

Facilitating Management of Opioid Use Disorder: A Review of Mobile Apps and mHealth Tools

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Abstract

Background: Advances in technology engender investigation of technology solutions to Opioid Use Disorder (OUD). However, in comparison to chronic disease management, the application of mobile health (mHealth) to OUD has been limited.

Objective: The objectives of this paper are to (1) document the currently available opioid-related mHealth applications (apps) and (2) review past and existing technology solutions that address OUD.

Methods: We used a two-phase parallel search approach: (1) app search to determine availability of opioid-related mHealth apps, and (2) focused review of literature to identify relevant technologies and mHealth apps used to address OUD.

Results: The app search revealed a steady rise in app development, with the majority of apps being clinician-facing. A majority of the apps were designed to aid in opioid dose conversion. Despite the availability of these apps, the focused review found no study that investigated the efficacy of mHealth apps to address OUD.

Conclusions: Our findings highlight a general gap in technological solutions of OUD management, and the potential for mHealth apps and wearable sensors to address OUD.

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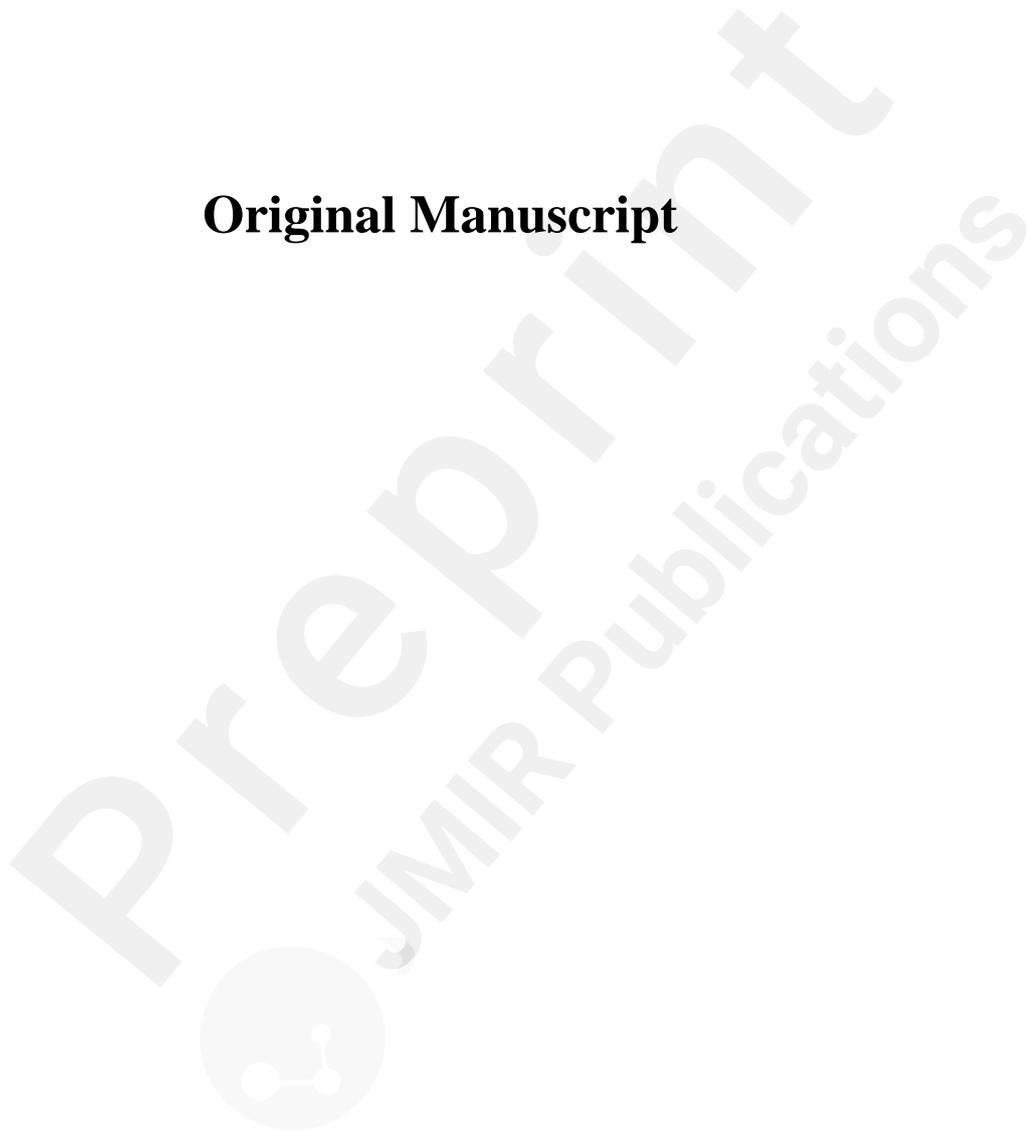
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Title: Facilitating Management of Opioid Use Disorder: A Review of Mobile Apps and mHealth Tools

