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REVIEW ARTICLE

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Systematic review: Wearable remote monitoring to detect nonalcohol/nonnicotine-related substance use disorder symptoms

CME

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Abstract

Background and Objectives: Substance use disorders (SUDs) are chronic relapsing diseases characterized by significant morbidity and mortality. Phenomenologically, patients with SUDs present with a repeating cycle of intoxication, withdrawal, and craving, significantly impacting their diagnosis and treatment. There is a need for better identification and monitoring of these disease states. Remote monitoring chronic illness with wearable devices offers a passive, unobtrusive, constant physiological data assessment. We evaluate the current evidence base for remote monitoring of nonalcohol, nonnicotine SUDs.

Methods: We performed a systematic, comprehensive literature review and screened 1942 papers.

Results: We found 15 studies that focused mainly on the intoxication stage of SUD. These studies used wearable sensors measuring several physiological parameters (ECG, HR, O_2, Accelerometer, EDA, temperature) and implemented study-specific algorithms to evaluate the data.

Discussion and Conclusions: Studies were extracted, organized, and analyzed based on the three SUD disease states. The sample sizes were relatively small, focused primarily on the intoxication stage, had low monitoring compliance, and required significant computational power preventing "real-time" results. Cardiovascular data was the most consistently valuable data in the predictive algorithms. This review demonstrates that there is currently insufficient evidence to support remote monitoring of SUDs through wearable devices.

Scientific Significance: This is the first systematic review to show the available data on wearable remote monitoring of SUD symptoms in each stage of the disease cycle. This clinically relevant approach demonstrates what we know and do not know about the remote monitoring of SUDs within disease states.

INTRODUCTION

Substance use disorders (SUDs) are chronic illnesses characterized by relapse, remission, and treatment resistance. Remote monitoring is a well-established component of most chronic disease management approaches.[1] However, it has been difficult to apply standard chronic disease management strategies to treatment models of SUDs.[2] For patients with chronic diseases like asthma, diabetes, heart disease, hypertension, and many others, remote monitoring has been shown to increase their disease-specific knowledge, prompt earlier clinical assessment/treatment, improve self-management, increase satisfaction, improve quality of life and increase a sense of responsibility for their illness.[1] Remote monitoring of chronic disease has also been associated with lower mortality and reduced hospital admissions.[3] Despite evidence indicating individuals with SUDs are open to remote monitoring from health care professionals,[4] it remains unused.[1,5]

"Stages of addiction" cycle

In 2016 the Surgeon General's Report on Alcohol, Drugs, and Health described SUD as a repeating cycle of three stages or disease states. These stages include binge/intoxication, withdrawal/negative affect, and preoccupation/anticipation (see Figure 1). Each disease state is associated with distinct brain regions, circuits (or networks), and neurotransmitters. Subsequently, these stages link to distinct physiological features. Individuals may go through these stages over hours, days, weeks, or even months. Variation in how people progress through these states contributes to assessment and treatment challenges. However, these cycles tend to intensify over time, leading to greater physical and psychological consequences if left untreated.[6] Although this "three-stage model" is a simplified way of viewing the complexity of SUDs, it provides an essential, clinically relevant framework to organize the current clinical understanding of the disease.[6]

