

**WILLINGNESS-TO-TRY VARIOUS
TOBACCO CESSATION METHODS AMONG
US ADULT CIGARETTE SMOKERS**

BY

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Willingness-to-try various tobacco cessation methods among US adult cigarette smokers

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ABSTRACT

Introduction: Long-term smoking cessation success rates without substantive intervention remain abysmal. Some studies suggest an association between sociodemographic factors and tobacco cessation success. We sought to explore US adult tobacco users' willingness-to-try diverse tobacco cessation methods by sociodemographics and tobacco use habits.

Methods: We electronically surveyed a convenience sample of 562 US adults to explore willingness-to-try various cessation methods among those who reported current tobacco cigarette use. Participants rated their willingness-to-try different cessation methods. Logistic regression models examined associations between willingness-to-try tobacco cessation methods based on sociodemographic and tobacco use characteristics.

Results: Non-whites were more likely to report willingness-to-try counseling (RR 1.32, 95% CI 1.14, 1.52) and those with high school education or less were less likely to report willingness-to-try counseling (RR 0.78, 95% CI 0.64, 0.95). Those with lower income were less likely to report willingness-to-try any medication (RR 0.84, 95% CI 0.73, 0.98). High nicotine dependence was associated with a high likelihood of reporting willingness-to-try any evidence-based method (RR 1.07, 95% CI 1.04, 1.10) and a history of quit attempts was associated with likelihood to report willingness-to-try any evidence-based method (RR 1.31, 95% CI 1.10, 1.56).

Conclusion: Sociodemographics and nicotine dependence may affect preferences for tobacco cessation methods and should be considered when counseling patients on tobacco cessation.

INTRODUCTION

Smoking accounts for an estimated 6 million deaths every year globally. By 2030, the mortality rate is expected to increase to approximately 8 million deaths annually[1-3]. According to the 2016 National Health Interview Survey, up to 15.5% of adults in the US smoke cigarettes, an improvement from 20.9% in 2005 [4]. The success rate of smoking cessation ranges from 5 - 7.4 % [5-7]. Evidenced-based methods are less frequently used than non-evidence-based methods,[8] yet studies have shown that treatment with pharmacotherapy and counseling support, either individually or when combined together, increase the likelihood of success by greater than 10% [9,10].

There is considerable variability among people who smoke in terms of smoking cessation methods used and successful quitting [11,12]. In the 2010 National Health Interview Survey, low income and non-Hispanic blacks indicated a higher interest in smoking cessation than non-Hispanic whites but had lower rates of success [13,14]. In a separate study, Hispanics were half as likely to seek assistance with tobacco cessation compared with whites and heavy smokers were more likely to seek assistance compared with light smokers [11]. Tobacco users who smoke more than 19 cigarettes per day have been found to have a higher likelihood of success with smoking cessation while electronic nicotine delivery system (ENDS) users are associated with lower likelihood of smoking cessation success [12].

Gaps exist in the understanding of different subgroups of tobacco users' willingness-to-try tobacco cessation methods including counseling and pharmaceutical products [15]. Identifying effective strategies for tobacco cessation, integrated with patients' preferences especially in a sociodemographically diverse setting, is beneficial and may lead to a reduction in tobacco-related morbidity and mortality [16]. The current study examines a convenience sample of U.S. adult tobacco users' self-report of their willingness-to-try various forms of evidence-

based and non-evidence-based cessation methods. Our study investigates whether differences in participants' preferences of tobacco cessation methods is associated with sociodemographic and tobacco use factors.

MATERIALS AND METHODS

Design

We conducted a cross-sectional online survey of various tobacco cessation methods. The study included a pre-test phase using an academic email system. Twelve individuals participated in the pretesting of the survey between May 9th and May 14th, 2016. We revised and simplified the language of the survey based on feedback from the pretest phase. To improve the clarity of the survey, we carried out a second round of testing with 75 participants who were recruited from a survey panel via Research Now, a market research group, between August 15th and 16th, 2016. After this round of testing, we revised the survey language again and fielded the final version of the survey between August 26th and August 31st, 2016. Participants from the Research Now panel were compensated per the marketing group's rates at the time. This study was approved by the UNC Chapel Hill School of Medicine Institutional Review Board.

Sample

The team enlisted and enrolled 900 participants, aged 18 and older, who were members of an online survey panel of a market research group - *Research Now*. The current analysis was limited to 562 participants who reported current tobacco cigarette use—defined as use in the past 30 days. Participants who reported ENDS use within the last 30 days in addition to tobacco cigarette use were also included in the study. Participants who reported current ENDS use were classified as dual users. All participants had to live in the United States and able to complete an online

survey in English. *Research Now* does not provide data on how many people receive the initial invitation to participate in a study, thus we cannot report a response rate.

