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REVIEW

Artificial intelligence interventions focused on opioid use disorders: A review of the gray literature

Tara Beaulieu[a,b], Rod Knight[a,c], Seonaid Nolan[a,c], Oliver Quick[d], and Lianping Ti[a,c]

[a]British Columbia Centre on Substance Use, Vancouver, BC, Canada; [b]Graduate Programs in Rehabilitation Sciences, Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada; [c]Department of Medicine, Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada; [d]University of Bristol Law School, Bristol, UK

ABSTRACT

Background: With the artificial intelligence (AI) paradigm shift comes momentum toward the development and scale-up of novel AI interventions to aid in opioid use disorder (OUD) care, in the identification of overdose risk, and in the reversal of overdose.

Objective: As OUD-specific AI interventions are relatively recent, dynamic, and may not yet be captured in the peer-reviewed literature, we conducted a review of the gray literature to identify literature pertaining to OUD-specific AI interventions being developed, implemented and evaluated.

Methods: Gray literature databases, customized Google searches, and targeted websites were searched from January 2013 to October 2019. Search terms include: AI, machine learning, substance use disorder (SUD), and OUD. We also requested recommendations for relevant material from experts in this area.

Results: This review yielded a total of 70 unique citations and 29 unique interventions, which can be sub-divided into five categories: smartphone applications (n = 12); healthcare data-related interventions (n = 7); biosensor-related interventions (n = 5); digital and virtual-related interventions (n = 2); and 'other', i.e., those that cannot be classified in these categories (n = 3). While the majority have not undergone rigorous scientific evaluation via randomized controlled trials, several AI interventions showed promise in aiding the identification of escalating opioid use patterns, informing the treatment of OUD, and detecting opioid-induced respiratory depression.

Conclusion: This is the first gray literature synthesis to characterize the current 'landscape' of OUD-specific AI interventions. Future research should continue to assess the usability, utility, acceptability and efficacy of these interventions, in addition to the overall legal, ethical, and social implications of OUD-specific AI interventions.

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Introduction

Globally, an estimated 27 million individuals meet the criteria for opioid use disorder (OUD), a condition associated with significant morbidity, mortality, and economic consequence (1–3). Despite a number of effective evidence-based treatments for OUD, including oral and injectable opioid agonist treatment (OAT) (1,4–8), it is estimated that the majority of those living with OUD remain undiagnosed, and less than 10% of those living with OUD receive treatment (3,9,10).

In recent decades, artificial intelligence (AI) interventions have experienced an era of explosive growth across the healthcare market, and have become a source of substantial surgical and non-surgical innovation within various fields including neurology, radiology and cardiology (11–14). In response to the ongoing opioid overdose epidemic plaguing North America, this paradigm shift is also creating momentum toward the development, evaluation, and scale-up of novel AI interventions to aid in the diagnosis and treatment of OUD, in the identification of opioid overdose risk, and in the reversal of opioid overdose. For example, a recent prognostic study involving 560,057 Medicare beneficiaries in the United States (US) found that machine learning algorithms performed well in predicting opioid overdose risk (15). A recent study using all Payer Claims Data in Massachusetts found that machine learning based approaches can also be leveraged to predict OAT concordance (16). Several studies have also shown that digital and virtual-related interventions supported by AI may play an important role in encouraging behavior modification, curbing opioid cravings (17,18), and aiding in the provision of opioid overdose training (e.g., naloxone training) (19–21).

In 2020, a scoping review of the peer-reviewed literature in the field of addiction AI interventions found

CONTACT Lianping Ti bccsu-lt@bccsu.ubc.ca British Columbia Centre on Substance Use, Vancouver BC V6Z 2A9, Canada

a number of additional emerging technologies which could prove useful for improving SUD care (22). Most of the research which examines OUD-specific interventions has resulted in promising findings (22). For example, the Affectiva Q sensor, a wearable sensor which employs machine learning algorithms was found to detect opioid use with 99% accuracy in a study involving 30 individuals in a hospital setting (22,23). It is likely that a number of non-OUD specific interventions could be applied or adapted to OUD as well; however, further research appears necessary to determine precisely how.

Key opportunities exist for gray literature (i.e., information published outside of traditional peer-review channels) (24) to supplement the knowledge in this area – particularly given that AI interventions in the field of addiction are relatively recent, dynamic, and may not yet be captured in the peer-reviewed literature (e.g., due to publication lag). Therefore, the objective of the current review is to synthesize the gray literature to identify OUD-specific AI interventions being developed, implemented, and evaluated. Outcome data were also captured when available (Table 1).

Methods

Eligibility criteria

The search was restricted to publications in English from January 2013 to October 2019. Publications referring to any type of AI (i.e., machine learning, natural language processing, expert systems, planning, speech, vision, and robotics) were included; however, those with a focus on SUD in a broader sense were excluded (i.e., OUD was not specifically mentioned), as were publications that spoke to AI more generally (e.g., only 'machine learning algorithms' were specifically mentioned). As a recent literature review was conducted that focused on peer-reviewed publications (134), these were also excluded. Setting, or population restrictions (e.g., age, socio-demographic status) were not applied.