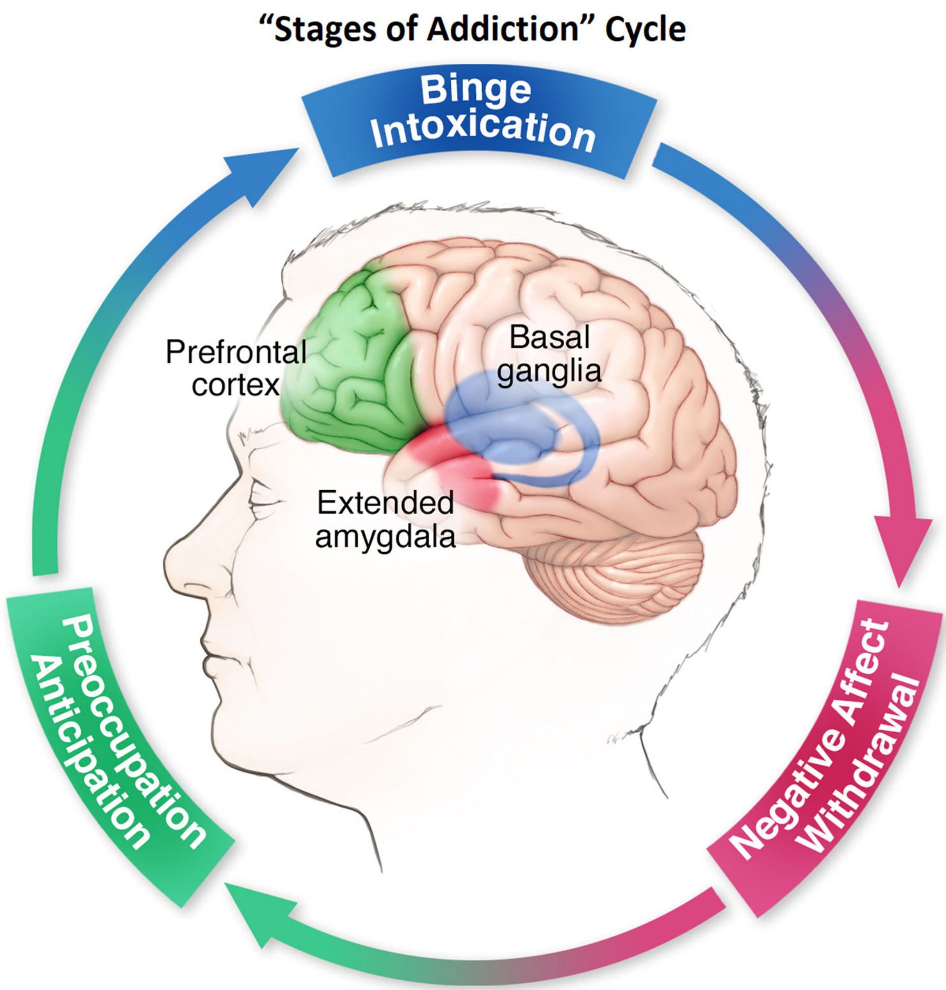

FIGURE 1 The three stages of the "addiction cycle" and associated brain regions. Used with permission of Mayo Foundation for Medical Education and Research, all rights reserved

Most of the research in remote monitoring of SUD has focused on alcohol use in the binge intoxication stage of the disease.[7] This stage begins when an individual experiences the rewarding/pleasurable effects of the addictive substance mediated by the activation of the brain's "reward centers" through the release of dopamine (either directly or indirectly) in neurons located in the basal ganglia.[8]

Remote monitoring of the binge/intoxication stage has focused on detecting the presence of an addictive substance in an individual's sweat. Exogenous substances are metabolized and excreted from the body. Most intoxicants produce excretion through the skin with sweat. Sweat collection through patches has been a viable clinical tool to measure substance use for decades. Sweat patches absorb and collect sweat over a distinct period (typically over a week to a month). When removed, the patches are processed to extract and analyze for the presence of intoxicants. Although relatively reliable, these results are far from "real-time."[9] Approximately 30 years ago, the technology for active identification of alcohol through the skin was developed. Today "Secure Continuous Remote Alcohol Monitoring" (SCRAM) is a wearable device that takes measurements every 30 min and is the most widely researched alcohol remote monitoring device.[10] However, several other alcohol-detecting devices have been available for over a decade, and others are under development to be commercially available.[11] A new age of wearable sensors offers a more advanced ability to better analyze the contents of sweat in real-time; however, these sensors do not reliably detect nonalcohol drug abuse.[7]

With the lack of widely available electrochemical sensors to detect drugs of abuse, most researchers have turned towards measuring physiological parameters representative of physical states associated with active use. Physiological changes associated with intoxication are typically substance-specific. For example, sedatives (benzodiazepines, selective benzodiazepine receptor subtype agonists [z-drugs], and barbiturates) can lead to physical changes, including nystagmus, decreased reflexes, and unsteady gait that could be measurable through remote monitoring.[12]

Withdrawal occurs when an individual with physiological tolerance and dependence on a substance stops using the substance. In the absence of an addictive substance that has regularly triggered the intoxication phase, an individual will experience negative physical and emotional consequences. The physical manifestations of withdrawal can be complex and, as with intoxication, are often substance dependent. For example, withdrawal from CNS depressant agents, such as alcohol and benzodiazepine, can vary from more subtle symptoms like sleep disturbance, irritability, increased tension, anxiety, tremor, diaphoresis, sweating, difficulty in concentration, to more severe symptoms, including delirium, hallucinations, seizures, and even death.[13] Stimulant withdrawal is thought to be associated with sedation, fatigue, anhedonia, depression, and hypersomnia.[14] Opioid Withdrawal is associated with lacrimation, rhinorrhea, piloerection "goose flesh," myalgia, diarrhea, nausea/vomiting, pupillary dilation with photophobia, insomnia, autonomic hyperactivity (tachypnea, hyperreflexia, tachycardia, sweating, hypertension, hyperthermia), and yawning. The negative emotions associated with all substance withdrawal come from two sources, hypoactivation of the reward circuitry in the basal ganglia and hyperactivation of the brain's stress response system in the amygdala.[15]

Following the withdrawal stage, a person with SUD transitions to a period of abstinence. At this point, they will begin the preoccupation and craving phase. This stage of addiction causes increased activity of the neurotransmitter glutamate and disruptions of dopamine influxes in the frontal cortex. These changes contribute to a feeling of discomfort associated with the lack of the addictive substance combined with a lower capacity to resist compulsions to use (driven by the disruption to executive functioning).[16] This coincides with the overactivation of the prefrontal (habit) areas of the brain that reinforce habitual behaviors like substance use. The combination of these forces can lead to a relapse into addictive substances.[17] Preoccupation with the addictive substance, especially during times of stress, is also a hallmark feature of this stage. Preoccupation leads to higher levels of cue-induced cravings.[18]