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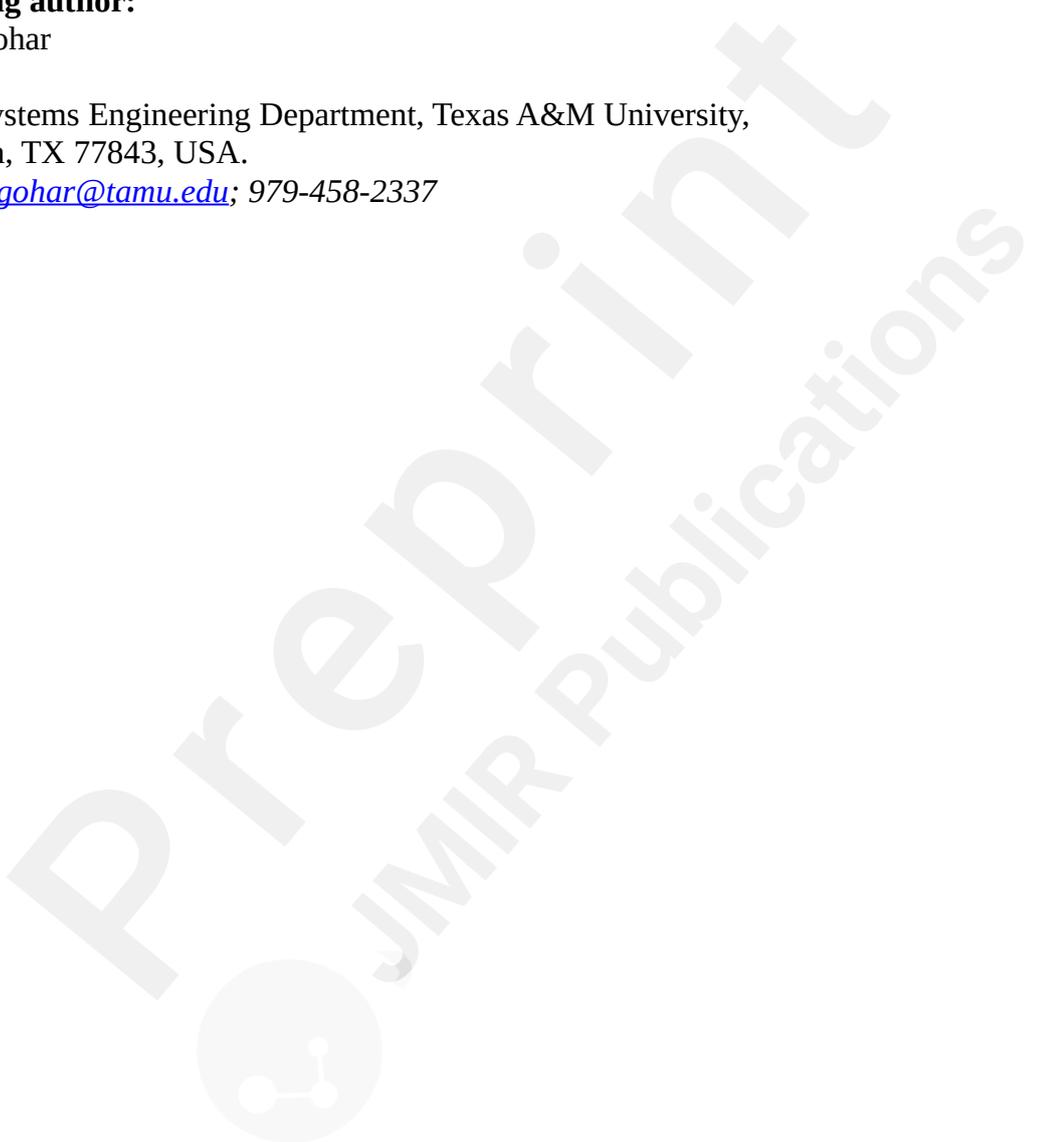
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Conclusions: Our findings highlight a general gap in technological solutions of OUD management, and the potential for mHealth apps and wearable sensors to address OUD.

Keywords: mHealth; apps; wearable sensors; substance abuse disorder

Introduction

On average 5 people in the United States die every hour from an opioid overdose [1]. In 2017 alone, over 70,000 drug overdose deaths occurred [2]. This problematic pattern of opioid use, often referred to as opioid use disorder (OUD), is considered a public health emergency [1, 3] with significant negative impacts on healthcare [4-5] and criminal justice costs [6]. Misuse of opioids can occur among patients who are initially exposed to opioids in a perioperative period—time periods immediately before, during, and after a surgical operation—or through a prescription for the treatment of acute or chronic pain [7]. In addition, opioids attract illegal users and individuals who profit by selling them unlawfully [8]. Such illegitimate use of prescription opioids has exacerbated the increase in OUDs [9-11].

Treatment exists for OUD, consisting of pharmacotherapy and behavioral therapies [12-13]. Opioid-dependent users may experience challenging and often severe withdrawal symptoms including restlessness, muscle aches, and depression, when they abruptly discontinue or reduce opioid intake [14]. Irrespective of the OUD treatment path, opioid withdrawal management, which includes regularly monitoring patients for symptoms, is the crucial first step after opioid use cessation or dose reduction [1]. A review of opioid withdrawal monitoring methods [15] revealed that the current method of assessing opioid withdrawal using various scales (tools to monitor and rate common signs and symptoms of withdrawal) is self-reported, needs frequent observations, may suffer from recall bias (see [16] for more details) –unintentional or intentional underreporting of information by respondents, and is ineffective outside of clinic or research environments. Moreover, opioid withdrawal scales differ with respect to the number of scale items and rating criteria. While technologies such as electronic prescription systems for controlled substances [17], medication history repositories, exchange of clinical records, and clinical direct messaging [8] have been proposed as useful methods to address opioid management, an opioid monitoring method that noninvasively and continuously monitors patients' symptoms as they occur in real time would provide several distinct advantages over these existing methods [18].

Advancements in technology have allowed for the ability to continuously monitor diseases outside of clinical settings. Mobile health (mHealth), one such advancement, involves use of mobile devices to collect health data, monitor signs and symptoms, deliver remote care, and/or educate patients [19]. mHealth interventions allow medical content to be delivered anytime and anywhere to patients [20]. mHealth applications (apps) have been used in managing chronic diseases including monitoring and managing day-to-day symptoms of sickle cell disease [21, 22], monitoring patients undergoing cardiac rehabilitation [23], monitoring blood pressure measurements to control hypertension [24], monitoring blood glucose, blood pressure, physical activity to prevent metabolic syndrome [25], and monitoring patients with chronic obstructive pulmonary disease [26] (also see [27] for a systematic review of mHealth apps for chronic disease management). However, in comparison to chronic disease management, the application of mHealth to OUD has been limited. Digital health technologies, including mHealth apps have the potential to play a unique role in tackling OUD. These include enabling care providers to create digital profiles of patients in order to provide personalized care regardless of time and place, monitoring patients' vital trends and issuing alerts to them or their caregivers, and providing insights into what triggers patients' behaviors.

Inspired by this gap, the overarching aim of our research is to design OUD management technologies that utilize wearable sensors to provide continuous monitoring capabilities. In particular, this research addresses the missed opportunity in monitoring withdrawal symptoms given their acute nature, salient physiological correlates, and their importance to long-term sobriety. As the first step in investigating novel technological solutions for remote monitoring and management of OUD and in particular withdrawal symptoms, we investigated the availability and evidence to support the efficacy of current OUD mHealth and wearable sensor solutions. The objective of this paper is to (1) document the currently available opioid-related mHealth apps, (2) review past and existing technology solutions that address OUD, and (3) discuss opportunities for technological withdrawal management solutions. To the best of our knowledge, no such review or landscape analysis of technologies that address OUD has been conducted to date.

Methods

A two-phase parallel search approach was used that involved an app search to determine availability of opioid-related mHealth apps and a scoping review of literature to identify relevant technologies and mHealth apps used to address OUD. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines [28] were used.

mHealth App Search Method

A search was conducted on Apple App Store and Google Play for apps published until May 10, 2019 using a combination of search terms that included "opioid", "opiate", "substance use disorder", "technology", OR "addiction". The inclusion criteria were: relevance to opioid, opioid prescription, opioid training, opioid monitoring, opioid overdose, opioid addiction support or substance use disorder including opioids. Apps that used a non-English language, apps that solely address substance use disorder (SUD) but not specific to opioids, and apps that require a Web browser to use were excluded.