Search strategy

Consistent with previous reviews of gray literature, we conducted our search within four different platforms: gray literature databases; customized Google search engines; targeted websites; and consultation with experts in the field (135). Specifically, the Turning Research into Practice (TRIP) medical database; Open Grey; Des Libris; clinicaltrials.gov; and Google were searched using a combination of relevant keywords including 'AI', 'machine learning', and 'opioid use disorder'. We then initiated contact with experts in the field to determine whether there were additional AI interventions that were not captured in our gray literature search.

Data extraction and synthesis

The first author (TB) conducted the gray literature search by examining the titles and full-text publications concurrently, and key information from publications which met the eligibility criteria were extracted (i.e., developer(s), setting, year of publication, intervention name, intervention type, intervention description, development stage, and any preliminary findings to date) and summarized in a table. Findings from the search strategies were combined, grouped by intervention type category, comprehensively analyzed and synthesized.

Results

Shown in Table 1, this review yielded a total of 70 citations and 29 unique interventions, which can be subdivided into five categories: smartphone applications (n = 12); healthcare data-related interventions (n = 7); biosensor-related interventions (n = 5); digital and virtual-related interventions (n = 2); and 'other', defined as those which do not fit into the other categories (n = 3). Of the 29 unique interventions, 27 (93%) were developed in the US, 1 (3%) was developed in Sweden, and 1 (3%) was developed in partnership between the US and Canada. While it was often difficult to determine the date the intervention was developed as there was no date corresponding to the specific source, 49 (70%) of the citations were published between 2018 and 2019. Of the 29 unique interventions yielded from the gray literature, only 6 were found to be captured in the peer-reviewed literature (20,21,50,110,114,119).

Smartphone applications

Twelve smartphone applications were identified: Addicaid; AiCure; Alexa; DynamiCare; Hey, Charlie; reSET-O; Second Chance, Sober Grid; Trigger Health; TryCycle; WorkIt Health; and Addiction Comprehensive Health Enhancement Support System (ACHESS) (25,27,28,31,32,34,36,39,42,47–49,52,53,57,60–62,65,66,70,136,137). Smartphone applications comprised a wide breadth of aims (e.g., the provision of recovery support including a digital connection between those in recovery and their counselors, monitoring oral OAT concordance, and overdose detection) (25,27,28,31,32,34,36,39,42,47–49,52,53,57,60–62,65,66,70,136,137). ReSET-O has become the first FDA-cleared prescription digital therapeutic for those living with

Table 1. Artificial intelligence interventions focused on opioid use disorder (OUD).

Developer(s)	Setting	Year of publication	Intervention Name	Intervention Type	Intervention description/purpose	Stage of development	Preliminary findings in the context of OUD specifically
Smartphone applications							
Sam Forns (25,26).	US	2017, 2018, 2019 (25,27–29).	Addicaid	Smartphone application	Addicaid uses a combination of machine learning, adaptive AI and clinical research to personalizes programs (25,27–29). Addicaid predicts when users are at risk of addictive behavior and intervenes – offering personalized treatment options (25,27–29).	Now available in commercial app stores (30).	None found.
Ai Cure Technologies (31,32).	US	2013, 2014 (31,32).	AiCure	Smartphone application	Ai Cure's platform, AiView-HRTM, uses facial recognition software to confirm that the right medication (e.g., oral OAT) has been ingested at the right time (i.e., a medication concordance intervention) (31–33).	Now available in commercial app stores (30).	None found.
Amazon (34,35).	US	2018 (34,35).	Alexa	Smartphone application	Amazon has recently programmed Alexa to answer questions such as "Alexa, what is an opioid?" and "Where can I go for help with opioid addiction?" (34). The primary intention of this programming is to aid in educating people about the opioid epidemic, and in linking them to care (34,35).	Now available through any Alexa compatible device (34,35).	None found.
DynamiCare Health (36,37).	US	2019 (36).	DynamiCare	Smartphone application	This app, used for random drug testing, prompts users to record the results of drug tests conducted via saliva test strips or Bluetooth-connected breathalyzer for drugs including opioids. This app is centered around abstinence and accountability. There is also a built-in rewards system to help support motivation.	Now available in commercial app stores (38).	None found.
Emily Lindemer (39).	US	2018 (39).	Hey, Charlie	Smartphone application	Hey, Charlie uses social contacts and location information to help encourage positive social connections, and to offer reminders for staying engaged with recovery (39). The primary intention of this app is to support abstinence (39).	Piloted in treatment centers and clinics in Boston (40,41). Appears in the development stage.	A pilot study involving 24 people with OUD reported that participants "felt positively toward the app" (39).
Pear Therapeutics (36,42–44).	US	2018, 2019 (36,42,43).	reSET-O	Smartphone application	reSET-O is a 12-week cognitive behavioral therapy program designed for those living with OUD. The primary intention if this app is to support treatment concordance (36,45).	Now available in commercial app stores (46).	A clinical trial has found that participants using reSET-O had better treatment concordance than participants not using reSET-O (47).

(*Continued*)

Table 1. (Continued).

Developer(s)	Setting	Year of publication	Intervention Name	Intervention Type	Intervention description/purpose	Stage of development	Preliminary findings in the context of OUD specifically
Dr. Jacob Sunshine, and researchers Rajalakshmi Nandakumar and Shyamnath Gollakot (48,49).	US	2018, 2019 (48,49).	Second Chance	Smartphone application	Second Chance monitors breathing patterns with sonar. The primary intention of this app is to detect an opioid overdose, and to immediately contact emergency services (48,49).	Researchers are in the process of obtaining FDA approval and commercializing this intervention (48). Appears in the development stage.	The Second Chance app was recently evaluated at a supervised injection site in Vancouver (InSite) – and that it detected opioid-induced respiratory depression with 87% sensitivity and 89% specificity; which is indeed promising (49–51).
Beau Mann (27,29,52–54).	US	2018, 2019 (27,29,52,53).	Sober Grid	Smartphone application	Sober Grid has been designed to help those living with OUD by connecting them with resources including sharing and tracking of progress resources. 24/7 peer coaching is also available (27,29,52–55). The primary intention of this intervention is to help build a strong social network, and to provide additional resources to support abstinence (27,29,52–55).	Now available in commercial app stores (56).	None found.
John Haskell (27,57,58).	US	2017, 2018 (27,57).	Triggr Health	Smartphone application	Triggr Health's machine learning system was designed to predict relapses and provide prevention strategies (27,57,58). The primary intention of this intervention is to support abstinence, and diminish the likelihood of overdose (27,57,58).	Now available in commercial app stores (59).	None found.
Developed in partnership with John MacBeth and Ken House (60–63).	US and Canada	2018 (60–62).	TryCycle	Smartphone application	TryCycle was designed to create a digital connection or "digital tether" between patients and their health care provider between their in-person visits (60–63). The primary intention of this intervention is to support abstinence, and diminish the likelihood of overdose (60–63).	Piloted in treatment centers in Old Saybrook and Meriden. Appears in the development stage (63,64).	None found.
Robin McIntosh, Lisa McLaughlin (65–68).	US	2018, 2019 (65,66).	WorkIt Health	Smartphone application	WorkIt Health provides digital triage and helps to link people to services. The intervention also provides digital therapy and telemedicine including OAT (67). The primary intention of this intervention is to help combat barriers to treatment.	Now available in commercial app stores (69).	A recent prospective cohort study involving individuals in WorkIt Health's telemidicine for OUD program reported that 93% of individuals achieved abstinence from opioids, and 84% of individuals sustained abstinence from opioids during a one-year period (68).

(*Continued*)

Table 1. (Continued).

Developer(s)	Setting	Year of publication	Intervention Name	Intervention Type	Intervention description/purpose	Stage of development	Preliminary findings in the context of OUD specifically
Dr. David Gustafson (70,71).	US	2017 (70).	A-CHESS	Smartphone application	A-CHESS provides digital recovery support including regular check-ins, medication reminders, appointment reminders, access to peer support, and 24/7 support (70,72). The intervention also monitors for risk of relapse. Similar to WorkIt Health, a primary intention of this intervention is to help combat barriers to treatment.	Now available in commercial app stores (73).	None found.
Healthcare data-related interventions							
Hc1.com (29,74–78).	US	2017, 2018, 2019 (29,74–77).	Hc1 Opioid Dashboard	Healthcare data-related intervention	Hc1 Opioid Dashboard, a cloud-based service, uses machine learning to analyze healthcare data to predict opioid misuse, and addiction across the US. The primary intention of this intervention is to better understand what is occurring at a population level – providing opportunity to optimize the allocation of resources (29).	Now available on the hc1 website (79).	None found.
ZeOmega (80,81).	US	2019 (80,81).	Jiva Opioid AI	Healthcare data-related intervention	Jiva Opioid AI, a machine learning algorithm, predicts opioid misuse using claims data, other medical data, and social determinants of health data, and guides patients toward care. The primary intention of this intervention is to support linkage to care (80,81).	Now available on the ZeOmega website (82).	None found.
Appriss Health (83,84).	US	2018 (83,84).	NarxCare and PMP AWARxE	Healthcare data-related intervention	Together, NarxCare and PMP AWARxE, synthesize and analyze prescription information, providing risk scoring and analytic insights. The primary intention of this intervention is to lessen inappropriate opioid prescribing, and to improve patient outcomes (83,84).	NarxCare is now in operation across much of the US in places such as Walmart, