verification
Cotinine
Internet

ABSTRACT

*Background and aims:* Cogent arguments have been made against the need for biochemical verification in population-based studies with low-demand characteristics. Despite this fact, studies involving digital interventions (low-demand) are often required in peer review to report biochemically verified abstinence. To address this discrepancy, we examined the feasibility and costs of biochemical verification in a web-based study conducted with a national sample.

*Methods:* Participants were 600 U.S. adult current smokers who registered on a web-based smoking cessation program and completed surveys at baseline and 3 months. Saliva sampling kits were sent to participants who reported 7-day abstinence at 3 months, and analyzed for cotinine.

*Results:* The response rate at 3-months was 41.2% (n = 247): 93 participants reported 7-day abstinence (38%) and were mailed a saliva kit (71% returned). The discordance rate was 36.4%. Participants with discordant responses were more likely to report 3-month use of nicotine replacement therapy or e-cigarettes than those with concordant responses (79.2% vs. 45.2%, p = 0.007). The total cost of saliva sampling was $8280 ($125/sample).

*Conclusions:* Biochemical verification was both time- and cost-intensive, and yielded a relatively small number of samples due to low response rates and use of other nicotine products during the follow-up period. There was a high rate of discordance of self-reported abstinence and saliva testing. Costs for data collection may be prohibitive for studies with large sample sizes or limited budgets. Our findings echo previous statements that biochemical verification is not necessary in population-based studies, and add evidence specific to technology-based studies.

## 1. Introduction

Accurate measurement of smoking status is imperative to evaluate the effectiveness of cessation interventions. Self-report surveys can underestimate smoking status (Connor Gorber, Schofield-Hurwitz, Hardt, Levasseur, & Tremblay, 2009), especially in high-demand trials where misreporting is more likely. High-demand trials are those involving populations with social pressures to quit (e.g., pregnant smokers (Shipton et al., 2009), or those with smoking-related diseases (Gerritsen et al., 2015; Hilberink et al., 2011; Pell et al., 2008)), and in intensive interventions with frequent contact that may create social desirability among participants to report success (Clark, Zyambo, Li, & Cropsey, 2016; Velicer, Prochaska, Rossi, & Snow, 1992). In such trials, biochemical verification is recommended. However, in low demand cessation trials such as studies with no face-to-face contact (West, Hajek, Stead, & Stapleton, 2005) and large population-based trials that require minimal interaction with study staff or effort by participants (Patrick et al., 1994; SRNT Subcommittee on Biochemical Verification, 2002; Velicer et al., 1992), rates of discordance between self-reported and biochemically verified abstinence have been shown to be small in magnitude (Patrick et al., 1994; Velicer et al., 1992) and comparable across intervention conditions. For these kinds of trials, biochemical verification has been determined to be unnecessary (SRNT Subcommittee on Biochemical Verification, 2002; Velicer et al., 1992).

Despite cogent arguments against the need for biochemical verification in low-demand, population-based studies, trials of digital smoking cessation interventions delivered via the Internet or text message are often required in peer review to include biochemically verified abstinence as a primary outcome. Several recent trials have included such measures (Abroms, Boal, Simmens, Mendel, & Windsor, 2014;

*Abbreviations:* PPA, point prevalence abstinence

* Corresponding author at: 900 G St NW, Fourth Floor, Washington, DC 20001, United States.
*E-mail address:* scha@truthinitiative.org (S. Cha).

http://dx.doi.org/10.1016/j.addbeh.2017.05.020
Received 7 March 2017; Received in revised form 3 May 2017; Accepted 19 May 2017
Available online 22 May 2017

Brown et al., 2014; Free et al., 2011; Johnson et al., 2016), while others that have relied on self-report have noted the lack of biochemical verification as a limitation of their findings (An et al., 2013; Berg et al., 2014; Bottorff et al., 2016; Bricker, Wyszynski, Comstock, & Heffner, 2013; Emmons et al., 2013; Fraser et al., 2014; Leykin, Aguilera, Torres, Perez-Stable, & Munoz, 2012; Mananes & Vallejo, 2014; Skov-Ettrup, Dalum, Bech, & Tolstrup, 2016). The emphasis on biochemical verification during peer review may be because digital interventions are newer than traditional face-to-face or telephonic approaches, and the perception that such studies should include more conservative metrics of abstinence to demonstrate their effectiveness. However, trials of digital interventions are often ill-suited for biochemical verification. Participants are usually recruited from the general population (vs. special populations) and have minimal direct interaction with study staff, and interventions are often self-guided and less intensive (Civljak, Stead, Hartmann-Boyce, Sheikh, & Car, 2013; Graham et al., 2016; Whittaker, McRobbie, Bullen, Rodgers, & Gu, 2016). Given the broad, national reach and scalability of digital interventions, such trials also often involve large, geographically diverse samples, posing additional challenges for biomarker collection.

The aim of this study was to address the discrepancy between recommendations regarding biochemical verification in population-based cessation trials and what we have observed to be the state of the science for digital cessation interventions. We also sought to add to the scant literature about the actual conduct of biochemical verification among participants whose entire study experience (recruitment, intervention, follow-up) occurred via the Internet. Specifically, we report the response rate, discordance rate, costs, and characteristics that distinguish those with discordant vs concordant results to inform the discussion about the utility of biochemical verification in trials of digital interventions.

## 2. Methods

### 2.1. Study sample

Participants were new registrants on BecomeAnEX.org, a free, publicly available smoking cessation website run by Truth Initiative since 2008 (McCausland et al., 2011; Richardson et al., 2013). Participants were recruited to a study that involved completing a baseline survey and 3-month follow-up assessment of smoking status. Recruitment information included details about biochemical verification and availability of incentives for completing each phase of the study. Eligibility criteria were age 18 or older, US residence, and smoking cigarettes “every day” or “some days”. There were no other inclusion/exclusion criteria.

### 2.2. Intervention

All participants had access to BecomeAnEX, which was developed in collaboration with Mayo Clinic (McCausland et al., 2011). Consistent with national guidelines (Fiore, Jaén, & Baker, 2008), BecomeAnEX helps users develop problem-solving and coping skills to quit smoking, educates about pharmacotherapy and assist users in selecting a cessation medication, and facilitates social support through a large online social network of current and former smokers.

### 2.3. Procedure

Study oversight was provided by Chesapeake IRB. Recruitment occurred immediately following registration. Users completed eligibility screening, provided informed consent, completed a baseline survey, and confirmed their e-mail address, all within 24 h of registration. The entire enrollment process was conducted online, automated by a proprietary clinical trials management system.

The follow-up survey was sent via e-mail 3 months after enrollment. Non-responders were sent email reminders at 3 and 6 days. Due to budget constraints, no other methods of follow-up data collection (e.g., phone, mail) were employed. Participants reporting 7-day point prevalence abstinence (ppa) were overnight mailed a swab saliva collection kit (SalivaBio Oral Swab from Salimetrics® (Salimetrics, 2015)) within 1 business day of survey completion. Depending on the timing of follow-up survey completion (e.g., end of day Friday), participants received the collection kit within 1–4 calendar days. Collecting saliva cotinine within 7 days is recommended as a reasonable interval to verify smoking status (SRNT Subcommittee on Biochemical Verification, 2002). Mailed saliva cotinine sampling is an accurate method to verify smoking status (Etter, Neidhart, Bertrand, Malafosse, & Bertrand, 2005; Foulds, Bryant, Stapleton, Jarvis, & Russell, 1994; Greeley, Valois, & Bernstein, 1992) and is most practical in studies with geographically diverse participants. Study staff notified participants by e-mail and text message when kits were mailed and delivered to encourage timely return. The kit included instructions to avoid foods high in sugar, acidity, or caffeine immediately before sample collection, and to wait at least 10 min after rinsing the mouth with water before collecting saliva. Participants were asked to document the presence of oral disease or injury, and to record past 12 h consumption of alcohol, caffeine, nicotine, and medications. This form was sent back with the saliva sample, which was stored in a dedicated freezer until it was overnighted to Salimetrics® (Salimetrics, 2015) for cotinine analysis. Cotinine levels of $< 15$ ng/mL were determined to be concordant with self-reported abstinence (SRNT Subcommittee on Biochemical Verification, 2002). Participants were compensated $20 for the baseline survey, $50 for the 3-month survey, and $25 for returning the saliva sample (Amazon giftcodes sent via email).

### 2.4. Measures and analysis

The baseline survey assessed sociodemographic characteristics (age, gender, race, ethnicity, education, employment, marital status, income); smoking history (current cigarettes per day, desire and confidence to quit, nicotine dependence (Borland, Yong, O'Connor, Hyland, & Thompson, 2010)); quitting history (number of quit attempts, quit methods); and curiosity about using e-cigarettes to quit. The 3-month survey assessed current smoking (30-day ppa, 7-day ppa); smoking and quitting history since enrollment; and smoking-related interactions with health professionals. Cotinine level and data on past 12-hour use of nicotine were included in analyses.

Bivariate tests were used to examine differences between participants with cotinine levels above or below the 15 ng/mL threshold on baseline characteristics, cessation-related behaviors, and smoking outcomes. Between group differences were examined with two-sample t-tests for normally distributed continuous and ordinal variables, Mann-Whitney $U$ test for skewed continuous variables, and two-sided Chi-square or Fisher's exact tests for categorical variables. All analyses were completed using SPSS v.21 (IBM Corporation, 2012).

## 3. Results

### 3.1. Study sample

From October 2015 to March 2016, 600 participants were enrolled. Participants were primarily white (81.5%), female (73.0%), and had some college education (72.2%). Most were 25–44 years old (42.2%) or 45–64 years old (42.8%); about half were employed full time (50.2%), had a spouse/partner (49.5%), and reported income higher than $30,000/year (56.8%). Smoking rate at enrollment was 18.2 cigarettes per day (SD = 9.8), and 74.5% reported smoking their first cigarette within 30 min of waking. Participants reported an average of 2 quit attempts in the past year (Interquartile range (IQR) = 0–3.0): the most common quit methods were “willpower/cold turkey” (55.5%) and medication (nicotine replacement therapy products and prescription