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# Digital health for assessment and intervention targeting tobacco and cannabis co-use

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## Abstract

**Purpose of review:** This article aims to summarize current research on digital health for assessment and intervention targeting tobacco and cannabis co-use and to answer the following questions: Which digital tools have been used? Which populations have been targeted? And what are implications for future research?

**Recent findings:** Ecological Momentary Assessment (EMA) via text messages or interactive voice response calls has been used to capture co-use patterns within a time window or co-administration of both substances via blunts among young adults. Feasibility of multicomponent interventions targeting dual cessation of both substances among adult co-users with cannabis use disorder, delivered via smartphone apps, online, and computer modules has been demonstrated.

**Summary:** Digital tools, particularly those using EMAs and mobile sensors, should be expanded to assess co-use of emerging tobacco and cannabis products. Digital cessation interventions should be tailored to different groups of co-users and address specific mechanisms underlying different co-use patterns.

#### Keywords

tobacco; cannabis; polysubstance use; digital health; mobile health

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#### INTRODUCTION

Co-use of tobacco and cannabis (marijuana) is common worldwide [1–3]. The use of both substances compounds health risks associated with each individual substance [4]. Co-users have worse health outcomes (e.g., mental health, respiratory symptoms) than exclusive users of either substance [5]. Recently, the tobacco landscape has expanded from conventional cigarettes, cigars/cigarillos, hookahs, and smokeless tobacco to e-cigarettes [6]. Likewise, cannabis is available in various forms, including combustible (e.g., joints, pipes, bongs), vaporized, and edible products [7]. In addition, the expanding cannabis legalization for medical and recreational use in the US may increase acceptance and availability of cannabis [8, 9]. In response to this changing context, research focusing on tobacco and cannabis co-use has ramped up recently [4, 10–12].

Co-use is an "umbrella" term that encompasses at least three patterns of substance use behavior : 1) simultaneous use at the same time (e.g., co-administration via blunts - cigar wrappers filled with cannabis, or spliffs - joints filled with both looseleaf tobacco and cannabis); 2) sequential use within the same occasion (e.g., "chasing" - smoking a tobacco cigarette right after smoking a cannabis joint); and 3) separate use within a certain time period (e.g., using any tobacco and cannabis products in the past 30 days or past 12 months) [11]. This complexity of product type and timeframe poses challenges for assessing co-use patterns. However, our understanding of co-use is limited due to traditional data collection approaches in substance use research (e.g., cross-sectional surveys or retrospective reports measuring co-use at one time point or over long time-intervals, such as over the past month) [13–16]. Data collected using these approaches can be subject to recall bias and lack specificity for how tobacco and cannabis are co-used. Newer data collection methods via digital tools, such as Ecological Momentary Assessment (EMA) and mobile sensing, have the potential to disentangle the complexity of co-use by providing data on specific products and timeframes via real-time assessments in natural environments [17•].

There is a demand for dual cessation interventions that target tobacco and cannabis simultaneously to improve cessation outcomes and reduce related health risks among co-users [18–20]. However, barriers to quitting the two substances include lack of available and accessible treatments, fear of stigma, desire for self-reliance, and limited options for personalized treatment [21, 22]. A growing area of research has highlighted the promising role of digital tools in overcoming these barriers [23–27]. For example, online interventions or mobile apps can deliver treatments to broader audiences, particularly hard-to-reach or underserved populations, in a wider array of settings compared to in-person interventions [25, 26]. In addition, the anonymity of these platforms can reduce stigma and facilitate self-disclosure with regard to sensitive information like substance use [27]. Furthermore, digital health can help to develop tailored interventions, which may be more effective to support quitting substance use compared to non-tailored interventions [26]. Collectively, the aforementioned advantages of digital health approaches make them promising for the assessment of co-use behavior and for the development of interventions that target dual cessation of both tobacco and cannabis.

To our knowledge, no existing work has reviewed digital health solutions for tobacco and cannabis co-use. Previous reviews on digital health research examined tobacco and cannabis separately, but did not focus on co-use of the two substances [22, 26]. A recent meta-analysis of interventions targeting co-users did not include assessment of co-use patterns and did not focus on digital health approaches [10•]. Thus, the current study aims to summarize current research using digital health for assessment and intervention targeting tobacco and cannabis co-use.

#### **METHODS**

#### Eligibility Criteria

We included published research in English that used digital health approaches alone or in combination with other components to assess tobacco and cannabis co-use (Assessment Research), or to provide cessation interventions for both substances (Intervention Research) regardless of study designs. We searched for digital health approaches that included, but were not limited to EMA, electronic diaries, text messaging, computer-based modules, online interventions, phone apps, and mobile sensors. Surveys administered online were not considered as a digital health approach in this review. We excluded studies that addressed both tobacco and cannabis use, if they did not provide information on co-use. For assessment studies, the outcomes were patterns (e.g., simultaneous use, sequential use, and co-use within a time period) and frequency of co-use. For intervention studies, the outcomes were changes in readiness to quit, reduction in use of either tobacco or cannabis, and cessation rates. A secondary outcome was participants' compliance with assessments or interventions.

#### Search methods and selection of studies

Relevant literature was searched on PubMed up to February, 2020. Search strategies were developed using a combination of terms relating to all types of tobacco use, all modes of cannabis use, treatment for tobacco and cannabis, and digital health approaches (see Supplementary materials for the full search strategy). Non-English articles were excluded. NN conducted the search and removed duplicates.

NN and CN conducted initial screening of titles and abstracts on Rayyan [28]. All studies retained after abstract screening were retrieved as full-text articles and assessed for eligibility. Each investigator conducted full-text review of half of the potential articles and then extracted data from included articles. The following study characteristics were extracted: research type (i.e., assessment vs. intervention), author and year of publication, sample characteristics (e.g., sample size, demographics, level of substance use, current treatment at baseline), study design, digital health approaches (e.g., EMAs, computer-based intervention), measures of substance use (e.g., patterns and frequency of co-use, changes in substance use), and participant compliance. JT reviewed included articles. Discrepancies were resolved by discussion.