Several studies have identified physiological parameters associated with cravings, including changes in heart rate (HR), skin temperature, blood pressure (BP), electrodermal activation/skin conductance (EDA/SC), and salivation.[19] In 2012, Zhao et al. studied 56 heroin-dependent patients who were either abstinent for less than 1 month or were abstinent at least for 12 months compared to 26 healthy controls in a controlled laboratory setting. They exposed cases and controls to videos showing active heroin use and monitored using laboratory equipment designed to capture EDA, muscle electromyography (MEG), skin temperature (TEMP), cardiovascular (CV) arousal (HR, systolic BP [HBP], and diastolic BP [LBP]). These measures were assessed at baseline and after exposure to the videos. Both heroin-abstinent groups showed increased heroin craving, EDA/SC, MEG, HR, SBP, and LBP after exposure to heroin-related video compared to the control group and the neutral video. The more recently abstinent group showed more HR changes. However, changes in heroin craving, EDA/SC, MEG, HR, SBP, and LBP after exposure to the heroin cue video were not different between the opioid-dependent cohort groups.[20] Another study showed similar results utilizing virtual reality devices to invoke craving episodes in participants with methamphetamine use disorder (MUD). HRV, EDA, and eye-tracking had significant differences between pre-VR stimulation and post-VR stimulation in MUD patients but not in healthy subjects.[21] Several reviews have addressed different aspects of remote monitoring of alcohol use with wearable sensors, emphasizing the utility of multiple types of sensors.[22] A relatively recent review of wearable sensors for monitoring cigarette smoking showed that most devices were researched in laboratory settings.[23] Remote monitoring of nonalcohol and nonnicotine substances of abuse has proven even more difficult.

What can we measure with wearable technology?

Wearable devices are a subset of unobtrusive remote monitoring devices, facilitating regular use and continuous monitoring of physiological activity associated with symptoms. To provide remote monitoring for SUDs, wearable wireless biosensors must be autonomous, provide continuous measurements, be user-friendly, noninvasive, and comfortable to wear for a long time close to the skin.[7] Currently available biosensors can passively measure an impressive array of parameters, including chemicals excreted in sweat, HR, BP, body/skin temperature, skin conductance/EDA, oxygen saturation (O_2), respiration rate (RR), and electrocardiogram (ECG).

Chemical sensors use electrochemical detection, which measures electrical currents or potentials at functionalized electrodes to transduce analyte concentrations.[24] Chemical sensors can identify chemicals excreted from the skin either actively or passively. These sensors are essential to the ankle bracelet monitors widely used in the criminal justice system to detect alcohol use.

Accelerometers can measure movement in multiple directions providing information on activity level and fine muscle movement. While not directly detecting substance use, these sensors detect substance-induced tremors and activity changes.[25]

Photoplethysmography measures HR and pulse oximetry readings using light directed at blood vessels under the skin. These sensors can identify substance use-related changes in HR and oxygen concentration, or they can be used to infer drug-induced autonomic changes through calculated perimeters like HR variability (HRV).[26]

Temperature sensors can measure subtle changes in skin temperature related to autonomic responses linked to substance use.[27] Another way to indirectly measure autonomic response affected by substance use is through skin conductance, also called electrodermal activation (EDA). EDA measures the varying electrical properties of the skin in response to sweat secretion.[28] Results show wearable EDA devices can accurately and reliably distinguish calm conditions from distress conditions.[29]

Although all these sensor types appear in various applications, from skin patches to ankle bracelets, wrist-worn products are by far the most popular and widely accepted due to their ease of use and functionality.[30] Commercially available wearable sensors include an ever-developing sensor array (accelerometers and photoplethysmography are the most common). Although these commercially available sensors can have varying degrees of quality, they are constantly improving.[25]

A proposed approach for remote monitoring in SUD clinics

Figure 2 describes a clinical scenario using a wearable device connected to a mobile phone application to enhance SUD clinical care through remote monitoring. Although this approach is not currently available to physicians, the technology and technical capabilities have been available for several years and will be the focus of this review.

This article represents a systematic review of research papers evaluating the efficacy of wearable biosensors in the remote monitoring of SUDs to identify the current capabilities of providing the care approach outlined in Figure 2.