Two reviewers independently applied the inclusion/exclusion criteria and identified the final set of apps for review. For each app, reviewers independently extracted the following: app name, app description, year published, publisher/seller, download estimate, rating and price. Reviewers transferred extracted data to a detailed Excel spreadsheet. Then, reviewers coded apps for operating system, i.e., Android operating system (henceforth Android) and/or iPhone operating system (henceforth iOS), clinical focus (opioid-specific OR SUD including opioid), audience (patient,

clinicians or anyone), and function (medicated-assisted treatment, education, prescription, professional support, peer support, withdrawal support and patient monitoring; see Table 1). Each app was assigned to one primary audience and clinical focus; however, each app could be categorized under more than one app function. Disagreements regarding exclusion/inclusion and coding of the apps were discussed with a third reviewer and agreement was reached through discussion.

Table 1. Taxonomy used for mHealth app coding.

Code	Category	Description
Audience		
	Patient-facing	App supports patient interactions and engagement
	Clinician-facing	App assists physician decision-making
	Anyone	App that is designed for general public including patients and caregivers
Clinical Focus		
	Opioid-specific	App related to only opioid
	SUD	App related to substances including opioids
App Function		
	Medicated-Assisted Treatment	App supports medication-assisted treatment of opioid use disorder
	Education	App provides educational information
	Conversion	App helps generate equivalent doses of various oral and intravenous opioids
	Professional support	App provides connections to outside professional support, e.g., send a message through the app to seek immediate emergency assistance, find services and resources that are available nearby
	Peer support	App provides connections to peer support, including individuals undergoing rehabilitation
	Withdrawal support	App supports patients as they go through withdrawal with e.g., reminders, supportive messages, symptom library
	Patient monitoring	App prompts patients to self-evaluate and submit regular personal assessments directly for the purpose of tracking progress and patterns of behavior

Scoping Review Method

PubMed, Embase, and Google Scholar were searched for articles published from inception until May 10, 2019 using a combination of search terms: [“wearable” OR “sensors” OR “technology” OR “mHealth” OR “app” OR “mobile”] AND [“opioid use disorder” OR “opioid” OR “opiate”]. Studies were included if they (1) were in English, (2) were peer-reviewed, and (3) employed wearable sensors, and/or mHealth. Animal studies and studies that did not include opioid were excluded.

Article selection was carried out in two stages. In the first stage, two reviewers independently

reviewed titles and abstracts against the inclusion and exclusion criteria using a web-based tool for systematic and scoping reviews called Rayyan [29]. The decision to fully review an article was made when both reviewers agreed to include the abstract. The reviewers resolved disagreements regarding article eligibility by discussing with a third reviewer.

In the second stage, the full-text articles were reviewed to determine eligibility. Furthermore, backward and forward reference search were conducted on all full-text articles that met the study selection criteria. Figure 1 below shows the process of searching and selecting articles included in the review. . Secondary searching yielded no unique results.

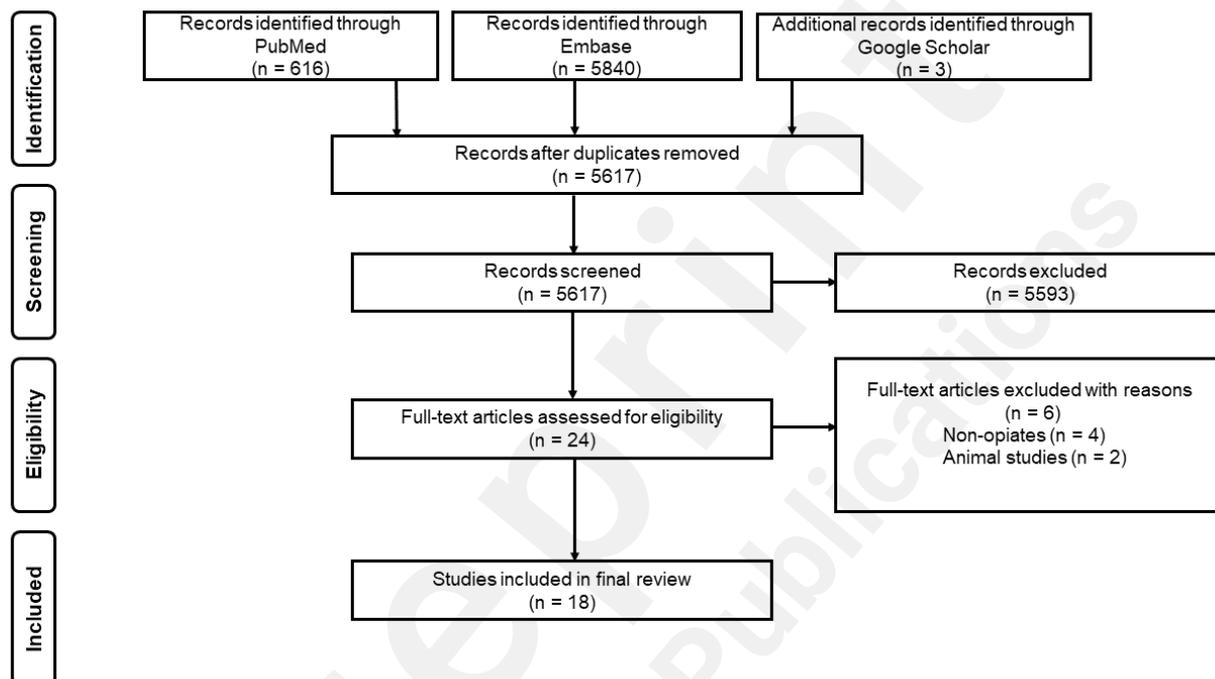


Figure 1. Process of searching and selecting articles included in the review.

Two reviewers independently read the full text of each article identified for inclusion in the review to extract pertinent data using a data extraction form. From each article, reviewers independently extracted the following: technologies used, physiological parameters, functions, research methods employed, and study findings. Reviewers transferred extracted data to a detailed Excel spreadsheet. Technologies used were further organized into ecological momentary assessment (EMA), global positioning system (GPS) information, wearable sensors, machine learning, and biomedical devices.

Results

mHealth App Search Results

The search yielded a total of 72 apps. Sixty-two apps (86%) were available for download at no cost. The remaining 10, all clinician-facing apps, had prices ranging from \$0.99 to \$9.99. Figure 2 shows the number of apps that were made available from 2009 to May 10, 2019 for both operating systems. Table 2 shows apps categorized by audience and operating system. Clinician-facing apps were most frequently available (43%) followed by apps that could be used by patients, caregivers, or general public (32%). As shown in Table 3 most of the available apps were opioid-specific (86%).