## RESULTS

The PubMed search resulted in 488 publications. Based on screening titles and abstracts, 28 articles were considered for full-text review (see Supplementary materials for PRISMA diagram). Of these, 19 were excluded due to addressing use of only a single substance or separate use of two substances rather than co-use of both substances together. A total of 9 studies met the inclusion criteria, including 4 assessment studies and 5 cessation intervention studies. These studies were published between 2014 and 2020. A brief description of the terminologies underlying the included studies is provided in Table 1. The characteristics of included studies were summarized in Table 2. Below, we provide a brief description of digital health approaches used and participants' compliance.

#### EMA approaches for assessment of co-use patterns

All four assessment studies employed EMA methods to collect data on co-use among young adults (18–29 years old) [29–32]. Of these, one study specifically targeted African American young adults due to their high risk of blunt use [30]. Except for Schuster et al.'s study [29], targeted populations were frequent substance users (e.g., currently use tobacco some days or every day, currently use cannabis at least 2 days per week). Regarding delivery modes, two studies sent EMA text messages to smartphones [30, 31], one prompted EMAs to handheld computers [29], and one used interactive voice response calls to mobile phones [32••]. The most common co-use patterns assessed were co-administration via blunts or spliffs [30, 31, 32••] and co-use within a specific time window (e.g., a 4-hour window) [29, 31, 32••]. Duration of assessments lasted from 1 to 4 weeks.

Co-administration of tobacco and cannabis via blunts was assessed in Chen-Sankey et al.'s study [30]. By examining 1205 cigar smoking moments, this study found that sweet-flavored cigars (vs. plain cigars) were more likely to be used for blunts, suggesting that reducing sweet-flavored cigar use may help curb blunt use. Likewise, Schuster et al. examined simultaneous use of tobacco and cannabis (measured as cannabis use in smoking prompts) and found that 16% of smoking prompts were simultaneous use with cannabis [29]. Furthermore, while this study revealed that working memory was poorer with cannabis use and better with tobacco use, no effects were found for simultaneous use of the two substances. This could suggest that tobacco use may compensate for working memory decrements from cannabis use, a potential reason for the use of tobacco in order to counteract unwanted effects of cannabis.

Berg et al. assessed both co-administration and co-use patterns within 4-hour windows [31]. Participants were asked to report the number of each tobacco and cannabis product, a mix of tobacco and cannabis, blunts, and spliffs used since the last assessment. This study found that use of cannabis was associated with 3–4 times greater odds of use of cigarettes, e-cigarettes, or any type of tobacco within a given time window. This finding suggests that the use of both substances happened in close temporal proximity and that conditioned cues associated with one substance may trigger use of the other. While this study assessed more patterns of co-use, it did not examine the order of substance use.

Compared to the above studies, Wilhelm et al. assessed co-use behavior more comprehensively [32••]. This study examined both traditional and emerging tobacco (cigarettes, cigars, hookah, and e-cigarettes) and cannabis products (combustible, vaporized, and edibles cannabis). Co-administration via spliffs and blunts was also addressed. Notably, the order of substance use was measured when both substances were used in the same epoch. This study found that participants reported co-use of cannabis and tobacco in 22.2% of epochs, only tobacco use in 19.3% of epochs, and only cannabis use in 17.6% of epochs. Use of blunts and spliffs was reported in half of epochs with co-use. Tobacco was used after cannabis 15.9% of the time, before cannabis 5.5% of the time, and both before and after cannabis 79.0% of the time. This suggests that tobacco use commonly followed rather than preceded cannabis use.

#### Digital health interventions targeting dual cessation of both tobacco and cannabis

Regarding cessation intervention research, two studies were randomized controlled trials [33, 34••] and the remaining were pilot studies [35–37]. Interventions were delivered via computer modules [34••, 36, 37], online sessions [33], or mobile apps [35]. Intervention length ranged from 6 to 24 weeks, except for one study, which included only a 26-minute single online session [33]. Overall, these interventions were feasible and acceptable. Efficacy for dual cessation was unclear, but tobacco cessation interventions did not impact cannabis cessation outcomes.

**Targeted populations**—Four studies targeted dual cessation among adult co-users with cannabis use disorder (CUD) [34–37], and one study targeted readiness to quit of both tobacco and cannabis among co-users regardless of substance use disorder severity [33]. Becker et al. developed interventions to enhance readiness to simultaneously quit both substances among co-users who were not seeking treatment [33]. Participants were included if they had used any tobacco during the past 4 weeks and any cannabis during the past 6 months. As such, it was possible that participants were not frequent users. The remaining studies targeted adult co-users in more advanced stages of the behavior change process, who were willing to quit smoking both cannabis and tobacco [35] or quit tobacco in the next 6 months [34••, 36, 37]. Participants had to be frequent users of tobacco and cannabis (e.g., daily use of cigarettes, blunts, or spliffs), had to meet criteria for CUD, and were currently seeking treatment for CUD.

**Intervention effects**—Intervention development was based on efficacious established treatments for each substance, including behavioral treatments (i.e., Motivational Enhancement, Cognitive Behavioral, and Contingency Management therapies) and pharmacological treatments (e.g., nicotine replacement therapy - NRT) [33–37].

The effectiveness of brief online interventions targeting readiness to quit both substances was evaluated in a three-arm randomized controlled trial [33]. This study used a fully automated web-based program to interact with participants and to tailor the content based on participants' responses. Compared to baseline, readiness to simultaneously quit tobacco and cannabis slightly increased right after the intervention, but effects disappeared at 8-week follow up. In addition, no differential effects were found across intervention arms,

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suggesting that the more individualized and interactive interventions performed no better than the psychoeducation intervention.

Abstinence Reinforcement Therapy, a multicomponent intervention targeting dual cessation among co-users with CUD, was examined in a pilot study [35]. This intervention included a smartphone app for contingency management, telephone counseling for cognitive behavioral therapy, and a telehealth clinic for NRT [35]. Results from 5 participants undergoing 6-week treatment indicated the feasibility and acceptability of recruitment, retention, and treatment completion. Preliminary data also suggested that the intervention may have led to abstinence from cannabis and/or tobacco. However, a larger randomized controlled trial is required to determine the efficacy of this approach.

Lee and colleagues employed computer-assisted modules to deliver their cessation interventions at community clinics or for remote access [34.., 36, 37]. They developed and evaluated two different approaches to help co-users with CUD quit using both substances. A simultaneous approach offered treatments of both tobacco and cannabis simultaneously over 12 weeks [36, 37], whereas a sequential approach offered treatment of cannabis (over the initial 12 weeks) before treatment of tobacco (over the following 12 weeks) [34••]. In both approaches, cannabis abstinence rates in dual cessation interventions were similar to previous CUD interventions without tobacco treatment. However, tobacco cessation outcomes were poor, which could be due to the fact that tobacco treatment was optional and without incentives. In their pilot trial, 56% of participants made at least one tobacco quit attempt; however, only 12.5% sustained tobacco abstinence during the final month of treatment [36]. Similar findings emerged in their subsequent randomized controlled trial, in which there was a lack of positive effects of tobacco treatment on tobacco quit attempts and cessation [34••]. Of note, no statistically significant differences were observed between the simultaneous and sequential intervention approaches on any tobacco and cannabis outcomes. However, the sequential approach had numerically better outcomes on cannabis cessation. Collectively, these findings indicated that simultaneously targeting dual cessation of both substances is feasible without negatively affecting cannabis cessation. More intensive treatment strategies are warranted to improve tobacco cessation.

#### Participant compliance

Compliance varied across studies. In assessment studies, support from researchers was used for low-compliance participants [30] and prompts were resent several times for missed EMAs [32••]. In Wilhelm et al.'s study, compliance with EMAs declined from ~80% on Day 1 to ~40% on Day 28 [32••]. In Becker et al.'s study, participation rates were higher for the shorter intervention (Normative Feedback, ~19 minutes) than the longer interventions (Psychoeducation and Motivational Interviewing, ~30 minutes) [33]. In Lee et al.'s study, engagement with tobacco treatment in the sequential approach was lower than the simultaneous approach (only 30% of participants engaged in the tobacco intervention offered during weeks 13–24) [34••]. These findings suggest that shorter and less burdensome assessments and interventions may be needed to keep participants engaged. In addition, common motivational strategies, such as incentives or vouchers, appeared to maintain high compliance during the study process or at follow ups [33].

## DISCUSSION

This review summarized current research on digital health approaches for assessment and intervention targeting tobacco and cannabis co-use. Although there is little empirical literature in this area, the existing evidence indicates the capability of EMAs in providing a nuanced understanding of co-use behavior as well as the feasibility, acceptability, and preliminary efficacy of digital interventions supporting simultaneous cessation of both tobacco and cannabis. There is much room for future research to leverage digital tools for research on tobacco and cannabis co-use. Below, we provide our evaluation of the existing literature.

#### Strengths of the current research

By using EMAs to collect a large amount of fine-grained data on tobacco and cannabis use multiple times per day, the current research disentangled the order of sequential use of the two substances and provided insights into co-use patterns beyond of what could be learned from traditional surveys. Indeed, Wilhelm et al. found that when both substances were used together, tobacco was commonly used after cannabis [32••]. In addition, all assessment studies focused on co-use among young adults, who have the highest rates of co-use compared to other age groups [2, 13]. Since young adulthood is a peak time for substance use, understanding co-use behavior during this developmental period is critical for preventing subsequent tobacco and cannabis use disorders.

The current cessation studies developed multicomponent interventions for dual cessation based on established treatments for each substance. Combining behavioral and pharmacological therapies is recommended for treating tobacco or cannabis use disorders [21, 38]. The delivery of these therapies via digital tools was feasible and acceptable to support simultaneously quitting of both substances due to the advantages of digital health in improving treatment access, reducing delivery costs, and ensuring treatment fidelity. For example, the web-based interventions in Becker et al.'s study were fully automated and therefore required no personnel for intervention delivery [33]. Likewise, computer-assisted interventions in Lee et al.'s studies were feasible for implementing cessation in community clinics and could produce comparable outcomes to therapist-delivered approaches at a decreased cost [37].

While targeting dual cessation at the same time adds complexity to the treatment process, we are in favor of the simultaneous approaches based on the existing evidence [33, 35, 36]. Lee et al. indicated that the simultaneous rather than sequential approaches were preferable since only 30% of participants engaged with the delayed tobacco treatment in the sequential treatment delivery approach [34••]. Becker et al. suggested setting one quit date for both substances since one substance may act as a behavioral cue for the other one. Moreover, participants could experience only one withdrawal phase by simultaneously quitting the two substances [33]. This approach may also be beneficial from a resource perspective given that both substances can be targeted during a single treatment program [36]. Since tobacco use is a predictor of poor CUD treatment outcomes, the simultaneous approach is particularly appropriate for co-users with CUD [18].