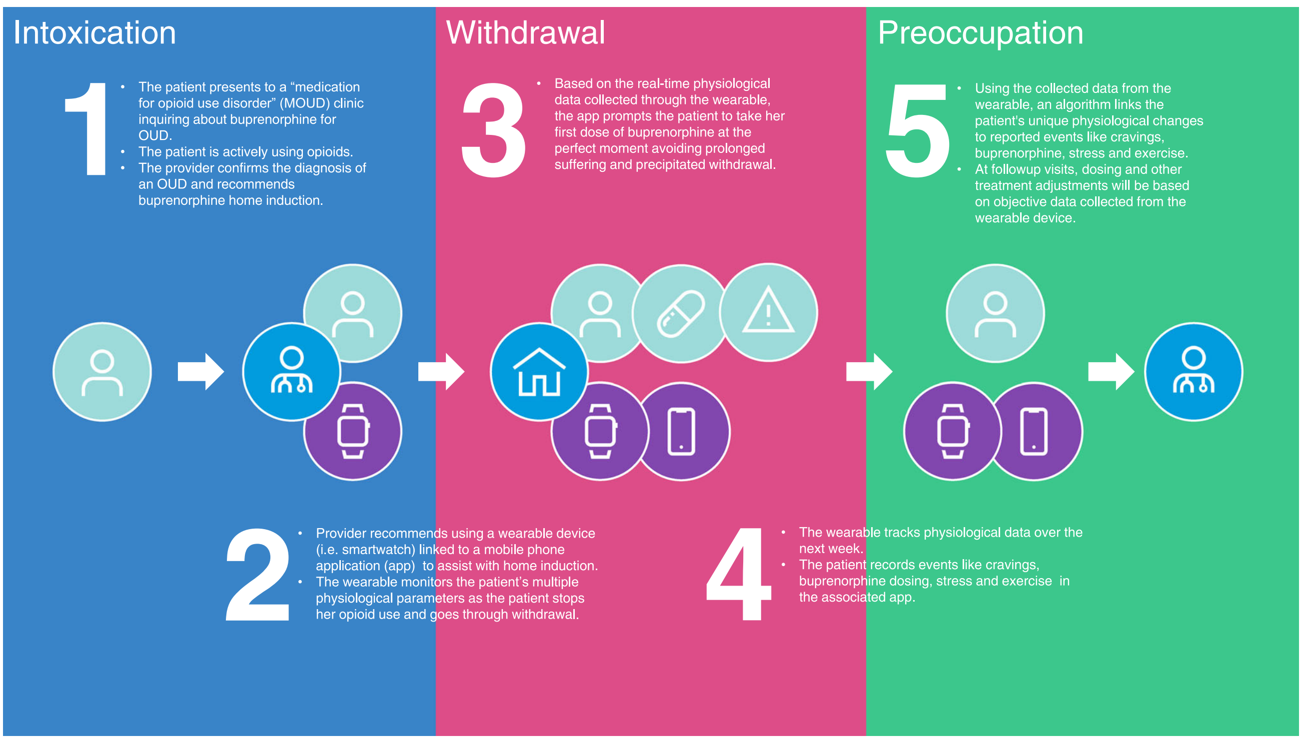

FIGURE 2 Using a wearable device in the clinical care of a patient with substance use disorder

METHODS

We searched the literature for the concepts of remote monitoring in patients with drug addiction. We used a combination of keywords and standardized index terms. We searched using specific terms in the medical subject heading and text words to identify candidate articles. Generally, the terms focused on remote monitoring, wearable devices, addiction, and SUD. The complete keyword and terms list were quite robust, so we included a detailed description of all the terms used in the appendix. (contact the corresponding author for a complete list of terms). We reviewed bibliographies of the relevant articles to search for additional studies. We ran searches in March 2021 in Ovid Cochrane Central Register of Controlled Trials (Central) (1991+), Ovid Embase (1974+), Ovid Medline (1946+ including epub ahead of print, in-process & other nonindexed citations), Ovid PsycINFO (1806+), and Scopus (1970+). Results were limited to the English language from 1980 forward, with most conference abstracts and animal and pediatric studies excluded. Central contained 78 references, Embase contained 1232 references, Medline contained 460 references, PsycINFO contained 69 references, and Scopus contained 756 references for a total of 2595 references. We exported all results to Covidence from Endnote, where we removed duplicates, leaving 1945 citations. We evaluated the papers' quality based on the EVIDENCE checklist (Publication Checklist for Studies Evaluating Connected Sensor Technologies: Explanation and Elaboration).[31]

Inclusion/exclusion criteria

As noted in the appendix, the general approach used words associated with "wearable," "remote monitoring," and "substance use." Due to an abundance of previous reviews focusing on remote monitoring of alcohol use disorder and nicotine, we chose to exclude alcohol/ smoking-related studies. We also excluded pediatric patients and studies focused on nonhuman subjects. We excluded articles focused on device development and not physical assessment in living humans. Furthermore, we excluded studies demonstrating wearables designed for law enforcement to detect drugs in the environment (i.e., drug sensors placed in gloves for handling suspicious material).

RESULTS

We screened 1945 studies at title and abstract for relevance to the research parameters. We removed 1333 studies due to titles indicating that they were beyond the scope of this review. We assessed 549 studies at the text level. Many of these had incorrect study designs (focusing on theoretical analysis or reporting on sensor development) or were the wrong patient population (nonsubstance-related patient population). Some had the wrong setting (lab studies that did not have a human component), and some were still ongoing. Figure 3 shows how we excluded studies from the current review. Ultimately, 15 studies met the inclusion criteria.

According to the EVIDENCE checklist[31] all studies appeared to be "proof-of-concept" with initial testing intended to indicate whether the use of a technology or the development of a digital measure may be feasible in each context of use.

Description of the studies and findings by stages of addiction

Intoxication stage

We could find no articles that evaluated biochemical sensors for the direct remote detection of nonalcohol, nonnicotine drugs of abuse in human participants. Our review did not reveal any studies looking at the physical symptoms of sedatives like barbiturates or benzodiazepines. However, we found multiple studies examining physical symptoms of stimulant (cocaine) and opioid use (see Table 1).

Cocaine

These studies begin with a 2013 pilot study ($N = 6$) that used a chest-worn halter monitor. This study utilized a lab setting where they administered controlled doses of cocaine to nontreatment-seeking individuals with cocaine use disorder. Chest worn Holter monitors measure ECG, HR, accelerometers, and RR. They evaluated HR ECG, accelerometers, and RR data using a computer-based algorithm that correlated halter data to the dose of cocaine. Using data collected from the same patients but not used in the development of the algorithm, they could use the algorithm to identify cocaine dosing accurately.[32] The following year, Yoon et al. employed a similar strategy of laboratory-controlled setting and halter monitor on a larger group of individuals ($N = 28$). They found that HR was significantly associated with cocaine dosing and the other parameters were not.[33] Hossain et al. employed a hybrid approach where they established and "trained" their algorithm on lab data using an approach similar to the studies mentioned above and then tested it in the field. The algorithm works reasonably well with a 100% "true positive" rate in "real-world" environments.[34] Angarita et al. employed a similar approach to the lab-based studies previously mentioned but specifically addressed distinguishing between potentially confounding events like exercise and methamphetamine use. They reported the ability of their algorithm as sensitive and specific to cocaine. Carreiro et al. used a wrist-worn device (rather than the chest-worn device of the other studies) that measured similar parameters (ECG, RR, Skin Temp, accelerometer, and EDA) in a "real world" setting and correlated sensor data with urine drug screens. Their algorithm was trained on initial positive urines and then tested on subsequent data. This approach was able to identify a few moments of active use and missed some others, and recorded too few events to establish statistical significance.[36] Natarajan et al. followed up their initial laboratory study to test their algorithm in the real world. They reported sensitivity of 80% and specificity of 90%

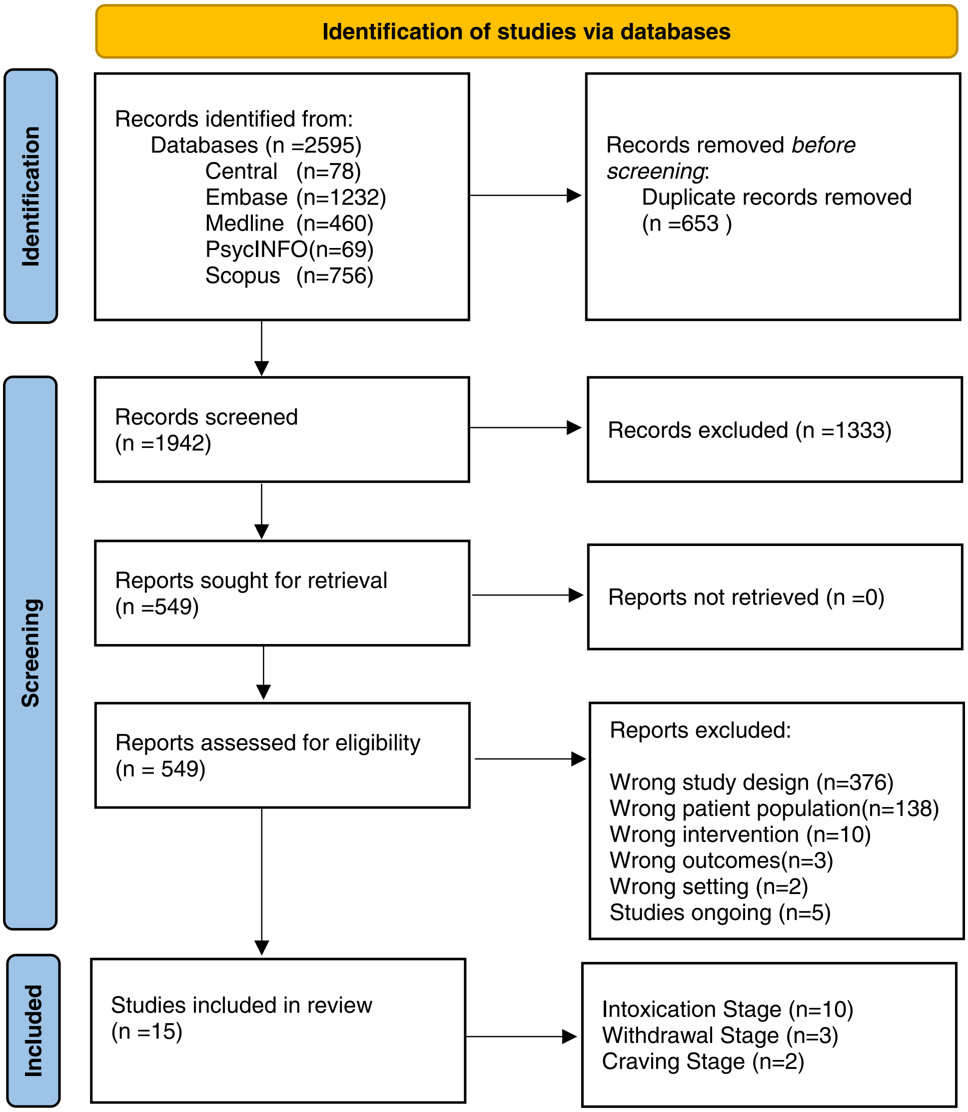

FIGURE 3 PRISMA flow diagram

based on urine drug screens. A unique study of this group addressed applying a novel algorithm to data initially acquired by the wrist-worn study by Carreiro et al.[38] Rather than using an algorithm that required significant computing power, they utilized a leaner formula that could identify events faster and with less input. See Table 1 for a full breakdown of the details of these studies.

Opioids

Our review revealed a series of studies looking at physiological parameters of opioid intoxication. All the studies came from the same researchers looking at opioid use in emergency rooms. They utilized a wrist-worn sensor that included EDA, skin temp, and accelerometer. The first study was a feasibility study showing that the approach was feasible within the described context.[39] The second study addressed correlations while in the emergency department.[40] They observed a significant change in locomotion and skin temp after opioid admin for pain. No other data points were significant.[40] All of these studies included algorithms to analyze the data and compare these results to intoxication events. The study by Mahmud et al. was a follow-up to the previous two studies.[39–41] This was a real-world study using the data gathered in the last two studies to test the algorithm trained in the previous studies. They developed a method that purportedly identified opioid use events with 99% accuracy. Identification relied heavily on only two parameters: the up and down (*Z*-axis) movement and the skin temperature of patients. See Table 1 for further details.

Withdrawal/negative affect stage

In our systematic review, we were able to find three studies associated with wearable devices monitoring withdrawal from addictive substances. The first study utilized a Holter monitor in a

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TABLE 1 Studies looking at remote monitoring in Binge/Intoxication

Study	Number of participants	Substance	Sensor type (measures taken)	Study design	Results
2013 Natarajan et al.[32]	6	Cocaine	Chest band (ECG, HR, accelerometer, RR)	Laboratory-controlled. Cocaine doses (8, 16, 32 mg) in three sessions (6 h total).	RR interval length most important feature but confounded by activity thus not viable. Waveform features better to use. AUC between 0.8 and 0.95 depending on dose.
2014 Yoon et al.[33]	28	Cocaine	Chest band (ECG, HR, accelerometer, RR)	Laboratory-controlled, double-blind, placebo-controlled, within-subject either placebo or 40 mg of cocaine over 30 min.	HR, but not RR, was significantly associated with substance use. For HR (top). No AUC reported as this wasn't the goal.
2014 Hossain et al.[34]	9 training study and 42 field study	Cocaine	Chest band (ECG, RR, Skin Temp, accelerometer, and EDA)	Laboratory-controlled training study. Cocaine doses (1, 10, 20, and 40 mg) every 30 min via a pump. Training model applied to field study.	Model performance in field study with sensitivity of 92.6% and specificity of 93.4%. No AUC reported.
2015 Angarita et al.[35]	5	Cocaine	Chest band (ECG, HR, accelerometer, RR)	Inpatient research study. Cocaine doses (8, 16, 32 mg/70 kg) given after methylphenidate use or during aerobic exercise to detect difference in activity and cocaine use.	Classifiers distinguished cocaine use from exercise and methylphenidate with AUC >0.9 and >0.95, respectively, and with sensitivity/specificity >90%.
2015 Carreiro et al.[36]	15	Cocaine	Wristband (ECG, RR, Skin Temp, accelerometer, and EDA)	Observational in real-world setting. Urine drug screening and drug use self-report measured cocaine use.	Data captured two drug use episodes reflected in urine screen but not self-reported and one drug use episode self-reported but not reflected in urine screen. No AUC reported.
2016 Natarajan et al.[37]	10 training study and 5 field study	Cocaine	Chest band (ECG, HR, accelerometers, RR)	Laboratory-controlled training study. Cocaine doses (8, 16, 32 mg) in three sessions (6 h total). Training model applied to field study.	Approach produces sensitivity of 80% and specificity of 90% when prior access to urine drug screen and per person cocaine exposure ECG data is available.
2017 Wang et al.[38]	See 2015 Carreiro et al.[36]	Cocaine	See Carreiro et al.[36]	Reanalyzed data from a previous study[36] with a sliding window technique.	Algorithm allows for real-time data interpretation and accurately identified cocaine use events within about 30 min.
2014 Carreiro et al.[39]	4	Opioid (4), Cocaine (1)	Wristband (EDA, skin temp, and accelerometer)	Pilot/feasibility study to measure opioid/cocaine use. Descriptive study.	Observed changes in EDA and skin temperature temporally associated with intravenous administration of opioids.
2016 Carreiro et al.[40]	30	Opioid	Wristband (EDA, skin temp, and accelerometer)	Observational study in the emergency department prescribed intravenous opioid medication for acute pain.	Significant decrease in locomotion and increased skin temperature associated with opioid administration within subject. Heavy users had greater decrease in short amplitude movements (i.e., fidgeting movements) compared to nonheavy users.
2018 Mahmud et al.[41]	30 (same cohort as 2016 Carreiro et al.[40]	Opioid	Wristband (EDA, skin temp, and accelerometer)	Observational study of 2016 Carreiro et al.[40] participants over a period of 4 months while the participants wore the device and tracked use events.	Using an algorithm derived from the 2016 Carreiro et al.[40] original data, identified opioid use events with 99% accuracy in cohort. Identification relied heavily on only two parameters; the up and down (*Z*-axis) movement and the skin temperature of patients.

laboratory setting to obtain ECG data.[42] Blinded physicians then evaluated this data. The following two studies were much more recent and evaluated opioid withdrawal in individuals presenting to the emergency room.[43,44] All the studies demonstrated statistically significant changes in physiological parameters during withdrawal. See Table 2 for full study details.

Preoccupation/craving

Our review revealed several studies evaluating wearable sensors' ability to measure similar parameters during long-term abstinence and sustained remission from substance use (see Table 3). Two studies were considered for inclusion but did not have sensor outcome data to report. In 2011 Fletcher et al. described a wearable sensor band worn on the ankle that could continuously monitor EDA, 3-axis acceleration, and temperature. They also described an ECG heart monitor worn on the chest as an optional part of the system. This article was simply a description of the device and did not contain any patient data from the device.[45] In 2012, the same group[47] reported on the results of a focus group of individuals with addiction that had a mostly favorable response to the concept of utilizing wearables to evaluate cravings longitudinally. The two included studies look at "real world" cohorts and rely on self-report episodes of cravings. One study utilized a chest band[26] and the other study utilized a wrist-worn device.[48] Both studies reported on algorithms able to identify episodes of cravings within the collected data. See Table 3 for full study details.

DISCUSSION

Thousands of individuals worldwide carry a wearable device daily that measures real-time physiological data like movement, HR, and so forth.[46] As noted earlier, remote monitoring has become an essential part of treatment modalities for chronic illnesses. Therefore, establishing remote monitoring to evaluate the various disease states of addiction is an important goal. Although remote monitoring of alcohol and even nicotine use disorders has advanced significantly in the last decade, remote monitoring of other SUDs has not. Like other reviews of alcohol and nicotine, the articles reviewed here are challenging to synthesize due to the utilization of different monitoring devices, different proprietary algorithms to analyze the data, and outcomes reported in very different ways. We narrowed down almost 2000 potential studies to a final 15 reflecting the significant amount of preclinical work that has been slow to move to clinical research. We expected device development research in a developing field that is very "device-dependent." While remote monitoring may someday significantly improve clinical outcomes of SUDs, several cautionary themes arose through the assessment of these studies. First, most studies focused on evaluating the active use/intoxication stage, which is a stage that occurs when preventative measures have failed. Second, continuous remote monitoring with sensors produces a significant variation in the amount and quality of the data collected.

TABLE 2 Studies looking at remote monitoring in withdrawal

Study	Number of participants	Substance	Sensor (measures)	Study type	Results
1989 Nademanee et al.[43]	21	Cocaine	Holter (ECG)	Observational study in a laboratory setting. Looking for ECG changes during cocaine use using blinded ECG physician raters.	No computer algorithm was used. Physicians were asked to evaluate ECG's. Eight of 21 patients with cocaine addiction had frequent episodes of ST elevation during Holter monitoring ST elevation during the first weeks of withdrawal.
2018 Chintha et al.[45]	20	Opioid	Wrist band (skin temp accelerometry, EDA, and HR).	Observational study in the emergency department for those with reported naloxone use before arriving. Patients followed for 90 min.	Physiologic changes were consistent with the onset of opioid drug effect, but only changes in heart rate and skin temperature research statistical significance.
2021 Kulman et al.[44]	16	Opioid	Wrist band (BP, EDA, skin temp, HR, and accelerometry).	Cohort who presented to the ED in opioid withdrawal. Researchers developed a set of machine-learning classifiers, using baseline data and then used those classifiers to evaluate unseen test data form the same patients.	Best performing model (Random Forest) had AUC = 0.9997. Model was able to detect withdrawal with just 1 min of biosensor data.

Abbreviations: AUC, area under the curve; BP, blood pressure; ECG, electrocardiogram; EDA, electrodermal activity; HR, heart rate.

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TABLE 3 Studies looking at remote monitoring in preoccupation/craving

Study	Number of participants	Substance	Sensors used (measures)	Study type	Results
2015 Kennedy et al.[9]	40	Polydrug	Chest band (accelerometry, EDA, skin temp, and HR)	Observational study in opioid-agonist maintenance for up to 4 weeks. Participants self-reported drug use and cravings.	HR was higher when participants reported cocaine use than when they reported heroin use and was also higher as a function of the dose of cocaine reported. HR was higher when participants reported craving heroin or cocaine than when they reported not craving. No AUC reported.
2020 Carreiro et al.[46]	N = 30	Polydrug	Wristband (accelerometry, EDA, skin temp, and HR)	Observational study in outpatient program. Participants self-reported episodes of stress and craving.	A total of 41 craving and 104 stress events were analyzed. The differentiation accuracies of the top performing models were as follows: stress versus nonstress states 74.5% (AUC = 0.82), craving versus no-craving 75.7% (AUC = 0.82), and craving versus stress 76.8% (AUC = 0.8).