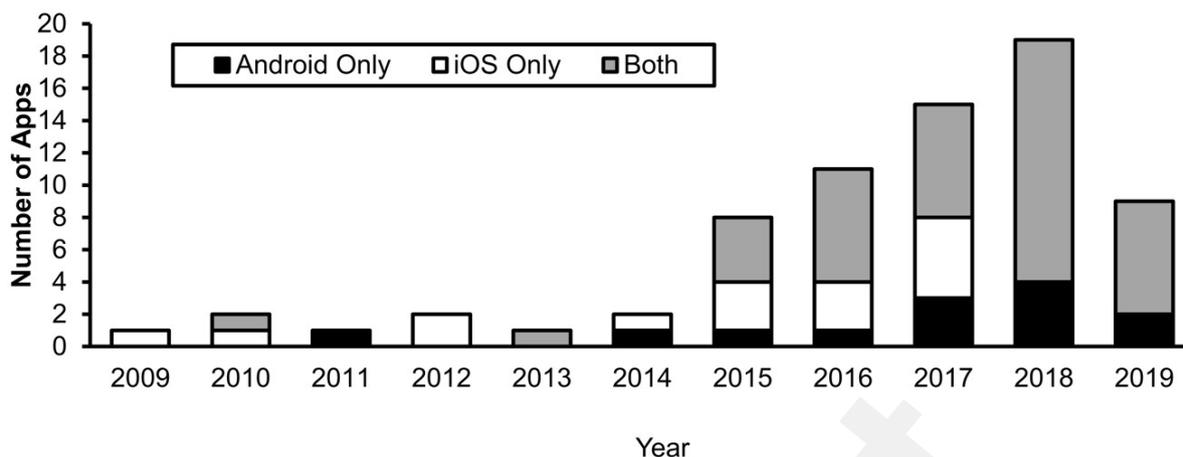


Figure 2. Number of apps published from 2009 – May 10, 2019.

Table 2. Apps categorized by audience and operating system.

Operating System	Audience			Total
	Patient-facing	Clinician-facing	General Audience	
Android only	3	8	2	13
iOS only	1	14	2	17
Both Android and iOS	14	9	19	42
Total	18	31	23	72

Table 3. Apps categorized by clinical focus and operating system.

Operating System	Clinical Focus		Total
	Opioid-specific	Substance Use Disorder	
Android only	11	2	13
iOS only	15	2	17
Both Android and iOS	36	6	42
Total	62	10	72

Furthermore, apps were analyzed for utilities (see Table 4). While most apps provided opioid conversion support (35%) or educational content (29%), only two opioid-specific apps (3%), namely FlexDek for MAT and MATx by SAMHSA, were designed to support medication-assisted treatment, and four (5.6%) provided support for patient monitoring.

Table 4. App tallies for different function categories (utilities are not mutually exclusive).

App Function							
Medicated-Assisted Treatment	Education	Converter	Professional support	Peer support	Withdrawal support	Patient monitoring	Other

Clinical Focus

Opioid-specific (62)	2	16	25	8	4	2	4	1
SUD (10)	1	5	0	1	2	0	0	1
Total	3	21	25	9	6	2	4	2

The majority of apps (35%), all clinician-facing and opioid-specific, were developed to convert from one opioid to another. These were also the most downloaded apps (Table 5). For example, Opioid Converter (Figure 3), the app with the highest number of downloads, is a free app supported by Emory University and designed to aid with opioid dose conversions. The app has a slider that allows for adjustments to be made for incomplete cross-tolerance. Opioids covered include buprenorphine, butorphanol codeine, fentanyl, hydrocodone, morphine, and oxycodone.

Table 5. Most downloaded Android apps.

App name	Year published	Rating (out of 5)	Number of reviews	Download Estimate
Opioid Converter	2011	4.0	170	50,000+
Orthodose	2013	4.6	56	10,000+
Opioid Calculator	2016	4.0	34	10,000+
CDC Opioid Guideline	2016	2.8	17	10,000+
Painkiller Calculator	2014	4.2	21	5,000+
FEND by Preventum	2018	4.2	32	5,000+

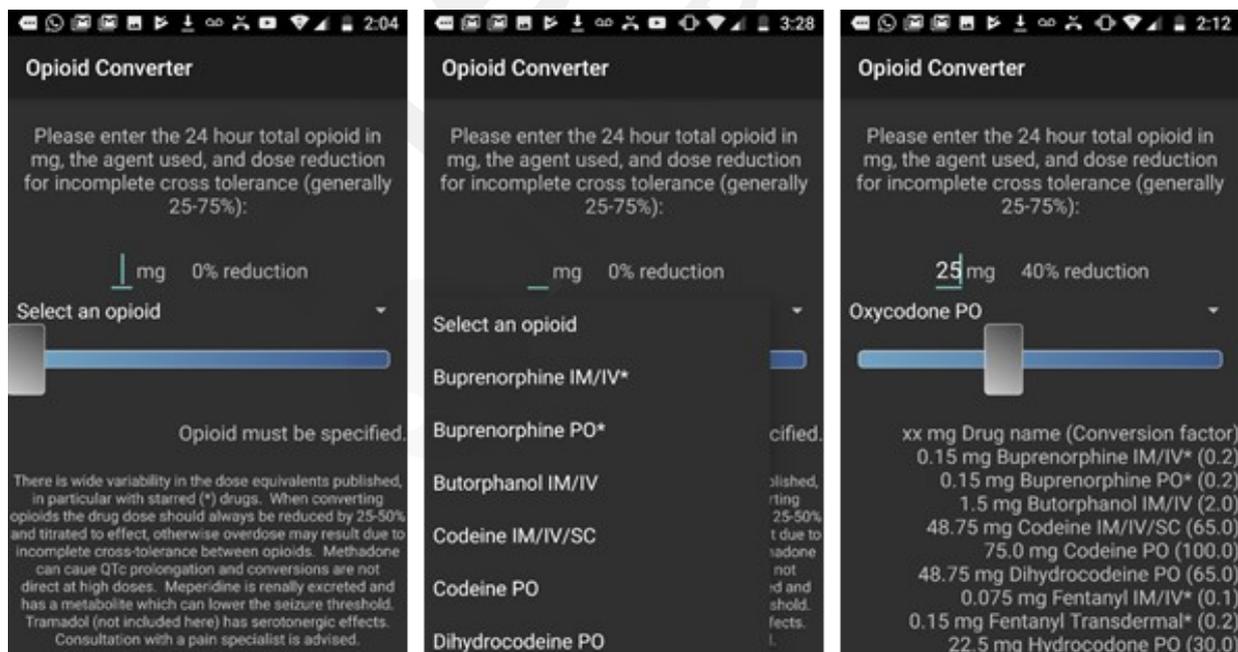


Figure 3. Opioid Converter: Main interface (left), selecting an opioid (center), 25mg oxycodone adjusted at 40% for incomplete cross-tolerance (right)

Nine out of 72 apps (12.5%) were designed to provide professional support including connecting users with a network of service providers and finding naloxone carriers in an overdose emergency.

Six out of 72 apps (8.3%) were designed to provide peer support in the form of reminders, supportive messages, and symptom library. Four out of 78 apps (5.6%) were designed to provide patient monitoring by prompting patients to self-evaluate and submit regular personal assessments directly for the purpose of tracking progress and patterns of behavior. Two out of 78 apps (2.7%) were categorized as “other”. One of these, DIRE, was designed for clinicians to use the DIRE tool [30] in their decision-making process when considering prescribing opioids. The DIRE tool allows clinicians to rate 7 factors (diagnosis, intractability, psychological risk, chemical health risk, reliability risk, social support risk, efficacy) each on a scale of 1, 2 or 3, with 1 being the least favorable case for prescribing, and 3 being the most favorable case for prescribing. The total score, the sum of the ratings, is used to determine a patient’s suitability for opioid maintenance analgesia. The other is THRIVEE, a virtual platform system designed to help patients overcome addiction. THRIVEE delivers virtual MAT to addicts, including opioid abusers. It utilizes virtual telemedicine sessions, such as video conferencing, between patients and providers to leverage proven clinical practices.

Total number of downloads was used as a measure of app prevalence. While download statistics was not available for iOS apps, statistics for Android apps varied from as low as 5+ downloads to as high as 50,000+ downloads (see Figure 4). Table 5 below shows 7 most downloaded Android apps and their respective ratings.

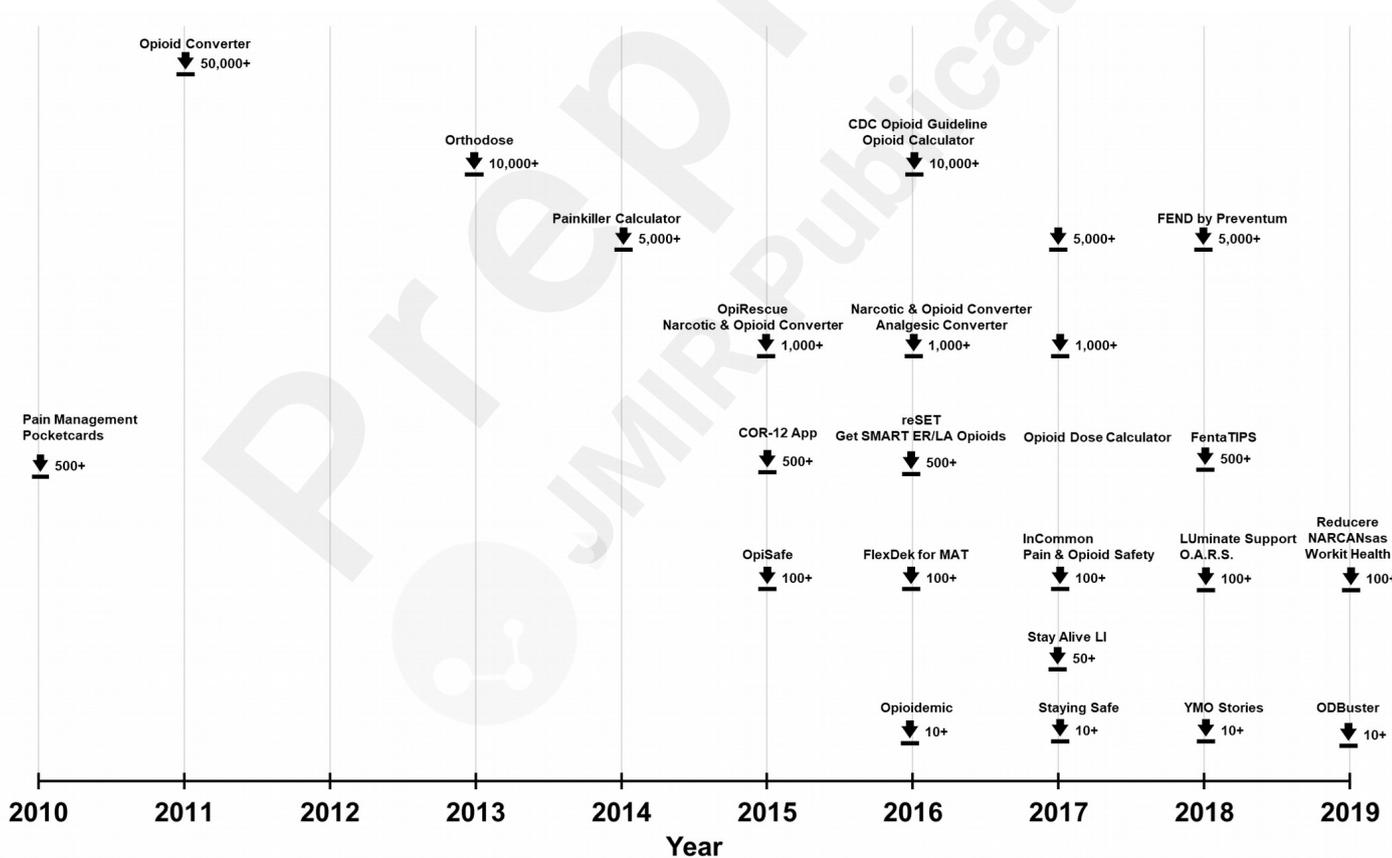


Figure 4. Shows for each app, year app was first published (on the horizontal axis) versus estimated number of downloads from the date app was published to the search date (on the vertical axis). Timeline for most downloaded Android apps showing number of downloads from January 2010 – May 10, 2019. Download statistics are not available for iOS apps.

Focused Review Results

Our initial search yielded 6459 articles. These were exported to the Zotero reference management software where 842 duplicates were removed. Title and abstract screening resulted in the exclusion of 5593 articles. The remaining 24 articles were fully reviewed. Out of these 24 articles, 18 met the inclusion criteria and were included in the final review.

Our search yielded 18 papers that documented relevant technologies used to address OUD. Of the 18 studies, 9 (50%) were lab-based studies, 8 (44%) were field studies, and 1 (6%) was a clinical trial. We did not find studies that employed mHealth apps to address OUD. Table 6 presents a summary of the technologies identified in the scoping review.

Ecological momentary assessment (EMA)

Six studies (33%), all field-based, employed ecological momentary assessment (EMA)—a method that uses electronic diaries and/or questionnaires deployed on mobile devices [31] to monitor, in near-real-time, craving for and use of opioids by outpatients receiving methadone treatment [32], assess stress in outpatients at work [33], investigate gender-based treatment strategies [34], study relationship between opioid use and craving and affect [35], investigate gender differences in the influence of stress on opioid use and craving [36], and examine the relationship between daily hassles and stressful events in opioid-dependent men and women [37]. Epstein and Preston [33] found opioid outpatients to be less stressed at the workplace than elsewhere, demonstrating utility of EMA to rate stress in outpatients. Kennedy et al. [34] found that males and females with substance use disorder differ in daily functioning during addiction treatment, highlighting the need to develop gender-based treatment strategies. Similarly, Moran et al. [36] found that stress-induced craving differs between opioid-dependent men and women, suggesting that gender-based tailoring of treatment should consider individual differences. Kowalczyk et al. [35] found that cravings increased when participants were using opioids, indicating utility of EMA to investigate the relationship between opioid use and craving. Overall, EMA has shown promise in enabling measurement of momentary experiences and states of cravings and misuse in natural settings.

Global positioning system (GPS) information

Two studies (11%), both field-based, combined EMA with GPS location information to monitor, in real-time mood, stress and drug craving in geographical context [38], and to study neighborhood effects on substance use [39]. EMA provided participants' momentary experience while GPS provided participants' location during those experiences. Epstein et al. [38] found negative association between environmental disorder (defined as lack of order and social control within the neighborhood) [39] and mood, stress, and drug craving, suggesting that mood, stress, and drug craving can be monitored in real-time in geographical context. Mennis et al. [40] found significant positive association between neighborhood disadvantage, higher perceived stress, lower perceived safety, and greater substance use, suggesting that GPS information can be combined with EMA to study neighborhood effects on substance use.

Wearable sensors

Advances in wearable technologies have enhanced researchers' ability to monitor physiological changes associated with opioid intake, and/or drug craving. Eight out of the 18 studies (44%) employed wearable sensors. Of these 8, three studies [41-43] combined EMA and wearable sensors to detect drug cravings [41, 42], deliver personalized prevention interventions [41], and determine stress episodes in opioid users [43]. Kennedy et al. [42] reported higher heart rates when participants reported craving than when they reported no craving, suggesting the potential efficacy of using heart rate data for continuous monitoring of craving. The "iHeal" system [41]—a system architecture

intended to provide personalized interventions—combines EMA, wearable sensors, and a deep belief network model to detect drug cravings and to deliver personalized drug prevention interventions. However, this study did not implement their "iHeal" system.

The remaining five studies [18, 44, 45, 46, 47] used wearable biosensors for real time detection of opioid use [44, 45], to detect physiological changes associated with opioid use [18], to evaluate physiological changes associated with wearing off of naloxone [46], and to automatically detect opioid intake [47]. Studies using Q sensors, worn on the participants' wrists, have found an increase in EDA is associated with opioid use [45], accurately detected substance use events within 30 minutes [45], and significant within-subjects increase in skin temperature and decrease in locomotion immediately after opioid administration [18]. However, they found that physiologic changes varied between subjects with level of opioid use—heavy opioid users showed greater decrease in fidgeting movements than non-heavy opioid users. Chintia et al. [46], used an E4 device (Empatica, Milan, Italy) worn on participants' wrists, and found that heart rate and skin temperature differed significantly between before and after naloxone administration. Finally, Linas et al. [48] combined EMA and wearable sweat patches, PharmChek Drugs of Abuse Patches (PharmChem, Inc., Fort Worth, TX), to concurrently collect momentary data and sweat in the field from 109 adults with recent opioid use and found moderate to good agreement of EMA to sweat patches and self-report methods in capturing drug use events.

Machine learning

Four studies (22%) used machine learning techniques to analyze and predict opioid use. Three of these studies [43, 45, 47] predicted opioid intake. The remaining study [40] developed a model to provide personalized interventions. Sarker et al. [43] combined EMA, location information, the cStress model (see [49]), which uses electrocardiogram and respiration data, and the Moving Average Convergence Divergence method to predict stress episodes associated with opioid intake. Their model predicted stress episodes with an accuracy of 94.8% and kappa of 0.444. Wang et al [45] used a sliding window technique to process streams of EDA, skin temperature and acceleration data collected from wrist-worn Q sensor, and distance-based outlier algorithm to detect substance use events. Their model accurately detected substance use events within 30 minutes. Using two parameters, movement in the z-axis and skin temperature collected from wrist-worn Q sensor, Mahmud et al. [47] compared three classifiers' (decision tree, k-nearest neighbors and eXtreme Gradient Boosting) ability to automatically detect opioid intake, obtaining an accuracy of 99.4% with eXtreme Gradient Boosting.

Biomedical devices

Miranda and Taca [50] investigated the effect of an auricular neurostimulation device, the BRIDGE[®], in treating opioid withdrawal symptoms. The device was placed behind the ears of 73 opioid-dependent outpatients for a maximum of 5 days to treat opioid withdrawal symptoms by stimulating nerves in brain and spinal cord. Reduction in opioid withdrawal scores, measured with clinical opioid withdrawal scale, was associated with the use of BRIDGE[®].

Table 6. Technologies identified in the scoping review.

	Physiological parameters				
[32]	PDA (Palm PZ21), software	Zire, diary	Not applicable	Monitoring	5 random prompts/day (5 weeks), 2 random prompts/day (20 weeks)

Physiological parameters					
[41]	Smartphones, wearable sensors, machine learning		EDA, acceleration, skin temperature, heart rate	Real-time detection of drug craving and interventions	Self-annotation of Physiological changes and machine learning
[33]	PDA (Palm Zire, Palm Zire 21), diary software		Not applicable	Momentary ratings of stress in outpatients at work	5 random prompts/day (5 weeks), 2 random prompts/day (20 weeks)
[34]	PDA(Palm Zire, PZ21), diary software		Not applicable	Gender-based treatment strategies	Random prompts (2-5 a day) for location, activities, and companions
[38]	PDA (PalmPilot), GPS (BT-Q1000X)		Not applicable	Real-time monitoring of mood, stress, drug craving	Time-stamped GPS data; EMA ratings of mood, stress, and drug craving
[42]	Biosensor (AutoSense); Smartphone		Heart rate	Continuous monitoring of heart rate	Wireless HR sensor data and self-reports
[44]	Biosensor (Q sensor)		EDA, skin temperature, acceleration	Real-time detection of drug use	Continuous monitoring of EDA, skin temperature, acceleration
[48]	PharmChek Drugs of Abuse Patches, Palm Z22, Smartphone		Sweat patches detect traces of cocaine or heroin secreted in sweat during period it is worn	Agreement of EMA methods to other methods -i.e., biological and ACASI- of assessing drug use	Palm Z22 PDA (3 trials), Motorola Droid X2 phone (1 trial); self-reports of heroin or cocaine; sweat patches (weekly); ACASI (weekly)
[40]	Smartphone, GPS		Not applicable	Integration of GPS information with EMA to study neighborhood effects on OUD	Combined GPS information with EMA to find association between neighborhood disadvantage, perceived stress, perceived safety, and substance use; generalized estimated equations for analysis.
[43]	Biosensor, smartphone, GPS, machine learning		ECG, Inspiratory :Expiratory ratio	Time series health data to determine timing of interventions; links to prevention of drug craving and relapse	Smartphone-initiated 32-item EMA (random); modeling R-R intervals and HRV from ECG data
[18]	Biosensor (Q sensor)		EDA, skin temperature, acceleration	Biosensors may be used in drug addiction treatment	Hilbert transform analyses combined with paired t-tests

