Lessons learned from unsuccessful use of personal carbon monoxide monitors to remotely assess abstinence in a pragmatic trial of a smartphone stop smoking app – A secondary analysis

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ABSTRACT

Introduction: Verifying abstinence remotely in trials of digital cessation interventions remains a major challenge. This study reports on using personal carbon monoxide (CO) monitors to assess abstinence in a pragmatic trial of a standalone cessation app involving automated recruitment with no researcher contact.

Methods: The study involved secondary data analysis of remote CO testing in a randomized trial (ISRCTN10548241) comparing two versions of a cessation app (BupaQuit). Trial participants were adult UK-based smokers interested in quitting, who were recruited online (02/2015–03/2016). Participants were followed-up through the app, email or phone at 4 weeks. Fifty-nine participants reporting not smoking were posted a personal CO monitor with instructions, and emailed two reminders. The monitors required installing software on a Windows PC. Participants were not reimbursed but retained the device. We recorded the proportion of CO tests returned, test results, self-reported ease of use, correct use, acceptability, and reasons for missing results.

Results: Fifteen (25.4%) CO results were returned, of which 86.6% were < 10 ppm and 53.3% were < 5 ppm, indicating abstinence (corresponding to 20.9% and 12.9% of all trial participants self-reporting abstinence, respectively). These 15 participants found the test easy, acceptable and believed they conducted it correctly.

Conclusion: Remote validation using personal CO monitors may not yet be feasible in pragmatic studies of cessation apps in which participants are recruited with no reimbursement or direct contact with researchers.

1. Introduction

Verification of self-reported abstinence is important in evaluating cessation interventions (Benowitz et al., 2002; West et al., 2005). However, it is especially challenging in studies of digital interventions that rely on remote recruitment and follow-up, with participants often spread across vast geographical locations. In result, many of such studies rely on self-reports (Taylor et al., 2017; Ubhi et al., 2015; Whittaker et al., 2016), which may over-estimate the actual quit rates (West et al., 2007), although the bias may be lower in low-intensity interventions, and should not differ across study arms (Glasgow et al., 1993; Patrick et al., 1994). In this study we report findings from using one type of a personal carbon monoxide (CO) monitor, which connected to Windows computers, to remotely validate self-reported abstinence in a trial of a smartphone stop smoking app. The trial involved no contact with the researchers during enrolment, and only minimal contact at follow-up.

Several methods for remote verification of abstinence are available. One approach involves analysing samples of saliva for nicotine metabolites (cotinine or anabasine). These can be collected through post, and sent by participants to the researchers or directly to biochemical labs (Brown et al., 2014). Previous studies offered participants reimbursement for providing saliva samples (e.g. reimbursement of value of £20/$28) (Brown et al., 2014). The costs of conducting lab-based tests of saliva samples can be at least £25–£40/$34–$55 per participant, excluding reimbursement (in 2015, the costs of cotinine tests started at £20–£35 per sample, depending on the level of processing required, over £30 for anabasine tests, and around £5 for first class postage, envelopes and salivettes; the prices could change depending on lab and the number of tests, and certain items may need to be purchased in

Trial registration: ISRCTN10548241 (http://www.isrctn.com/ISRCTN10548241).

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Assessment of carbon monoxide (CO) in the exhaled breath has been among the most commonly used methods in many cessation programmes (Goldstein et al., 2018; West et al., 2010), with readings lower than 10 particles per million (ppm) commonly accepted as confirmation of abstinence (Brose et al., 2013; West et al., 2005), but with lower cut-off levels of 5 ppm suggested more recently (Perkins, Karelitz, & Jao, 2013). CO testing has important advantages over the other methods as it is non-invasive, and insensitive to concurrent use of nicotine products or e-cigarettes, although its temporal applicability is limited due to rapid elimination of CO from the body (Benowitz et al., 2002; Goldstein et al., 2018). Measuring CO levels may be especially difficult if participants cannot travel for in-person testing. Some studies have accomplished remote CO testing by having research staff travel to participants’ homes or organizing verification at local clinics (Kim et al., 2005), or by providing traditional CO monitors for home-based testing and requiring participants to share videos of the procedure (Dallery & Glenn, 2005; Hertzberg et al., 2013; Karelitz et al., 2017). However, such a method may not be feasible or affordable in many contexts.