#### Limitations of the current research and gaps of knowledge

The current assessment studies had a more detailed emphasis on tobacco than cannabis. While different tobacco products (e.g., cigarettes, cigars, e-cigarettes) were examined explicitly, cannabis use was mostly examined as "any cannabis", "combustible cannabis products", or only tetrahydrocannabinol (THC) products. Other forms, such as vaporized and edible cannabis or other cannabinoids (e.g. cannabidiol/CBD), remain understudied. Moreover, there is a lack of evidence on specific mechanisms associated with different couse patterns (e.g., synergistic and compensatory effects, conditioned cues associated with same routes of administration). The limited understanding of relationship between the two substances may hinder development of effective dual cessation interventions. Current interventions predominantly seemed to integrate treatments for each individual substance into one cessation program rather than targeting potential mechanisms underlying the interrelationship between the two substances. In addition, the included intervention studies focused more on cannabis treatment than tobacco treatment, since their targeted population was co-users seeking treatment for CUD. These interventions may not be applicable for other groups of co-users, such as those with less problematic cannabis use. Moreover, there is limited and inconclusive evidence on the efficacy of these interventions, since only two of the included studies were evaluated in a randomized controlled trial design. The limited efficacy of existing interventions is also indicated in a recent meta-analysis, which reported that cessation interventions (both single and dual cessation), regardless of whether or not they used digital health approaches, had small effects on reducing cannabis use, but no clear effects on tobacco cessation [10•]. In addition, response burden (~8 EMAs per day, 4-week data collection periods) may result in poor participant compliance in the assessment studies, with potentially declining compliance over time [32]. Similarly, regular clinical visits for validating abstinence (e.g., twice a week for urine tests of cannabis abstinence) may impact participants' engagement in the cessation interventions. Finally, inconsistent measures of substance use behaviors and cessation outcomes, as well as various terminologies of co-use patterns made it difficult to compare the study results and to summarize the evidence.

#### CONCLUSION

Digital health research addressing tobacco and cannabis co-use is nascent. Given the popularity of co-use, more research is needed to assess and treat the use of both substances. Here, we provide potential directions for future research.

#### Combination of active and passive data collection to improve co-use assessment

Alongside active data collection requiring participant input (e.g., EMAs), passive data collection approaches that automatically log data (e.g., mobile or wearable sensors) should be considered in future co-use research [39]. While EMA has been used widely in substance use research, mobile sensing has been employed mostly in alcohol use research [40•]. A recent review called for applying these tools in research on other substances [40•]. In addition, combining both active and passive data collection approaches can be powerful for improving our understanding of co-use behavior as well as its real-time triggers [17•]. For instance, sensor and EMA data could be combined to iteratively train a machine learning algorithm to recognize high-risk situations that precede substance craving or use [41]. These

situations include both internal factors (e.g., affect, arousal) and external factors (e.g., location, people present, specific time on a day, week day vs. weekend) [39]. If a smartphone app detects data collected from sensors that may indicate substance craving or use (e.g., increased body motion, skin temperature, or heart rate), it can trigger an EMA to collect information on situational variables. Moreover, since data are collected passively via sensors, response burden in EMAs can be reduced.

In addition to the use of novel methods, future studies should assess co-use more comprehensively. As the emerging product landscape may change the ways people use both substances (e.g., co-vaping via electronic devices) [9], co-use should be characterized in wider ranges of products beyond cigarettes, joints, and blunts. Frequency, order, and physical and psychological effects of co-use should also be captured more specifically to elucidate the reciprocal relationship between the two substances and to understand potential mechanisms sustaining different co-use patterns. Such data can be helpful for addressing which products and co-use patterns most likely impede cessation of substance use, and can guide future treatment development efforts that target specific mechanisms of co-use.

#### Tailored interventions for different groups of co-users

Interventions should be tailored to different groups of co-users, who have different preferred patterns and levels of substance use, motivation to change, and interest in quitting. Like assessment, cessation interventions should take co-use patterns into account, since patterns may vary by substance use severity and reasons for use, and thus, require different treatment approaches  $[10^{\bullet}, 42-44]$ . For example, co-use within the same occasion (through sequential use and co-administration) is associated with worse mental health symptoms compared to co-use within a certain time period [5]. Thus, individuals with closer temporal patterns of co-use could be supported to quit both substances simultaneously by including mental health support. In addition, a brief screening for substance use and rapid referral may create early treatment opportunities for co-users [45]. Digital tools, such as computerized adaptive testing, can be used to reliably assess problematic substance use in different health-care settings without clinician burden or remotely via the Internet, and subsequently refer individuals to treatment [17•, 45].

Regarding the level of substance use, brief psychoeducation interventions may be offered to infrequent co-users, while intensive and multicomponent interventions may be needed for more frequent co-users. Unlike interventions for co-users with CUD, interventions for non-treatment seeking co-users may consider providing tobacco treatment before cannabis treatment, since this group indicated greater interest in quitting tobacco compared to cannabis and preferred quitting tobacco first before reducing their cannabis use, compared to simultaneous dual cessation [46]. Furthermore, to prevent relapse among heavy co-users, future research may consider just-in-time interventions, which provide timely and adaptive support via smartphones to meet an individual's needs in real time [47•]. This approach has been used for smoking cessation by using EMAs to identify predictors of relapse and then delivering real-time interventions to prevent a relapse in naturalistic settings [48]. Similar principles can be applied to develop just-in-time dual cessation interventions for tobacco and cannabis co-use.

Moving forward, fully-powered randomized controlled trials are needed to examine the efficacy of digital health interventions, and interventions that sustain long-term effects need to be developed [24•]. Moreover, given the vulnerability of sensitive information (e.g., illegal substance use) to data breaches, implementation and dissemination of interventions should consider the privacy and security of data collected using digital tools [49]. Finally, to reduce participant burden and enhance retention, digital health approaches to biochemically validate cessation outcomes should be tested in future interventions, such as mobile phonebased breath carbon monoxide monitors to validate smoking status [50] or video-recording of saliva cotinine or cannabinoid testing [35].

In summary, additional applications of digital tools in research of tobacco and cannabis couse are warranted to better understand co-use of novel products and mechanisms underlying co-use patterns, and effectively treat broader groups of co-users.

#### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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#### REFERENCES

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- •• Of major importance
- Hindocha C, Freeman TP, Ferris JA, Lynskey MT, Winstock AR. No Smoke without Tobacco: A Global Overview of Cannabis and Tobacco Routes of Administration and Their Association with Intention to Quit. Front Psychiatry. 2016;7:104. doi:10.3389/fpsyt.2016.00104. [PubMed: 27458388]
- Schauer GL, Berg CJ, Kegler MC, Donovan DM, Windle M. Assessing the overlap between tobacco and marijuana: Trends in patterns of co-use of tobacco and marijuana in adults from 2003–2012. Addict Behav. 2015;49:26–32. doi:10.1016/j.addbeh.2015.05.012. [PubMed: 26036666]
- Goodwin RD, Pacek LR, Copeland J, Moeller SJ, Dierker L, Weinberger A et al. Trends in Daily Cannabis Use Among Cigarette Smokers: United States, 2002–2014. Am J Public Health. 2018;108(1):137–42. doi:10.2105/AJPH.2017.304050. [PubMed: 29161058]
- Meier E, Hatsukami DK. A review of the additive health risk of cannabis and tobacco co-use. Drug Alcohol Depend. 2016;166:6–12. doi:10.1016/j.drugalcdep.2016.07.013. [PubMed: 27476751]
- Tucker JS, Pedersen ER, Seelam R, Dunbar MS, Shih RA, D'Amico EJ. Types of cannabis and tobacco/nicotine co-use and associated outcomes in young adulthood. Psychol Addict Behav. 2019;33(4):401–11. doi:10.1037/adb0000464. [PubMed: 30985164]
- Spinner JR, Araojo R, Zeller M. Changing the Tobacco Landscape: FDA's Role in Addressing Tobacco and Nicotine Use. Health Promot Pract. 2020;21(1\_suppl):5S–8S. doi:10.1177/1524839919888993. [PubMed: 31908199]

Nguyen et al.

- 7. Goodman S, Wadsworth E, Leos-Toro C, Hammond D, International Cannabis Policy Study t. Prevalence and forms of cannabis use in legal vs. illegal recreational cannabis markets. Int J Drug Policy. 2020;76:102658. doi:10.1016/j.drugpo.2019.102658. [PubMed: 31927413]
- Wang JB, Ramo DE, Lisha NE, Cataldo JK. Medical marijuana legalization and cigarette and marijuana co-use in adolescents and adults. Drug Alcohol Depend. 2016;166:32–8. doi:10.1016/ j.drugalcdep.2016.06.016. [PubMed: 27460859]
- Nicksic NE, Do EK, Barnes AJ. Cannabis legalization, tobacco prevention policies, and Cannabis use in E-cigarettes among youth. Drug Alcohol Depend. 2020;206:107730. doi:10.1016/ j.drugalcdep.2019.107730. [PubMed: 31759233]
- 10•. Walsh H, McNeill A, Purssell E, Duaso M. A systematic review and Bayesian meta-analysis of interventions which target or assess co-use of tobacco and cannabis in single- or multi-substance interventions. Addiction. 2020. doi:10.1111/add.14993.This meta-analysis of interventions for single- or multi-substance use indicated no clear effects on tobacco or cannabis cessation outcomes among co-users. However, multi-substance interventions might be more effective than cannabis-only interventions on cannabis cessation.
- Rabin RA, George TP. A review of co-morbid tobacco and cannabis use disorders: possible mechanisms to explain high rates of co-use. Am J Addict. 2015;24(2):105–16. doi:10.1111/ ajad.12186. [PubMed: 25662704]
- Schlienz NJ, Lee DC. Co-use of cannabis, tobacco, and alcohol during adolescence: policy and regulatory implications. Int Rev Psychiatry. 2018;30(3):226–37. doi:10.1080/09540261.2018.1465399. [PubMed: 29944032]
- Cohn AM, Abudayyeh H, Perreras L, Peters EN. Patterns and correlates of the co-use of marijuana with any tobacco and individual tobacco products in young adults from Wave 2 of the PATH Study. Addict Behav. 2019;92:122–7. doi:10.1016/j.addbeh.2018.12.025. [PubMed: 30623805]
- Schauer GL, Peters EN. Correlates and trends in youth co-use of marijuana and tobacco in the United States, 2005–2014. Drug Alcohol Depend. 2018;185:238–44. doi:10.1016/ j.drugalcdep.2017.12.007. [PubMed: 29471228]
- Coleman-Cowger VH, Schauer GL, Peters EN. Marijuana and tobacco co-use among a nationally representative sample of US pregnant and non-pregnant women: 2005–2014 National Survey on Drug Use and Health findings. Drug Alcohol Depend. 2017;177:130–5. doi:10.1016/ j.drugalcdep.2017.03.025. [PubMed: 28599211]
- Seaman EL, Green KM, Wang MQ, Quinn SC, Fryer CS. Examining prevalence and correlates of cigarette and marijuana co-use among young adults using ten years of NHANES data. Addict Behav. 2019;96:140–7. doi:10.1016/j.addbeh.2019.04.014. [PubMed: 31078741]
- 17•. Ferreri F, Bourla A, Mouchabac S, Karila L. e-Addictology: An Overview of New Technologies for Assessing and Intervening in Addictive Behaviors. Front Psychiatry. 2018;9:51. doi:10.3389/ fpsyt.2018.00051. [PubMed: 29545756] This review described new technologies (e.g., digital phenotyping, biofeedback and virtual reality) that can improve assessment and interventions in the field of addictive disorders.
- Peters EN, Budney AJ, Carroll KM. Clinical correlates of co-occurring cannabis and tobacco use: a systematic review. Addiction. 2012;107(8):1404–17. doi:10.1111/j.1360-0443.2012.03843.x. [PubMed: 22340422]
- McKelvey K, Thrul J, Ramo D. Impact of quitting smoking and smoking cessation treatment on substance use outcomes: An updated and narrative review. Addict Behav. 2017;65:161–70. doi:10.1016/j.addbeh.2016.10.012. [PubMed: 27816663]
- Agrawal A, Budney AJ, Lynskey MT. The co-occurring use and misuse of cannabis and tobacco: a review. Addiction. 2012;107(7):1221–33. doi:10.1111/j.1360-0443.2012.03837.x. [PubMed: 22300456]
- Sherman BJ, McRae-Clark AL. Treatment of Cannabis Use Disorder: Current Science and Future Outlook. Pharmacotherapy. 2016;36(5):511–35. doi:10.1002/phar.1747. [PubMed: 27027272]
- 22. Gulliver A, Farrer L, Chan JK, Tait RJ, Bennett K, Calear AL et al. Technology-based interventions for tobacco and other drug use in university and college students: a systematic review and meta-analysis. Addict Sci Clin Pract. 2015;10:5. doi:10.1186/s13722-015-0027-4. [PubMed: 25928221]

- 23. Marsch LA, Campbell A, Campbell C, Chen CH, Ertin E, Ghitza U et al. The application of digital health to the assessment and treatment of substance use disorders: The past, current, and future role of the National Drug Abuse Treatment Clinical Trials Network. J Subst Abuse Treat. 2020;112S:4–11. doi:10.1016/j.jsat.2020.02.005. [PubMed: 32220409]
- 24•. Arigo D, Jake-Schoffman DE, Wolin K, Beckjord E, Hekler EB, Pagoto SL. The history and future of digital health in the field of behavioral medicine. J Behav Med. 2019;42(1):67–83. doi:10.1007/s10865-018-9966-z. [PubMed: 30825090] This paper provides a comprehensive review of digital health tools and research methods in behavioral medicine.
- Budney AJ, Borodovsky JT, Marsch LA, Lord SE. Technological Innovations in Addiction Treatment. In: Danovitch I, Mooney LJ, editors. The Assessment and Treatment of Addiction: Best Practices and New Frontiers. St. Louis, Missouri: Elsevier; 2019. p. 75–90.
- Vilardaga R, Casellas-Pujol E, McClernon JF, Garrison KA. Mobile Applications for the Treatment of Tobacco Use and Dependence. Curr Addict Rep. 2019;6(2):86–97. doi:10.1007/ s40429-019-00248-0. [PubMed: 32010548]
- 27. Tofighi B, Abrantes A, Stein MD. The Role of Technology-Based Interventions for Substance Use Disorders in Primary Care: A Review of the Literature. Med Clin North Am. 2018;102(4):715–31. doi:10.1016/j.mcna.2018.02.011. [PubMed: 29933825]
- Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev. 2016;5(1):210. doi:10.1186/s13643-016-0384-4. [PubMed: 27919275]
- Schuster RM, Mermelstein RJ, Hedeker D. Ecological momentary assessment of working memory under conditions of simultaneous marijuana and tobacco use. Addiction. 2016;111(8):1466–76. doi:10.1111/add.13342. [PubMed: 26857917]
- Chen-Sankey JC, Choi K, Kirchner TR, Feldman RH, Butler J 3rd, Mead EL. Flavored cigar smoking among African American young adult dual users: An ecological momentary assessment. Drug Alcohol Depend. 2019;196:79–85. doi:10.1016/j.drugalcdep.2018.12.020. [PubMed: 30754022]
- Berg CJ, Haardorfer R, Payne JB, Getachew B, Vu M, Guttentag A et al. Ecological momentary assessment of various tobacco product use among young adults. Addict Behav. 2019;92:38–46. doi:10.1016/j.addbeh.2018.12.014. [PubMed: 30579116]
- 32••. Wilhelm J, Abudayyeh H, Perreras L, Taylor R, Peters EN, Vandrey R et al. Measuring the temporal association between cannabis and tobacco use among co-using young adults using ecological momentary assessment. Addict Behav. 2020;104:106250. doi:10.1016/j.addbeh.2019.106250. [PubMed: 31918167] This paper assessed co-use patterns the most comprehensively, including various products and order of substance use.
- Becker J, Haug S, Sullivan R, Schaub MP. Effectiveness of different Web-based interventions to prepare co-smokers of cigarettes and cannabis for double cessation: a three-arm randomized controlled trial. J Med Internet Res. 2014;16(12):e273. doi:10.2196/jmir.3246. [PubMed: 25486674]
- 34••. Lee DC, Walker DD, Hughes JR, Brunette MF, Scherer E, Stanger C et al. Sequential and simultaneous treatment approaches to cannabis use disorder and tobacco use. J Subst Abuse Treat. 2019;98:39–46. doi:10.1016/j.jsat.2018.12.005. [PubMed: 30665602] This trial found no significant differences between the simultaneous and sequential approaches for dual cessation interventions among co-users seeking treatment for cannabis use disorder.
- Beckham JC, Adkisson KA, Hertzberg J, Kimbrel NA, Budney AJ, Stephens RS et al. Mobile contingency management as an adjunctive treatment for co-morbid cannabis use disorder and cigarette smoking. Addict Behav. 2018;79:86–92. doi:10.1016/j.addbeh.2017.12.007. [PubMed: 29268146]
- Lee DC, Budney AJ, Brunette MF, Hughes JR, Etter JF, Stanger C. Outcomes from a computerassisted intervention simultaneously targeting cannabis and tobacco use. Drug Alcohol Depend. 2015;155:134–40. doi:10.1016/j.drugalcdep.2015.08.001. [PubMed: 26307942]
- Lee DC, Budney AJ, Brunette MF, Hughes JR, Etter JF, Stanger C. Treatment models for targeting tobacco use during treatment for cannabis use disorder: case series. Addict Behav. 2014;39(8):1224–30. doi:10.1016/j.addbeh.2014.04.010. [PubMed: 24813547]

Nguyen et al.