Measures

Data on sociodemographic characteristics collected included questions about race, education level and yearly household income. The survey also collected details about each participant's tobacco use characteristics including number of cigarettes per day, time to first smoke after wake and past attempts to quit. The heaviness of smoking index (HSI) which estimates the level of nicotine dependence as mild, moderate and high based on the number of cigarettes smoked per day and time to first smoke after waking was calculated for each participant [17].

Outcome Measures

Participants were asked to rate their willingness-to-try different forms of evidence-based and non-evidenced-based tobacco cessation methods. Response options included “would definitely use”, “likely to try”, “unlikely to try” and “would definitely not try”. Evidence-based methods listed were medications including nicotine containing products, wellbutrin/zyban and chantix, and different forms of counseling support, including individual counseling, support group or class, telephone quitline, online program, texting program and any counseling. Non evidenced-based methods included forms of complementary and alternative therapy, other tobacco or nicotine delivery systems and quitting without any assistance. Participants were not informed of which methods are evidence-based or non-evidence-based.

Analysis

The analytical sample contained only current tobacco cigarette users and dual users. Some sociodemographic variables were dichotomized. Race was collapsed into non-white and white

and race was not further classified by ethnicity due to the low number of Hispanic participants. Education was classified as high school degree/GED or less and some college or higher and income was classified as less than \$30,000 and \$30,000 or greater. HSI was further dichotomized into high or moderate/low while quit attempts in the past year and ENDS use was categorized as yes or no. Positive responses for the use of tobacco cessation methods - “will definitely use” and “likely to try” - were categorized as willingness-to-try for the analysis.

Bivariate associations between ENDS use (yes/no) and baseline characteristics (i.e. sociodemographic characteristics and tobacco use characteristics) were examined using t-tests for normally distributed continuous variables, Wilcoxon-Mann-Whitney tests for non-parametric continuous variables, and Chi-square tests for categorical variables. Unadjusted and adjusted effects were estimated for willingness-to-try cessation methods using logistic regression. Purposeful selection method was used [18] to determine variables to include in adjusted models, which involved an iterative process of examining all covariates as potential significant predictors or confounders. In the iterative process, covariates were removed from the model if they were non-significant at $\alpha=0.1$ and not a confounder (i.e., did not result in a parameter estimate change greater than 15%). The final model included only significant covariates and confounder. Data were analyzed using SAS version 9.4 (SAS Institute, Inc.) with a two-tailed significance level ($p<.05$). Risk ratios are reported rather than odds ratios because the outcome events are relatively common (incidence of more than 10%) and thus risk ratios offer more appropriate approximations [19].

RESULTS

From the larger sample of 900 participants who completed the survey, a total of 562 were tobacco cigarette or dual users. Mean age was 47 years. Most participants were white (82%), 47% were female and 76% had a college education or higher. Approximately 24% of participants

had an annual household income of less than \$30,000. Of this sample, 88% reported smoking less than 20 cigarettes per day, 14% reported less than 5 minutes to first smoke after wake and 6.2% had a high HSI score. Eighty-three percent reported making an attempt to quit smoking in the past year and almost half (48%) were dual users.(Table 1)

Adjusted logistic regression analysis showed that non-white participants were more likely to report willingness-to-try any counseling method (RR 1.32, 95% CI 1.14, 1.52) compared to whites and participants with a high school education or less were less likely to report willingness-to-try any counseling method compared with those with a college education or higher (RR 0.78, 95% CI 0.64, 0.95). Participants with an annual income of less than \$30,000 were less likely to report willingness-to-try any medication (RR 0.84, 95% CI 0.73, 0.98) and any counseling (RR 0.82, 95% CI 0.67, 0.99) when compared with participants with higher annual income.

Participants with a high HSI score were more likely to report willingness-to-try any medication, any counseling and any evidenced-based method (RR 1.07, 95% CI 1.04, 1.10) and less likely to report willingness-to-try cold turkey (RR 0.90, 95% CI 0.87, 0.94). Those who had attempted to quit in the past were also more likely to report willingness-to-try any medication, any counseling and any evidenced-based method (RR 1.31, 95% CI 1.10, 1.56) compared with those with no history of quit attempts. Although, dual users were more likely to report willingness-to-try any counseling and any evidenced-based method compared with tobacco cigarette only users, these associations lost statistical significance after adjusting for other variables in the final model (Table 2).

Table 3 represents a breakdown of comparison of willingness-to-try different tobacco cessation methods among tobacco cigarettes only users and dual users. Dual users were more likely to report a willingness-to-try wellbutrin when compared with tobacco-only users with

similar non-significant trends for other medications (41% vs 30%; p value = 0.005). Dual users were significantly more likely to report willingness-to-try any type of counseling support listed, except for individual counseling, which did not reach statistical significance. Overall, dual users were more likely to report a willingness-to-try any evidence-based method compared with tobacco cigarette only users (82% vs 73%; p= 0.01). Dual users were also more likely to report willingness-to-try non-evidenced-based methods including different forms of complementary and alternative methods and other tobacco or nicotine delivery systems.