A new generation of personal CO monitors (e.g. devices manufactured by Bedfont® Scientific Ltd., https://www.bedfont.com/shop/smokerlyzer) are smaller, lighter and more affordable (under £50/$69 in the UK) than traditional CO monitors (cost starting at around £170/$230 in the UK), which means they could be purchased and posted to smokers for home-based testing at a price similar to the saliva testing that includes reimbursement.

Remote CO testing using these new devices offers several advantages. CO testing is not easily accessible, but has been shown to be valued by smokers (Beard & West, 2012; Goldstein et al., 2018; Shahab, West, & McNeill, 2011), and acceptable for regular remote assessment of smoking status (McClure et al., 2015), and thus could be attractive to study participants, enabling them to assess their quitting progress. Retaining such a device for future use could be a form of compensation for participants’ time and inconvenience, especially in the absence of other reimbursement. Importantly, a single CO device could be used for multiple tests and follow-up waves. Moreover, CO testing in itself may provide an incentive for smokers to remain abstinent (Beard & West, 2012; Shahab et al., 2011). Finally, using the new generation of personal CO monitors could be cost-effective, and appropriate when saliva testing or use of traditional CO monitors is not possible. However, feasibility of using this method to assess self-reported abstinence during follow-up in trials of digital interventions is yet to be ascertained.

In this study we assessed feasibility of remote verification of abstinence using personal CO monitors that connect to Windows PCs, and which were posted to participants who were self-reporting not smoking in a pragmatic trial of a stop smoking smartphone app (BupaQuit). One of the key underlying aims for the BupaQuit trial was to evaluate the app in a more ecological setting than previous studies had done (Bricker et al., 2014; Bricker et al., 2017; Buller et al., 2014), namely one with limited contact with the researcher throughout the trial. The procedures of CO testing were aligned with those used in an earlier trial of a web-based stop smoking intervention conducted by some of the authors, and which involved saliva sampling (Brown et al., 2014). These included automatic posting of the testing kit to the postal address provided by the participants during enrolment into the trial, using first class mail, and offering guidance to participants in the form of written instructions. The main difference in the procedures was the lack of incentives in the current trial beyond the possibility to keep the CO device for private use. Adopting similar procedures for CO testing was judged to be important - if CO testing was to be a feasible alternative to saliva testing, it should be used in a context with similar funding level and research staff time.

2. Methods

2.1. Design

The study involved secondary analysis of data related to remote CO testing from a pragmatic, randomized controlled trial comparing effectiveness of a cessation app for iOS and Android called BupaQuit, to a version of the app providing minimum support. The trial was approved by UCL Research Ethics Committee (6212/001), and was prospectively registered with the ISRCTN Register (ISRCTN10548241). The trial outcomes are reported elsewhere (submitted for review). Trial protocol and additional information are available on Open Science Framework (https://osf.io/ge6vh/). The study was conducted in collaboration with Bupa (www.bupa.com) who developed the app and provided support for data collection.

2.2. BupaQuit trial recruitment and participants

Between February 2015 and March 2016, we recruited into BupaQuit trial a total of 425 adult, UK-based daily smokers interested to quit, who downloaded the app, and completed registration (including provision of informed consent and full contact details) via the app. Participants were recruited online and with no researcher contact, primarily through paid advertisement on social media, as well as through UK iTunes and Google Play app stores. Interested participants were directed to a project website with study information that outlined the follow-up procedures (including the follow-up procedures at 2 and 7 months), and asked to confirm reading it before registering via the app.

2.3. Study sample

Among BupaQuit trial sample, 62 (14.6%) participants self-reported not smoking in the past 14 days at 4-week follow-up (primary trial outcome). The current study concerned a sample of 59 trial participants who (i) self-reported not smoking, and (ii) were posted the CO monitor (three participants were not posted a monitor due to one participant declining to receive one, and the other two due to administrative reasons).