Physiological parameters						
					and pain management	to compare biosensor data
[45]	Biosensor (Q sensor), urine drug screens, patient self-report of substance use	(Q)	EDA, temperature, acceleration	skin	Detect and set up thresholds of parameters in real-time drug use event detection for wearable biosensor data streams	Sliding window technique to process data stream, and distance-based outlier algorithm to detect substance use events
[46]	Biosensor (Empatica E4)		Skin temperature, acceleration, heart rate		Identify physiologic change that marks wearing off of naloxone effect	90-minute post naloxone time point evaluated with Hilbert transform
[35]	PalmOne Zire 21, Palm Tungsten E2, or HTC TyTN II smartphone		Not applicable		Investigate relationship between opioid use and craving and affect	Mobile devices used to rate craving four times randomly each day
[47]	Biosensor (Q-sensor), machine learning	(Q-)	EDA, temperature	skin	Automatic detection of opioid intake; classification of pre- and post-opioid health conditions	Time and frequency domain feature analysis; decision tree, <i>k</i> -nearest neighbors (KNN) and eXtreme Gradient Boosting classifiers
[36]	Smartphone		Not applicable		Gender differences in the influence of stress on opioid use and craving	Entry initiated, and causes, context, stress and craving severity rated each time participant felt more stressed than usual
[37]	Smartphone		Not applicable		Relationship between daily hassles and stressful events in opioid-dependent men and women	Randomly prompted entries, self-initiated reports of drug use, self-initiated reports of stressful events, end-of-day entries
[50]	BRIDGE®-auricular neurostimulation device	an	Not reported		Treat opioid withdrawal symptoms without the use of antiopioids	Patients wore device behind the ear to stimulate nerves in brain and spinal cord

Discussion

The goal of the app search in the present study was to determine the availability of opioid-related mHealth apps. The search revealed the availability of 72 Android and revealed a steady rise in app development within the same period, with most of the apps designed to support clinicians. Our findings suggest that majority of the apps have been developed to help clinicians convert from one opioid to another at equianalgesic dose. Opioid conversion, a common but challenging clinical practice [51], is required when patients do not respond therapeutically, develop adverse effect to an opioid, or need an alternative route of administration [52]. Prescription error has been identified as a significant risk factor for opioid-related deaths [53], and so opioid conversion apps that run on mobile devices may help improve patient safety [54]. Although these apps are not geared toward OUD, they help primary care providers safely prescribe opioids.

The United States Food and Drug Administration (FDA) has the mandate to regulate mHealth apps that meet certain statutory criteria as medical devices. Under the existing FDA regulatory framework, it is difficult to determine whether an mHealth app is a medical device or not [55]. The FDA has long exempted apps considered as "low-risk" from its approval process [56]. It is unclear how many of the opioid conversion apps identified in the current study have approval from the FDA. For example, although Pear reSET-O, a prescription app, was first published in 2016, it is only recently that the FDA cleared it as the first prescription digital therapeutic for patients with OUD [57]. This app provides cognitive behavioral therapy to patients enrolled in an OUD treatment program.

Although a majority of the apps identified in this study are free to download, many healthcare providers and patients may not be aware of the availability of such apps. Future studies should investigate such awareness and adoption rates. Factors that influence the adoption of mHealth apps by health professionals include lack of clinical evidence [58], security [59], and inability to integrate apps with other systems [60]. Factors that influence patient's adoption of mHealth apps include security and privacy concerns [61, 62], social contacts [63], and cost of smartphones and data plans [62, 64]. Failure to balance system demands of apps with end user needs and resources undermines the adoption of mHealth apps [65]. Conducting content analyses, usability testing, observational studies, and efficacy testing will contribute to increased adoption of mHealth apps in clinical practice [66].

mHealth app privacy, the right for users to know how their information is collected and used, is an issue worthy of discussion. In the present study, majority of the apps identified in the search were free to download. For users of these apps, there is a likelihood that their information is passed around to third parties, thereby exposing them to privacy risks [67]. A recent study investigated data sharing practices in the mHealth ecosystem and found 79% of the sampled apps shared user data with 55 entities, including third parties [68]. This presents a major concern for mHealth users since they do not know how their data will be used and by whom. Furthermore, the aggressive medicolegal system in the United States deters many health care providers from using mHealth apps. Recent studies (e.g., [69]) have suggested the need for standards that can ensure mHealth app user privacy.

Despite the availability of opioid-related apps, the scoping review, which sought to document relevant technology solutions that address OUD, found no study that employed mHealth apps to address OUD. Most of the studies employed EMA to capture participants' opioid use patterns as they occurred in real time. Few studies combined EMA with a range of data types, including

physiological changes and location information to detect opioid intake. These findings highlight a general lack of empirical evidence to support the efficacy of mHealth apps for OUD management. However, our findings show the potential for wearable sensors, especially in opioid withdrawal management, to facilitate remote monitoring of signs and symptoms of OUD.

Opioid withdrawal management, which includes regularly monitoring patients for symptoms, is the crucial first step after opioid use cessation or dose reduction [1]. Relapse rates during in-patient treatment of opioid dependence indicate that as many as 91% of those in recovery experience an opiate relapse, 59% of whom within the first week of sobriety, and 80% within a month after discharging from a detox program [70]. Results from the scoping review revealed that a majority of the studies employed EMA or combined EMA with a range of data types to detect opioid use patterns. These studies focused on opioid intake and use patterns. Only one study [50] from the review focused on developing technology to help treat opioid withdrawal symptoms. Indeed, the BRIDGE® device used in that study is the first of its kind approved by the FDA. It is crucial that technology solutions be provided not only to help healthcare professionals monitor and manage patients' withdrawal symptoms but also to help the patients themselves as they go through withdrawal.