DISCUSSION

The current study explores a convenience sample of tobacco users' willingness-to-try different tobacco cessation methods by sociodemographics and level of nicotine dependence. Our findings reveal that preferences for tobacco cessation methods exist based on race/ethnicity, level of income, education and severity of nicotine dependence. While non-white participants were significantly more likely to report willingness-to-try counseling over other cessation methods, those with lower education level were less likely to report willingness-to-try counseling and those with an annual household income of less than \$30,000 were less likely to report willingness-to-try any medication. Participants with a higher HSI, higher tobacco dependency, were more likely to report willingness-to-try any evidence-based cessation method over non-evidence-based methods. The data also indicates that dual users were more likely to report willingness-to-try any evidenced-based method compared with tobacco cigarette only users.

Our results have implications for public health practice, primary care clinician counseling services and future research. Our finding that non-white participants had a higher likelihood to report willingness-to-try counseling compared with whites is similar to previous studies that show a higher utilization of quitlines, telephone counseling, by non-whites compared with white

tobacco users in studies to assess for variations in quitline reach by ethnicity and race [20,21]. This preference for counseling over other methods may arise from lack of knowledge or awareness about pharmacological therapies, their perceived costs, harms or their effectiveness, leading to a perceived preference for counseling. Some studies have shown that, compared with white tobacco users, non-whites are less likely to be screened for tobacco use or advised to quit by a healthcare provider [22, 23] and hence, may not be aware of all their options. Another study to assess ethnic minority group's beliefs and perspectives for recommended treatment options for tobacco cessation found that many participants were not fully aware that medications are beneficial and were concerned about risks of side effects [24]. These concerns may have contributed to findings in the current study and may explain non-whites reported willingness-to-try counseling over other methods.

We found that participants with an annual income less than \$30,000 were less likely to report willingness-to-try any medication and any counseling. This finding may be related to costs associated with medication and counseling especially for low-income smokers who may be uninsured. While the daily cost of cessation medications may be similar to the cost of cigarettes, these medications tend to come in weekly or monthly supply, making it unaffordable for low income smokers who may need to pay out of pocket [25]. This association has been mentioned in other studies that showed that low-income patients with chronic disease cut back on essential medications or are non-adherent due to cost [26, 27]. Removal of the cost barrier or the offer of free treatment may increase preference and hence, utilization of pharmacotherapy for tobacco cessation among low-income patients [28].

Although we found that participants with lower levels of education were less likely to indicate a willingness-to-try any counseling, other studies have shown mixed results, indicating a positive, negative or non-significant association between low education and participation in

counseling.[11,29,30,31] Our findings could also be the result of the low likelihood of people with low educational status to receive smoking cessation advice [23,32] and hence may not be aware of counseling as an option.

Tobacco use characteristics seem to play a role in willingness-to-try different cessation methods. Participants with a high level of nicotine dependence were more likely to report a willingness-to-try any evidence-based method and less likely to report willingness-to-try to quit cold turkey. This is similar to findings by Zhu et al who found that heavy smokers were twice as likely to seek assistance as light smokers. In this study, the assistance involved both evidence-based and non-evidenced-based methods such as self-help materials [11]. The fact that those with high level of nicotine dependence are less likely to quit cold turkey may stem from previous failed attempts to quit without assistance or concerns that their severity of nicotine dependence may make it challenging to quit independently.

In addition, participants with history of previous quit attempts were more likely to report willingness-to-try any evidence-based method. A similar study that assessed preferences for future quit attempts showed that a history of previous quit attempt with medications was associated with interest in pharmacotherapy for future quit attempts [33]. Another showed that smokers tend to use same cessation methods that they tried at their baseline quit attempt [34]. It is unclear if participants in our study reported willingness-to-try evidence-based methods based on cessation methods used during previous quit attempts.

Our study also showed that dual users were more willing to report a willingness-to-try both evidence and non-evidenced-based methods compared with tobacco cigarette only users. The significant difference noted between the two groups suggests that dual users are willing to try any method in an attempt to stop smoking. This is similar to findings from various studies

have shown that e-cigarette users are likely to attempt to quit [35, 36], although this may not translate to successful quitting.

Limitations of this study include its cross-sectional design and restriction to those able to complete an online survey. Since the study was on volunteer participants, the findings may not be applicable to the general population. The cross-sectional nature also limits the ability to explore causality and to capture other factors that may affect responses of participants. Participants were not asked about their knowledge of smoking cessation methods and may not have been aware of all methods or their efficacy, which may have affected their report of willingness-to-try different methods. Another limitation is the reliance of self-reported information about smoking status and habit, which may not reflect true characteristics. Our findings are reflective of participants' willingness-to-try different methods and may not correlate with actual choices. Responses to questions may have been affected by participants' recall bias. Furthermore, we were unable to analyze for differences between minority race and ethnicities due to the limited number of non-white or Hispanic individuals in our sample.

Conclusion

Despite improvement in the availability of interventions for smoking cessation, success rate is still suboptimal. To close this gap, efforts have been made to increase access to evidence-based methods of cessation but some methods remain preferred over others. Findings of this study highlight preferred methods for smoking cessation based on sociodemographics and level of nicotine dependence. The implication is that medical providers and those involved in the provision of tobacco cessation programs need to be mindful that individuals can differ in their preference for a smoking cessation method based on factors such as sociodemographics and nicotine dependence. In addition, increased education on evidenced-based tobacco cessation

methods for smokers trying to quit will be beneficial. Further studies to evaluate methods actually used by former tobacco users of different sociodemographics and level of nicotine dependence will be helpful and may aid in the development of targeted therapies for patients to increase the likelihood of success in their smoking cessation efforts.

Table 1: Demographic Characteristics, N=562

Characteristics	Total, N (%) or mean (SD)
Age, years	47 (20)
Female	263 (47%)
White	460 (82%)
Hispanic or Latino/a	61 (11%)
High school or less	135 (24%)
<\$30,000 annual income	134 (24%)
Days of tobacco use in past 30-day period	21 (11)
21 or more cigarettes/day	67 (12%)
Time to smoke after wake	
5 minutes or less	78 (14%)
6-30 minutes	237 (42%)
31-60 minutes	83 (15%)
>60 minutes	164 (29%)
History of quit attempts	466 (83%)
Current ENDS use	269 (48%)

ENDS = electronic nicotine delivery system; N = sample size; SD = standard deviation from the mean

Table 2: Association between baseline characteristics and willingness-to-try cessation methods among tobacco cigarette users (n=562)

Baseline Characteristics	Willingness-to-try any medication	Willingness-to-try any counseling	Willingness-to-try any evidence-based method	Willingness-to-try “cold turkey”
	Adjusted RR (95% CI)	Adjusted RR (95% CI)	Adjusted RR (95% CI)	Adjusted RR (95% CI)
Age	-	0.99 (0.99, 1.00)	1.0 (0.99, 1.00)	0.99 (0.99, 1.00)
Gender (female vs. male)	-	-	1.07 (0.98, 1.16)	-
Race (non-white vs. white)	-	1.32 (1.14, 1.52)	-	1.00 (0.88, 1.13)
Hispanic (Yes vs. No)	-	-	-	0.95 (0.82, 1.11)
Education (HS or less vs. Some college or higher)	-	0.78 (0.64, 0.95)	0.94 (0.84, 1.05)	-
Annual household income, (<\$30,000 vs. \$30,000+)	0.84 (0.73, 0.98)	0.82 (0.67, 0.99)	0.93 (0.82, 1.04)	-
Heaviness of Smoking Index score (High vs Low/Medium)	1.11 (1.07, 1.15)	1.06 (1.02, 1.12)	1.07 (1.04, 1.10)	0.90 (0.87, 0.94)
Ever tried to quit (Yes vs. No)	1.30 (1.06, 1.58)	1.36 (1.07, 1.72)	1.31 (1.10, 1.56)	1.15 (0.98, 1.35)
Current ENDS use (Yes vs. No)	-	-	1.05 (0.95, 1.15)	-

CI = confidence interval; ENDS = electronic nicotine delivery system; N = sample size; RR = risk ratio

Table 3. Willingness-to-try tobacco cessation methods, n (%)

Tobacco Cessation Methods	Total, n=562	Current tobacco cigarette only users, n = 293	Current tobacco cigarette and ENDS users, n = 269	P-value
Evidence-Based Methods				
Medications				
Nicotine containing products	329 (58%)	161 (55%)	168 (62%)	0.07
Wellbutrin/Zyban (bupropion)	197 (35%)	87 (29%)	110 (41%)	0.005
Chantix (Varenicline)	222 (39%)	107 (36%)	115 (43%)	0.13
Any Medication	388 (69%)	194 (66%)	194 (72%)	0.13
Counseling support				
Individual counseling	221 (39%)	106 (36%)	115 (43%)	0.11
Support group/group class	185 (33%)	80 (27%)	105 (39%)	0.003
Telephone Quitline	147 (26%)	61 (21%)	86 (32%)	0.003
Online program	220 (39%)	98 (33%)	122 (45%)	0.004
Texting program	145 (26%)	60 (20%)	85 (32%)	0.003
Any counseling support	320 (57%)	154 (53%)	166 (62%)	0.03
Any Evidence-Based Method (Medication or Counseling)	434 (77%)	214 (73%)	220 (82%)	0.01
Non-Evidence-Based/Alternative Methods				
Complementary and Alternative Methods				
Mindfulness therapy/meditation	269 (48%)	121 (41%)	148 (55%)	0.001
Hypnosis	256 (46%)	119 (41%)	137 (51%)	0.01
Acupuncture	241 (43%)	114 (39%)	127 (47%)	0.05
Any complementary and alternative method	357 (63%)	171 (58%)	186 (69%)	0.008
Other Tobacco or Nicotine Delivery Systems				
Smokeless tobacco	121 (21%)	28 (10%)	93 (35%)	<0.0001

Electronic vaping devices (e-cigarettes, e-hookahs, vape pens, e-pens)	402 (71%)	164 (56%)	238 (88%)	<0.0001
Any other tobacco or nicotine delivery system	410 (73%)	167 (57%)	243 (90%)	<0.0001
Quit on My Own				
Cold turkey (pick a date and quit)	385 (68%)	191 (65%)	194 (72%)	0.07
Cutting back gradually	467 (83%)	233 (79%)	234 (87%)	0.02
Any independent quitting method	511 (91%)	262 (89%)	249 (93%)	0.19

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Appendix I: Mobile phone and Web-Based Interventions for Smoking Cessation and Biochemical Confirmation of Abstinence : A Limited Systematic Review

INTRODUCTION

An estimate of 1 in 6 U.S adults are current smokers, a slight improvement from 20.9% in 2005[1]. It is well known that smoking leads to several health consequences including coronary heart disease, pulmonary diseases such as chronic obstructive pulmonary disorder and lung cancer, stroke, miscarriages and neonatal death [2]. Several studies have shown improvement in success rates associated with medications and counseling, either individually or combined for smoking cessation[3,4]. Without any intervention, success rates can be as low as 5-7 % [5,6].

A growing area of behavioral management for chronic diseases is in mobile health (mHealth) and web-based interventions. mHealth technology has the potential to enhance healthcare delivery, offers a wide range of flexibility, and benefits such as low cost and wide reachability [7, 8], given the large proportion of Americans with ownership or access to the internet and a cellular phone [9]. mHealth interventions are usually designed with increased convenience and patients' accessibility to care, including the flexibility to change intervention content based on the response or needs of users [8,10]. These interventions create opportunities to tailor services and reduce barriers to care [11].

mHealth technology has been applied in several smoking cessation programs [12-15]. While they tend to be successful based on participant report of abstinence or cessation, there are conflicting results about the association between mHealth interventions and biochemical confirmation of abstinence at different time points from one's quit date [14,16,17]. Biochemical confirmation is a more reliable assessment of abstinence at follow-up than self-report of abstinence and has been used in several studies [18].

The goal of this study is to provide a review of the evidence for mHealth and web-based interventions for smoking cessation and their association with biochemical confirmation of abstinence. The key questions (KQs) addressed here are: KQ1 - Do mHealth or web-based interventions for smoking cessation improve outcomes based on biochemical confirmation? and KQ2- does effectiveness vary by duration of intervention?

METHODS

Search Strategy and Data Sources

The literature search was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. PubMed and EMBASE were searched from inception through February 2019 for English-language articles in scientific journals of human adults using MESH terms and key words relevant to mHealth intervention terms and tobacco cessation. Searches were further limited to randomized trials.

Study Selection

Studies were included if they met the eligibility criteria developed with reference to PICOTSS (Appendix I, Table 1). Studies in which the intervention was any mobile or web-based health intervention including text messaging (SMS or MMS), downloadable mobile applications that targeted smoking cessation were selected. Studies with any of the above interventions in combination with other types of activities were also included. Studies in which the comparator or control group included another form of mobile or web-based interventions were excluded from this review. There was no limit on the publication time, duration of the intervention, participants' age, level of income or comorbid conditions.

For this review, primary outcome of interest was broadly defined as objective measures related to smoking cessation including cotinine level and exhaled carbon monoxide levels to confirm abstinence. This review did not focus on subjective outcomes such as reduction in

number of cigarettes smoked per day, self-report of abstinence and duration of abstinence from smoking cessation after the intervention.

Text Review and Data Extraction

All titles and abstracts were evaluated against the inclusion criteria by a single reviewer. Full texts were assessed for eligibility and abstraction of data from relevant full texts was done by a single reviewer. Extraction of the following data from eligible studies was performed: publication date, author name, study aims and objectives, number of participants in the intervention and control arms, components and duration of the intervention, and relevant outcomes. Outcome measures were extracted at all points of measurement for studies that had multiple time periods for outcome measurement.

Each included study was assessed for risk of bias using the Cochrane's tool for risk of bias assessment. Studies were rated as low, high risk of bias or unclear. In the assignment of a level of risk of bias, studies for which there was a high confidence in the treatment effects represented in the results were rated as low risk. Studies in which some risks of bias were noted but not enough to make the results invalid and those with significant errors in the study design or analysis that likely had a major impact on the results were rated as having a high risk of bias. Studies were rated as unclear risk of bias when the risk of bias could not be ascertained based on the available data.

RESULTS

The combined search strategies yielded 493 title and abstracts, of which 111 duplicates were removed and 382 were screened to assess for eligibility. Sixty-eight reports were found to be potentially eligible and their full texts were obtained for further assessment. Out of these eligible reports, 5 studies met the study inclusion criteria[12,16,17,19,10]. Reasons for excluding

studies were primarily due to wrong outcome, wrong setting, wrong study design and wrong comparator. Figure 1 is a representation of the flow diagram from the screening process.