2.4. Procedure

Trial participants were contacted at 4-week follow-up since their quit date, first via the app, and then email and phone to assess the primary outcome. Participants self-reporting abstinence were posted a 1st Class small parcel (normally delivered on the next business day within the UK; CO box size 25 × 15 × 5 cm plus padded envelope; stamp cost starting at £3.30/$4.50) with the COmpactUSB™ Smokerlyzer® developed by Bedfont Scientific Ltd. (the only such device available for purchase at the time). The package included additional mouthpieces (enabling hygienic sharing of the device), and instructions and information about CO testing (see Appendix A1). Participants were instructed to provide a single CO reading upon receiving the CO device, and were also informed that they may be asked to use the device again at the next follow-up at 6 months. However, due to the low return rate of CO readings during the short-term follow-up the biochemical verification at 6 months was suspended.

Only those participants, who were reporting not smoking over the phone (66.1% of the current study sample) could be opportunistically asked to update the postal address. Most of the participants contacted over the phone seemed positive about the CO test, but a longer discussion about the procedures was not possible, and the participants...
enrolled in BupaQuit trial (n=425)

Reporting abstinence at 4-week follow-up (n=62)

Posted CO Monitor (n=59)

CO Monitor not posted (n=3) declined to receive one (n=1) administrative reasons (n=2)

CO reading not returned (n=44) incorrect addresses provided (n=1) unable to accept large packages (n=1) device lost (n=1) forgotten about the test (n=1) refused to share result (n=1) not able to use Windows PC (n=3) unknown (n=36)

Fig. 1. Participant flow through BupaQuit trial and CO testing procedure.

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Fig. 1. Participant flow through BupaQuit trial and CO testing procedure.

are auxiliary to the present study.

2.6. Data analysis

Participants with and without the CO results returned were compared on baseline and process variables using chi-square and t-test for categorical and continuous data, respectively. We applied Sidak correction to account for multiple comparisons, and the p-value cut-off was set to 0.007. Data were analysed in SPSS (22.0).

3. Results

Fig. 1 presents the flow of participants. Fifteen out of 59 (25.4%) participants returned their CO readings (one participant sent two readings, and only the first reading was included in the analysis), of which five did so within two days, six within a week, and three after 9, 22 and 47 days since the device was posted (mean = 8.4 days, median = 5 days; for one participant the date was not available). Thirteen (86.6%) of the returned readings were below 10 ppm (meeting the Russel Standard criteria for abstinence (West et al., 2005)), and eight (53.3%) were below 5 ppm (a more conservative threshold suggested more recently (Perkins et al., 2013)). This corresponded to 20.9% and 12.9% of all trial participants self-reporting abstinence, respectively. Among those returning the readings, 12 (80.0%) reported they used the device correctly, 14 (93.3%) that it was easy to use, and 15 (100.0%) that it was acceptable.

There were no statistically significant differences between participants returning the CO tests or not with respect to baseline characteristics or the study arm, except for those who returned the CO readings being more likely to had used electronic cigarettes before (40.9% vs. 73.3%, p = 0.04; see Table 1). Participants with known app device system (Android: 35%, iOS: 22.7%) had marginally greater proportion of results returned than those with device status Unknown (17.0%). A significantly greater proportion of participants reporting abstinence via the app (53.8%) sent their readings in comparison to those reporting it via e-mail (0.0%), or phone (21.1%) (p = 0.01). There were no
and as an integral part of quitting or cutting down, rather than only as a sent study, and often implemented CO testing during study initiation implementing additional procedures (e.g. incentives).

Remote assessment of self-reported abstinence in trials of digital cessation interventions using personal CO monitors is a promising and, in theory, more attractive and cheaper alternative to other available methods. However, in this study only a quarter of participants provided results of biochemical verification, much fewer than around 60–80% observed in other studies (e.g. (Brown et al., 2014)). These findings suggest that using CO monitors that connect to computers to remotely assess abstinence in a smartphone-based cessation trial was not feasible as per this study’s protocol. Lack of affordable and practical means to trace package delivery, retrieve unused devices, and to systematically collect feedback or reasons for the missing results. Some of the underlying causes were common with other trials of digital interventions, including limited contact with participants, lack of a closer rapport or accountability, and little opportunity to discuss procedures (Brown et al., 2014). Several practical barriers to CO testing were also identified, although most cases remained unexplained. Some other possible reasons could include: (a) lack of reimbursement (retaining CO monitors might not be a sufficient incentive), (b) participants unavailable at the address provided – we were able to confirm only two-thirds of addresses, (c) having used the CO test but not sharing the results with the researchers, (d) over-reporting of abstinence at follow-up, and not willing to share CO result confirming smoking, and (e) low commitment to the study or limited app engagement.

Through subsequent opportunistic communication with some of the participants (e.g. when issuing invitation to follow-up telephone interviews or at 6 month follow-up) and thanks to one parcel being re-taioning CO monitors might not be a sufficient incentive), (b) participants other possible reasons could include: (a) lack of reimbursement (re- Hajiri et al., 2014)). For example, such studies could have nontrivial impact on the experience of testing itself. Among the main challenges in using CO monitors in this trial were lack of affordable and practical means to trace package delivery, retrieve unused devices, and to systematically collect feedback or reasons for the missing results. Some of the underlying causes were common with other trials of digital interventions, including limited contact with participants, lack of a closer rapport or accountability, and little opportunity to discuss procedures (Brown et al., 2014). Several practical barriers to CO testing were also identified, although most cases remained unexplained. Some other possible reasons could include: (a) lack of reimbursement (retaining CO monitors might not be a sufficient incentive), (b) participants unavailable at the address provided – we were able to confirm only two-thirds of addresses, (c) having used the CO test but not sharing the results with the researchers, (d) over-reporting of abstinence at follow-up, and not willing to share CO result confirming smoking, and (e) low commitment to the study or limited app engagement. The latter is further supported by the observations that the CO results tended to be returned more often by those reporting abstinence via the app, and those engaging with the app in the first place.

Indeed, studies that observed better engagement with remote CO testing adopted very different procedures in comparison with the present study, and often implemented CO testing during study initiation and as an integral part of quitting or cutting down, rather than only as a method to validate self-reported abstinence (Dallery & Glenn, 2005; Hertzberg et al., 2013; Karelitz et al., 2017). For example, such studies involved training with a researcher on using the CO device, offered incentives (e.g. cash or vouchers) for reporting any CO readings or for meeting certain CO thresholds, required or encouraged regular and video-recorded CO testing (e.g. daily, or twice daily), offered additional cessation resources (e.g. a website, pharmacotherapy, behavioural support), and involved other regular contact with the researchers (e.g. remote monitoring of the readings to identify falsifications, or lab visits) (Dallery & Glenn, 2005; Hertzberg et al., 2013; Karelitz et al., 2017). Finally, some studies also used a more expensive CO device (e.g. pICO Smokerlyzer developed by Bedfont for clinical use) (Dallery & Glenn, 2005; Karelitz et al., 2017), which could have nontrivial impact on the experience of testing itself.

The table below shows the baseline characteristics of BupaQuit trial participants who self-reported not smoking and who returned or did not return their CO readings.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n = 59)</th>
<th>Did not return CO readings (n = 44)</th>
<th>Returned CO readings (n = 15)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study arm in BupaQuit trial, % (N)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>42.4 (25)</td>
<td>40.9 (18)</td>
<td>46.7 (7)</td>
<td>0.77</td>
</tr>
<tr>
<td>Control</td>
<td>57.6 (34)</td>
<td>59.1 (26)</td>
<td>53.3 (8)</td>
<td>0.10</td>
</tr>
<tr>
<td>Age (years) Mean (SD)</td>
<td>33.0 (10.6)</td>
<td>33.1 (10.9)</td>
<td>32.7 (10.0)</td>
<td>0.90</td>
</tr>
<tr>
<td>Smokes within 5 min of waking up % (N)</td>
<td>20.3 (12)</td>
<td>18.2 (8)</td>
<td>26.7 (4)</td>
<td>0.48</td>
</tr>
<tr>
<td>Confidence to stop (1–7) Mean (SD)</td>
<td>4.9 (1.4)</td>
<td>4.8 (1.4)</td>
<td>5.3 (1.3)</td>
<td>0.17</td>
</tr>
<tr>
<td>Female % (N)</td>
<td>32.2 (19)</td>
<td>29.5 (13)</td>
<td>40.0 (6)</td>
<td>0.53</td>
</tr>
<tr>
<td>Occupation % (N)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manual</td>
<td>55.9 (33)</td>
<td>54.5 (24)</td>
<td>60.0 (9)</td>
<td>0.92</td>
</tr>
<tr>
<td>Non-manual</td>
<td>20.3 (12)</td>
<td>20.5 (9)</td>
<td>20.0 (3)</td>
<td>0.77</td>
</tr>
<tr>
<td>Other, incl. retired, unemployed, student</td>
<td>23.7 (14)</td>
<td>25.0 (11)</td>
<td>20.0 (3)</td>
<td>0.77</td>
</tr>
<tr>
<td>Recruitment channel</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Advertisement on Twitter/Facebook</td>
<td>33.9 (20)</td>
<td>29.5 (13)</td>
<td>46.7 (7)</td>
<td>0.42</td>
</tr>
<tr>
<td>App store searches</td>
<td>30.5 (18)</td>
<td>34.1 (15)</td>
<td>20.0 (3)</td>
<td>0.77</td>
</tr>
<tr>
<td>Other (email, word of mouth, poster)</td>
<td>35.6 (21)</td>
<td>36.4 (16)</td>
<td>33.3 (5)</td>
<td>0.77</td>
</tr>
<tr>
<td>Recruitment channel</td>
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<tr>
<td>Recruitment channel</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No aids</td>
<td>22.0 (13)</td>
<td>25.0 (11)</td>
<td>13.3 (2)</td>
<td>0.48</td>
</tr>
<tr>
<td>Medical aids</td>
<td>50.8 (30)</td>
<td>52.3 (23)</td>
<td>46.7 (7)</td>
<td>0.77</td>
</tr>
<tr>
<td>Other, incl. retired, unemployed, student</td>
<td>23.7 (14)</td>
<td>20.5 (9)</td>
<td>33.3 (5)</td>
<td>0.77</td>
</tr>
<tr>
<td>Smartphone operating system</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Android</td>
<td>33.9 (20)</td>
<td>29.5 (13)</td>
<td>46.7 (7)</td>
<td>0.46</td>
</tr>
<tr>
<td>iOS</td>
<td>37.3 (22)</td>
<td>38.6 (17)</td>
<td>33.3 (5)</td>
<td>1.00</td>
</tr>
<tr>
<td>Unknown</td>
<td>28.8 (17)</td>
<td>31.8 (14)</td>
<td>20.0 (3)</td>
<td>0.77</td>
</tr>
</tbody>
</table>

* p-Value from Fisher’s exact test for 2 × 2 tables, from chi-square test for other categorical variables, and from independent t-test for continuous variables.

** Participants could select one or more answers.
The study had limitations. First, it was an exploratory and observational study using secondary data from a randomized trial. Due to concerns about attrition and participant burden, a more detailed assessment of the CO testing procedure was not feasible. However, contacting participants over email or phone to collect other trial outcome data was challenging, and it is unlikely that attempts at collecting further data on CO test would be fruitful. Second, the PC-based COm pactUSB® Smokerlyzer® model used in this study has been discontinued and replaced by a model that connects to Android/iOS smartphones and tablets (iCO® Smokerlyzer®). Smartphone-enabled CO monitoring devices (Meredith et al., 2014) might be more accessible and thus could increase the proportion of CO tests returned in future studies of cessation apps. The feasibility of using these devices requires further research, but the observations from this study should nevertheless apply to other settings when the CO devices are posted as part of the follow-up and verification of abstinence.

In the present study, the CO monitors were posted to participants only once the follow-up had started, and to be used by them only at one time point. Among the key benefits of using personal CO monitors is that they allow for repeat testing and monitoring of progress in quitting (i.e. demonstrating a decline in ppm values from baseline), which this study has not explored. Providing participants with CO monitors at the start of the trial or at the initiation of a quit attempt could increase acceptability and engagement with the devices, as well as cessation outcomes (Beard & West, 2012; Dallery & Glenn, 2005; Shahab et al., 2011), which should be assessed in future research. Additionally, future studies could involve experimental designs, e.g. a head-to-head comparison of several methods of abstinence validations, to better assess the acceptability and feasibility of the individual tests.

The findings suggest that studies using remote CO testing to validate abstinence in trials may require separate reimbursement and establishing a better rapport with participants, as well as using software that enables recording of installation or initiation of device use without intrusive collection of non-trial data.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jabrep.2018.07.003.

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