Abbreviations: AUC, area under the curve; EDA, electrodermal activity; HR, heart rate.

Finally, remote monitoring produces a large amount of per-patient data that is not easily interpretable by standard data analysis and requires robust (often proprietary) computer algorithms that take time.

LIMITATIONS

A focus on intoxication

Of the 15 included studies, much of the research (67%) focused on addiction's active use or intoxication stage. Our introduction notes the dominance of remote alcohol use monitoring literature by studies of remote biochemical sensors identifying the intoxication stage. Subsequently, this focus on identifying active use through non-biochemical sensors may be a response to the lack of electrochemical sensors to identify active use of nonalcohol-related substances of abuse. It may also be related to broader efforts to identify alternatives to urine drug testing in assessing individuals with SUDs.[9,49] The 10 studies evaluating the intoxication stage primarily focused on cocaine use. Stimulants like cocaine have significant effects on the CV system with symptoms of tachycardia, dyspnea, hypertension, and dysrhythmias.[50] Subsequently, it is no surprise that our review revealed several studies that focused on remote monitoring of the CV system to assess stimulant intoxication.[32,35,37]

Sensor selection and data collection are still a work in progress

There is no clear standard currently for the remote monitoring of individuals with SUDs. Many of the studies used a similar set of sensors to evaluate physiological parameters remotely (ECG, accelerometry, EDA, skin temperature, O_2, and HR). However, these sensors were selected based on availability rather than a priori assessment of what type of data would be most beneficial. Some of these sensors were in chest-worn devices, and some were in wrist-worn devices. No consistent device was used among the studies, although studies produced by a particular research group used the same device. Most medical-grade devices need to be independently calibrated to make sure they are accurately collecting the data they purport to be measuring. No studies included data identifying the independent validation of the monitoring devices utilized. However, those studies that compared within-participant results to between participant results showed that some "self-calibration" occurred, creating more accurate results within subjects than between subjects.[39–41] Studies utilizing Holter monitors identified these as FDA-cleared devices, but the other studies utilizing wrist-worn devices indicated these were research devices only. CV-related data like HR and ECG appeared to be the most consistently valuable data in the predictive algorithms. CV data may be the most valuable data in the future, or it could be related to the fact that these parameters are the easiest to measure consistently at the time of these studies. All the researchers reported significant data gaps in their monitoring for several reasons, including poor compliance from the participant, failure of the sensor to detect the desired parameter, movement artifact, and sensor results outside of physiological probability. The researchers typically discussed their approach to accounting for data gaps through various statistical methods. However, inconsistent data extraction remains a significant limitation of continuous remote monitoring utilizing wearable devices.

Understanding "Big Data"

Continuous remote monitoring produces a large amount of data. This data must be analyzed and interpreted, typically through algorithms that assist in identifying trends and predicting future results. Many of the studies evaluated the efficacy of their algorithms and some even compared algorithms. The development of algorithms to characterize large data sets is an active area of research and development in and of itself that has developed independently of the wearable device field. When developing algorithms from data sets, the more data, the better and the more diverse the circumstances, and the more accurate and generalizable the algorithms predict rare events. Unfortunately, these studies represented a relatively small number of patients, with the most significant study incorporating just 40 patients. The relatively low sample sizes associated with these studies are related to the fact that most of these studies were pilot approaches designed to evaluate the approach's feasibility.

Furthermore, the algorithms are only as good as the data quality they model, making data loss particularly impactful. The reliance on algorithms also limits the clinical utility of the data extracted. Typically, these algorithms require robust computing power applied to essential data to predict an event accurately. Most of these studies used algorithms in a retrospective manner to "predict" an event within an already gathered data set, which is not clinically useful in real-time. One study by Mahmud et al. specifically attempted to address this limitation and demonstrated an algorithm with comparable efficacy that produced results much quicker.[41] These are significant efforts to streamline the algorithms to make them more useful in "real-time" so that they can produce actionable alerts to providers.

CONCLUSIONS

Most of the researchers in the studies included in this review acknowledge the nascent nature of their research. CV-related data like HR and ECG appeared to be the most consistently valuable data in the predictive algorithms. However, all the included papers identified the need for better, more consistent sensors and identified the need for larger, more diverse patient groups to further the development of their algorithms. This review represents the most up-to-date information about remote monitoring of the various disease states, primarily cocaine and opioid use disorders. Unfortunately, these studies represent small, pilot data utilizing unique algorithms that require significant computing power to analyze the data. Subsequently, the scenario outlined in Figure 2 is not yet possible. Future researchers would do well to learn from these initial efforts and utilize wearable devices that are desirable to wear, calibrated to the specific user, independently assessed for accuracy, and capable of a consistently accurate data stream. Despite the limitations of these studies, this review shows the early promise of noninvasive wearable devices as monitoring tools for SUD management.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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