Characteristics of studies

The total number of participant in all studies was 1537 with samples size ranging from 14 - 262 for intervention groups and 16 - 250 for control groups. Study duration ranged from 3 months to 12 months for all studies except one in which the duration was dependent on the medication used in addition to the mHealth technology or 8 weeks for those who opted out of pharmacotherapy. All studies had cell phone and text messaging as the main mobile health device and medium of communication respectively except one that used a web-based program that was not cell phone specific (Appendix I, Table 2). Mobile technology was applied in several ways including provision of motivational messages, education and link to resources and social support. Most programs were interactive and centered around the chosen quit date of participants. Three of the studies were directed towards smoking cessation during pregnancy and one of these studies used the platform of an already established text message program for pregnant women.

Outcomes

The focus of this review was on the biochemical confirmation of abstinence after self-report of cessation. Four studies assessed biochemical confirmation by examining the cotinine level of participants who self-reported smoking cessation at 3 months, 6 months or 12 months after their quit date[12,16,17,19]. Cotinine level indicating abstinence at different time points was set at less than or equal 13 ng/ml by 2 studies [17,19] and less than or equal to 15 ng/ml by 2 studies[12,16]. One of the studies that set a goal or less than or equal to 15 ng/ml also set a goal of less than or equal 18ng/ml for participants who reported living with a smoker[16]. One study

used expired carbon monoxide (eCO) level to verify biochemical abstinence at 2 weeks after quit date[20] and set the goal of eCO at less than 5 parts per million and less than 8 parts per million.(Appendix I, Table 3)

Results of one study showed a statistically significant difference in biochemically confirmation point prevalence abstinence between participants in the intervention group and control group at 3 months[12]. Although a larger percentage of participants in the intervention group had biochemical confirmed repeated point prevalence abstinence at 6 months follow-up period compared with the control group, the difference was not statistically significant[12]. For all other studies that used cotinine levels to verify 7 day or 30 day point prevalence abstinence at the 3 months - 12 months follow-up visit, a higher proportion of participants in interventions groups who had reported abstinence were biochemical confirmed compared with those in control groups but no statistically significant difference was noted[16,17,19]. The study that used exhaled carbon monoxide levels for biochemical confirmation also reported that a higher proportion of those in the intervention group met the goal compared with those in the control group but the difference between both groups was not statistically significant[20].

Risk of Bias Assessment

All studies had a low risk of bias for sequence generation except one which rated as high risk. One study had a low risk of bias for allocation concealment. All studies except one had a high risk of bias for blinding of personnel and participants while all studies had a high risk of bias for blinding of outcome assessors. Three out of five studies received a low risk of bias for incomplete data while all studies received a low risk of bias for selective outcome reporting. Three studies received a high risk of bias for other factors, one was for contamination of

intervention group, another for contamination of control group with intervention and the last was for an underpowered study. Risk of bias assessment can be found in appendix I, Table 4.