- 38. U.S. Department of Health and Human Services. Smoking Cessation. A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. 2020.
- Dallery J, Kurti A, Erb P. A New Frontier: Integrating Behavioral and Digital Technology to Promote Health Behavior. Behav Anal. 2015;38(1):19–49. doi:10.1007/s40614-014-0017-y. [PubMed: 27347477]
- 40•. Lauvsnes ADF, Langaas M, Toussaint P, Grawe RW. Mobile Sensing in Substance Use Research: A Scoping Review. Telemed J E Health. 2020. doi:10.1089/tmj.2019.0241.This scoping review gave an overview of the current state of published research on passive mobile sensing of substance use.
- Boyer EW, Fletcher R, Fay RJ, Smelson D, Ziedonis D, Picard RW. Preliminary efforts directed toward the detection of craving of illicit substances: the iHeal project. J Med Toxicol. 2012;8(1):5– 9. doi:10.1007/s13181-011-0200-4. [PubMed: 22311668]
- Berg CJ, Payne J, Henriksen L, Cavazos-Rehg P, Getachew B, Schauer GL et al. Reasons for Marijuana and Tobacco Co-use Among Young Adults: A Mixed Methods Scale Development Study. Subst Use Misuse. 2018;53(3):357–69. doi:10.1080/10826084.2017.1327978. [PubMed: 28792283]
- 43. Tucker JS, Pedersen ER, Seelam R, Dunbar MS, Shih RA, D'Amico EJ. Types of cannabis and tobacco/nicotine co-use and associated outcomes in young adulthood. Psychol Addict Behav. 2019. doi:10.1037/adb0000464.
- 44. Akbar SA, Tomko RL, Salazar CA, Squeglia LM, McClure EA. Tobacco and cannabis co-use and interrelatedness among adults. Addict Behav. 2019;90:354–61. doi:10.1016/j.addbeh.2018.11.036. [PubMed: 30522075]
- 45. Gibbons RD, Alegria M, Markle S, Fuentes L, Zhang L, Carmona R et al. Development of a computerized adaptive substance use disorder scale for screening and measurement: the CAT-SUD. Addiction. 2020. doi:10.1111/add.14938.
- 46. McClure EA, Tomko RL, Salazar CA, Akbar SA, Squeglia LM, Herrmann E et al. Tobacco and cannabis co-use: Drug substitution, quit interest, and cessation preferences. Exp Clin Psychopharmacol. 2019;27(3):265–75. doi:10.1037/pha0000244. [PubMed: 30556733]
- 47•. Nahum-Shani I, Smith SN, Spring BJ, Collins LM, Witkiewitz K, Tewari A et al. Just-in-Time Adaptive Interventions (JITAIs) in Mobile Health: Key Components and Design Principles for Ongoing Health Behavior Support. Ann Behav Med. 2018;52(6):446–62. doi:10.1007/s12160-016-9830-8. [PubMed: 27663578] This paper described key comonents and design principles of Just-In-time Adaptive Interventions for health behaviors.
- Hebert ET, Ra CK, Alexander AC, Helt A, Moisiuc R, Kendzor DE et al. A Mobile Just-in-Time Adaptive Intervention for Smoking Cessation: Pilot Randomized Controlled Trial. J Med Internet Res. 2020;22(3):e16907. doi:10.2196/16907. [PubMed: 32149716]
- 49. Filkins BL, Kim JY, Roberts B, Armstrong W, Miller MA, Hultner ML et al. Privacy and security in the era of digital health: what should translational researchers know and do about it? Am J Transl Res. 2016;8(3):1560–80. [PubMed: 27186282]
- Meredith SE, Robinson A, Erb P, Spieler CA, Klugman N, Dutta P et al. A mobile-phone-based breath carbon monoxide meter to detect cigarette smoking. Nicotine Tob Res. 2014;16(6):766–73. doi:10.1093/ntr/ntt275. [PubMed: 24470633]

#### Table 1:

#### Terminology underlying digital health research in tobacco and cannabis co-use

Terminology	Description
Substance	
Tobacco	Including both cigarettes and alternative tobacco products
Alternative tobacco products	Indicating non-cigarette tobacco products, such as e-cigarettes, cigars/cigarillos, smokeless tobacco, hookahs
Cannabis/Marijuana	Including various forms of cannabis consumption, such as combustible, vaporized, edible products
Co-use patterns	
Co-use within a time period	Using both cannabis and tobacco within the same period, such as within a 4-hour window or within past 30 days, but not simultaneously
Simultaneous use Co- administration	Using tobacco and cannabis simultaneously through blunts (cannabis rolled inside of a hollowed-out cigar or cigarillo wrapper) or spliffs (joints that contain both tobacco and cannabis)
Sequential use	Using one product while still feeling the effects of the other, such as co-use in close temporal sequence (e.g., "chasing" - consuming tobacco immediately after cannabis)
Assessment	
Ecological Momentary Assessment (EMA)	A data collection method that uses repeated assessments to collect real-time or near real-time data in real- world environments, thus minimizing recall bias, maximizing ecological validity, and allowing assessment of variables that influence substance use behaviors at a moment-to-moment time resolution
Interactive voice response (IVR)	Computerized and pre-programmed scripts to be used in interaction with participants via their own mobile phones
Cessation intervention	
CUD	Cannabis use disorder: Diagnosed with DSM-IV cannabis abuse or dependence. The more recent DSM-V includes different severities of CUD but no differentiation of abuse and dependence.
Treatment for CUD	Motivational Enhancement Therapy (MET) Cognitive Behavioral Therapy (CBT) Contingency Management (CM)
Treatment for tobacco cessation	Behavioral interventions: counseling Pharmacological interventions: Nicotine replacement therapy (NRT), Varenicline, Bupropion
Simultaneous intervention	Interventions for cannabis and tobacco cessation are provided over the same time period
Sequential intervention	Intervention for tobacco cessation is provided before/after intervention for cannabis cessation is completed

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Characteristics of the included studies