From the results of the present study it is evident that there is a gap in technologies available to manage opioid withdrawal. Advances in wearable and machine learning technologies have enhanced researchers' ability to monitor physiological changes associated with opioid intake, and/or drug craving [43, 45, 47]. In the same vein, wearable sensors can be employed to detect temporal and spectral patterns of physiological responses associated with opioid withdrawal symptoms. For example, joint/muscle aches lead to elevated heart rate [71], which can be measured with a wearable ECG; anxiety leads to elevated heart rate [72] and change in skin conductance [73], which can be measured respectively with wearable ECG and EDA sensor; and *cutis anserine*, defined as goose bumps, leads to a change in skin conductance [74], which can be measured with a wearable EDA sensor. Machine learning-based pattern detection algorithms may be used to explicitly detect and characterize specific features obtained from wearable sensor configuration and existing contextual information. This can provide real-time feedback to healthcare providers to facilitate interventions.

There are some limitations in the study that warrant discussion. First, the search may not be collectively exhaustive due to the limitations of the scoping review. The scoping review utilized relatively fewer, albeit relevant, number of search terms and databases to identify potentially eligible studies. Despite this limitation, we found saturation in the technologies used to address OUD, evidenced by the lack of additional results from the 19-article-based bibliographic secondary search. Second, availability of information about app downloads was limited to Android apps only. However, the data presented in this study is relevant given that Android has overtaken iOS as the number one operating system for mHealth apps [75]. Third, while the app rating information is reported, it is difficult to determine how many of the ratings were legitimately written by people who used the apps. Also, we were unable to determine how the apps were rated. Due to this lack of information, the present study did not include information on the quality of the apps. Furthermore, we did not focus on capturing app effectiveness. Given the proliferation of mHealth apps and technologies made available to target OUD, future studies should aim to investigate the quality and effectiveness of these apps on OUD management. Lastly, developers may be reluctant to publish research on their apps for IP reasons (if they have any); much of their results/algorithms may be considered "proprietary".

Conclusions

This study showed the availability of opioid-relevant mHealth apps, the majority of which are opioid conversion apps. Despite the availability of these apps, the scoping review found no study that employed mHealth apps to address OUD. Most of the studies employed EMA to capture participant's opioid use patterns as they occurred in real time. Few studies combined EMA with a range of data types, including physiological changes and location information to detect opioid intake. Our findings highlight the gap in technologies and the potential for using wearable sensors, especially in opioid withdrawal management, to address OUD.

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Authors' Contributions

RKM and FS conceptualized the study, JN conducted and analyzed the reviews and drafted the initial manuscript, RKM and FS interpreted review outcomes and refined the manuscript.

Conflicts of Interest

None declared.

Abbreviations

app: application
EDA: electrodermal activity
EMA: ecological momentary assessment
GPS: global positioning system
iOS: iPhone operating system
mHealth: mobile health
OUD: opioid use disorder
SUD: substance use disorder

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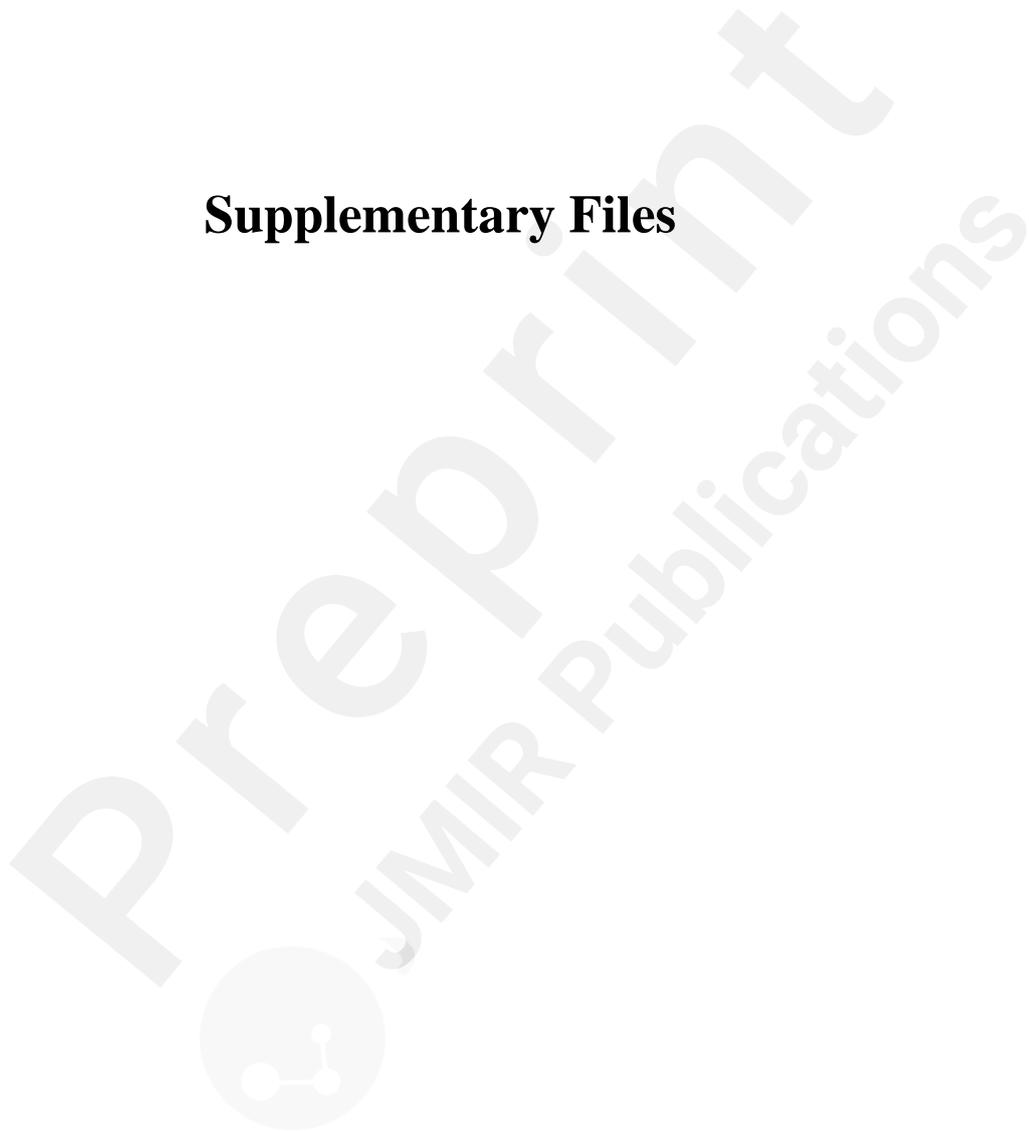
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