DISCUSSION

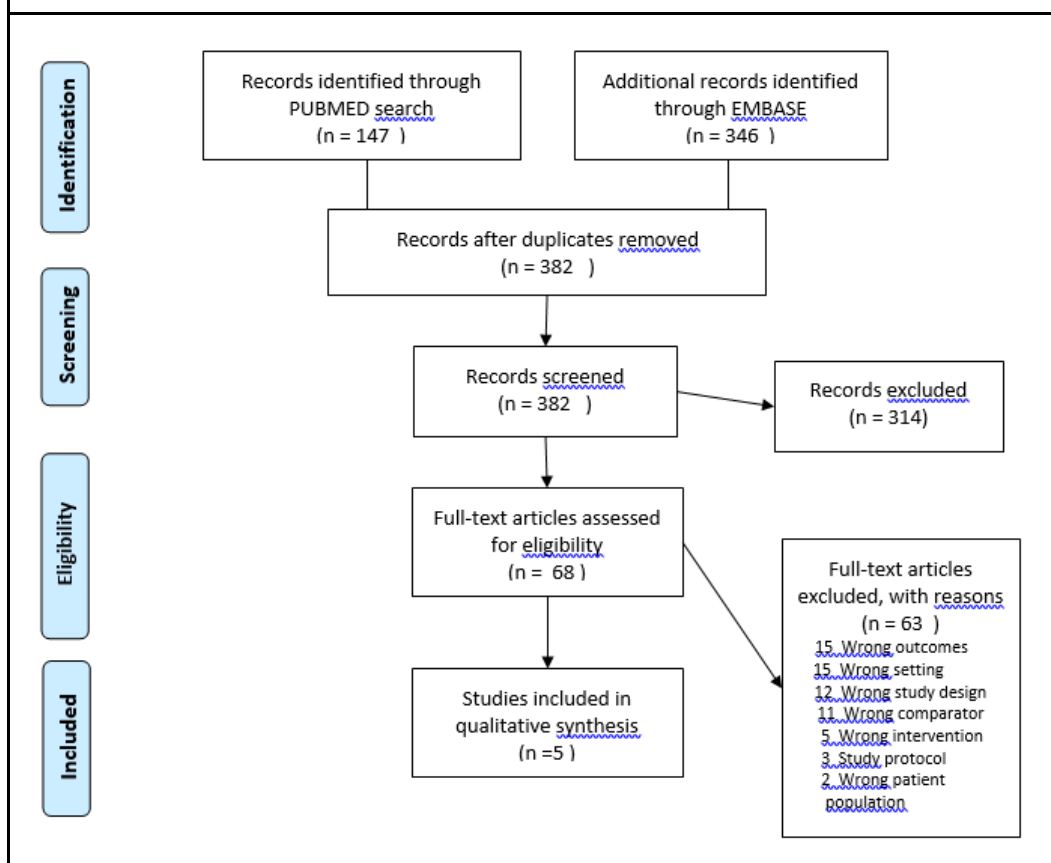
This systematic review evaluates the effectiveness of mHealth and web-based interventions for smoking cessation with biochemical confirmation after self-reported abstinence. All 5 studies were randomized trials and showed consistency in terms of biochemical confirmation of abstinence in a larger proportion of participants who received the mHealth or web-based interventions compared with those in control groups. However, only one study showed a statistically significant difference between the intervention and control group at 3 months. Although mHealth and web-based interventions for smoking cessation have shown significant benefits based on smokers' self-reports of abstinence, the association with biochemically confirmed smoking cessation has not been consistent. The inconsistency may be a result of other factors that may affect cotinine and exhaled carbon monoxide levels. For instance, cotinine levels may be affected by racial/ethnic differences in cotinine metabolism and genetic factors such as low UGT2B10 activity[21,22] and these factors may affect results depending on the timing of biochemical confirmation from last smoke. Biochemical confirmation using carbon monoxide in the blood can also be affected by the respiratory effort of participants[23]. Deep exhalation can lead to higher levels and low exhalation can lead to lower levels of carbon monoxide measured.

This systematic review has a number of limitations. The small number of studies that met eligibility criteria may limit the generalizability of the findings. Another limitation is that the review was performed by a single reviewer who performed database searches, review of articles for eligibility, extraction of data and assessment of risk of bias for all included study. The addition of a

second reviewer, with consensus agreement, will add to the validity of the review and findings. The single reviewer process reduces the applicability of the findings.

This systematic review showed mixed findings on the effectiveness of mHealth interventions on smoking cessation based on biochemical confirmation of abstinence. These findings are within the limitations of biochemical confirmatory tests and further studies done under improved and more reliable conditions are needed to increase the understanding of the association between mHealth interventions and biochemical confirmation of abstinence.

Figure 1 - PRISMA flow diagram



Appendix I, Table 1: Eligibility Criteria

Category	Include	Exclude
Population	Active smokers	Non-smokers, ex- smokers
Intervention	Controlled trials with any mobile phone and web-based intervention including text messages (SMS or MMS), downloadable apps, use of other hand-held devices, or the internet for any duration of time	Counseling sessions involving a counselor or therapist etc via telephone or mobile phones
Comparators	Usual care including face to face coaching, handouts, no intervention	Comparative effectiveness studies or studies in which both intervention and control groups had any form of mobile phone or web-based intervention.
Outcome(s)	Objective measures: biochemical confirmation of abstinence such as cotinine level or expired carbon monoxide level	All other outcomes, including self-reported smoking cessation
Timing	All years	N/A
Setting	Studies performed in the United States	Other countries
Study Designs	Randomized and non-randomized controlled trials	Other study designs

Appendix I, Table 2. Baseline characteristics of studies					
Author, year	Aim	Sample size	Intervention	Comparator	Duration of study
Abroms et al, 2014	To compare effectiveness of Text2Quit vs control on biochemically confirmed smoking abstinence	Control - 241 Intervention - 262	Text2Quit - text message, email and web-portal	A guidebook on smoking cessation	6 months
Abroms et al, 2017	To test the acceptability and feasibility of SmokefreeMOM, aimed at pregnant women	Control = 44 Intervention = 55	Messages with advice and tips on how to quit, social support, information on harms of smoking on a baby's development and advice from ex-smokers. Interactive texting program. Messages were scheduled around participant's quit date and baby's due date	A single text message that provided a referral to a telephone quitline and mailed self-help printed materials from the CDC about quitting smoking while pregnant	3 months
Abroms et al, 2017	Effect of adding a smoking cessation text message program, Quit4baby, to an established text message program, Text4baby.	Control = 250 Intervention = 247	1 - 8 text messages per day with highest number on the quit day and days immediately after. Afterwards, outgoing messages taper over time and stop at 3 months. Between 1 month prior to baby's arrival and 6 months after, messages related to postpartum relapse prevention are delivered. Participants can text keywords to the program for additional support	Usual care - only Text4baby. Nothing on smoking cessation	6 months
Calhoun et al, 2016	To compare the impact and cost-effectiveness of an	Control = 203 Intervention = 205	Free lifetime membership to the full version of	Referral to specialty clinic and appointment	12 months

	internet-based smoking cessation program paired with a telemedicine clinic to an assisted referral to specialty smoking cessation clinic -based care for veteran smokers		QuitNet, an internet based program- Includes tailored, online smoking cessation support that is personalized and based on readiness to quit. Provision of direct access to counselors, social support, and assistance with selecting a quit date and medication.	scheduled. Provision of group and telephone counseling by psychologists in the clinic and medication management by a psychiatrist. Smoking cessation aids also provided during clinic visits and renewals sent by mail	
Forinash et al, 2018	To evaluate the impact of text messaging on smoking cessation rates among pregnant women in addition to standard of care	Control = 16 Intervention = 14	Usual care plus motivational text messages focused on pregnancy and smoking cessation, starting 3 days prior to quit date, then 1 day prior, on the quit date and tapering until delivery.	Pharmacy-driven education with or without pharmacotherapy . Follow-up phone calls to patients within 3 days after quit date and weekly for 2 weeks.	Through completion of pharmacotherapy or 8 weeks for those who opted out of pharmacotherapy

Appendix I, Table 3. Effect estimates for outcome

Study	Biochemical Outcome	Results
Abroms et al, 2014	Biochemically confirmed repeated point prevalent abstinence i.e. not smoking in the past 30 days at 3 months and 6 months follow-up and cotinine level of ≤ 15 ng/ml at 6 months	<p>Biochemically confirmed repeated point prevalence abstinence Intervention (%) = 11.1% Control (%) = 5.0% RR (95% CI) = 2.22 (1.16, 4.26)</p> <p>Biochemically confirmed repeated point prevalence abstinence at 6 month follow-up Intervention (%) = 15.7% Control (%) = 11.2% RR (95% CI) = 1.40 (0.89, 2.20)</p>
Abroms et al, 2017	7 day biochemically confirmed point prevalence abstinence at 3 months i.e self report of no smoking in past 7 days on 3 month survey and a cotinine level of ≤ 13 ng/ml.	<p>Biochemically confirmed 7 day point prevalence abstinence Intervention (%) = 14.55% Control (%) = 9.09 %</p>
Abroms et al, 2017	7 day and 30 day biochemically confirmed PPA at 3 months follow-up i.e. self-report of no smoking in past 7 or 30 days and cotinine level < 13 ng/ml	<p>Biochemically confirmed 7-day point prevalence abstinence Intervention (%) = 39 (15.60) Control (%) = 27 (10.93) RR (95% CI) = 1.51 (0.89–2.55) (Missing data imputed to indicate smoking)</p> <p>Intervention (%) = 39 (19.90) Control (%) = 27 (13.04) RR(95% CI) = 1.53 (0.97–2.39) (Only complete cases)</p> <p>Biochemically confirmed 30-day point prevalence abstinence Intervention (%) = 32 (12.80) Control (%) = 26 (10.53) RR(95% CI) = 1.12 (0.83–1.52) (Missing data imputed to indicate smoking)</p> <p>Intervention (%) = 32 (16.33) Control (%) = 26 (12.56) RR(95%CI) = 1.30 (0.81–2.10) (Only complete cases)</p>

Calhoun et al, 2016	Biochemical confirmation of abstinence at 12 month follow-up - cotinine level of ≤ 15 ng/ml or ≤ 18 ng/ml if the participant reported living with a smoker	Percentage Intervention (%) = 5.4% Control (%) = 3.5% *missing data and untestable samples included in analyses as smoking
Forinash et al, 2018	Verification by exhaled carbon monoxide level 2 weeks after quit date	2 weeks cessation with eCO < 8 ppm Intervention - 57.1% Control = 31.3% OR(95% CI) = 2.93 (0.66, 13.09) 2 week cessation with eCO < 5 ppm Intervention - 35.7% Control = 12.5% OR (95% CI) = 3.89 (0.62, 24.52) ** eCO= exhaled carbon monoxide, ppm = parts per million

Appendix I, Table 4: Risk of Bias Assessment							
Author	Sequence Generation	Allocation Concealment	Blinding of personnel and participants	Blinding of outcome assessors	Incomplete data	Selective outcome reporting	Other bias
Abroms et al, 2014	Low	High	High	High	Low	Low	Unclear
Abroms et al, 2017	High	High	High	High	Low	Low	High *
Abroms et al ² , 2017	Low	High	High	High	Low	Low	High **
Calhoun et al, 2016	Low	Low	Low	High	High	Low	Low
Forinash et al, 2018	Low	Unclear	High	High	High	Low	High***
<p>* 2 participants from intervention group received a component of the control group ** Some level of contamination. At 3 month survey, 6 participants in control group had used the Text4baby for smoking cessation *** Study was underpowered to detect statistical differences</p>							

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