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	Compliance			66–100%			86%					92.6%		
	Findings Cannabis was a predictor of cigarettes, ENDS, and any tobacco.		Sweet- flavored cigars were more likely to be blunts, while alcohol flavored cigars were less ikely to be used, used, plain cigars.				16% of emoting	16% of smoking prompts reported co- use. Co-use had no effects on working memory despite positive effect of iobacco alone and						
04112	2100	Co-use			Co- administration	Co-use within 4 hours			Co- administration				Last-hour co-	nse
Substance mea		Cannabis		Combustible and vaporized			Blunt					Any		
		Tobacco			Cigarette ENDS	Ugar Hookah			Cigarette Cigar	0			Cigarette	0
		Duration		3 weeks			2 weeks					1 week		
annlication	appucauon	Delivery			Text	messages			Text messages	0			Handheld	computers
Dicital health		Component		Four 4-hour interval assessments/day, including:	Fixed-interval     EMAs for     substance use	Random-interval EMAs for momentary experience	Four 3.5-hour interval assessments/day with each interval including:	A "coverage"     survey     (substance use     and cuex) at the	and time every same time every day	<ul> <li>A "random" survey (affect and craving) at random times and preceding a "coverage" survey</li> </ul>		Two approaches: • Device-initiated	random prompts at 5–7 times/day	Subject-initiated prompts at smoking events
	z			31 participants Unreported number of EMAs		63 participants 1205 EMAs				287 participants 13266 EMAs				
	Population			College or university students		African American young aduts				Community young adults				
	Design	Design tudies) EMA			EMA				EMA					
	Study Assessment (4 s Berg et al. 2019 (US)		Berg et al. 2019 (US) (US) (US) (US) et al. 2019 et al. 2019 (US)					Schuster et al. 2016	(NS)					

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Compliance			55.1%		80.3%	100%	
Findings		of cannabis alone.	22.5% of EMAs reported concurrent use, half of those were co- administration. It was more common for tobacco to follow than to precede cannabis.		Significant increase in readiness to quit for both substances was observed right after intervention, but not at 8 weeks follow up. No significant frequency of substance use. No differential effectiveness effectiveness effectiveness effectiveness arms.	The intervention was feasible and acceptable, and was associated with initial cessation and reduction in use of tobacco and cannabis	
sure	Co-use		Co- administration Co-use within an epoch Order of co- use		Concurrent use of combustible products	Concurrent use: CUD + past-week use of cigarettes	
Substance meas	Cannabis	Combustible and vaporized			Combustible	Combustible	
	Tobacco		Cigarette ENDS Cigar Hookah		Cigarette	Cigarette	
	Duration		4 weeks		A brief single session (17– 29 minutes)	6 weeks	
application	Delivery		Automated interactive voice response calls		Website	Telephone Phone app	
Digital health a	Component		Three calls/day occurring randomly within 4-hour windows to collect data on 4 epochs		<ul> <li>Three separate interventions to enhance readiness to quit:</li> <li>Personalized normative feedback</li> <li>Motivational Interviewing</li> <li>Psychoeducation (control)</li> </ul>	A multi-component intervention that included: • CBT telephone • NRT • NRT	
2	2	90 participants 5550 EMAs			325 participants	5 participants	
Dounlotion	roputation		Young adult co- users		Co-users	Adults with CUD	
	Design		EMA	studies)	RCT	Pilot	
Study			Wilhelm et al. 2020 (US)	Treatment (5 s	Becker et al. 2014 (Switzerland)	Beckham et al. 2018 (US)	

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Compliance	computance	100%	66%	Varied by component. Lower compliance for the sequential intervention (30%)					
Findings	rmungs	Integrating thread to the second to acconduct on intervention intervention intervention did not megatively affect cannabis outcomes, but tobacco cessation was poor.	Compared to cannabis-only intervention, the simultaneous simultaneous showed a comparable rate for cannabis a greater reduction in cigarettes smoked per reduction in cigarettes smoked per reduction in cigarettes smoked per reduction in cigarettes smoked per reduction in cigarettes smoked per day, but no effects on tobacco	Cessation rates for cannabis and tobacco were poor. No difference between simultaneous and sequential intervention arms.					
sure	Co-use	Concurrent use: CUD + daily use of cigarettes or blunts/spliffs	Concurrent use: CUD + daily use of cigarettes or blunts/spliffs	Concurrent use: CUD + use tobacco on 5 days per week or use of blunts/ spliffs					
Substance meas	Cannabis	Any	Any	Any					
	Tobacco	Cigarette	Cigarette Cigarillo ENDS Smokeless tobacco	Cigarette Cigarillo ENDS Smokeless tobacco					
	Duration	12 weeks	12 weeks for the simultaneous approach 24 weeks for the sequential approach						
application	Delivery	Computer	Computer	Computer					
Digital health a	Component	<ul> <li>A simultaneous tailored intervention that included:</li> <li>Cannabis treatment: 9 MET/CBT modules + 3 supportive counseling supportive counseling therapist + abstinence-based CM</li> <li>Tobacco treatment: 5 modules of psychoeducation and counseling for tobacco use and counseling for tobacco use and counse + NRT</li> </ul>	<ul> <li>Cannabis treatment: 9 MET/CBT modules + 3 wupportive counseling sessions with a supportive based CM</li> <li>Tobacco treatment: 5 modules of psychoeducation and counseling for courseling for psychoeducation and counseling for course + NRT</li> <li>Same as Lee et al., 2014 above</li> </ul>						
N	L.	6 participants	32 participants	67 participants					
Dounlation	roputation	Adult co- users, seeking treatment for CUD	Adult co- users, seeking for CUD	Adult co- users, seeking treatment for CUD					
C	ncsign	Case series	Pilot trial with a historical control	RCT					
Ct.rd.	func	Lee et al. 2014 (US)	Lee et al. 2015 (US)	Lee et al. 2019 (US)					

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Comiliano	Computance						
Findings	Findings						
ure	Co-use						
Substance meas	Cannabis						
	Tobacco						
	Duration						
application	Delivery						
Digital health	Component	modules of	psychoeducation	and counseling	for smoking, co-	use, and ENDS	use + NRT
7	Z						
Dourlotton	Population						
	neagu						
C4	Śmme						

Note: CBT: Cognitive Behavioral Therapy; CM: Contingency Management; CUD: Cannabis Use Disorder; EMA: ecological Momentary Assessment; END; Electronic nicotine delivery system; MET: Motivational Enhancement Therapy; NRT: Nicotine Replacement Therapy; RCT: Randomized Controlled Trial.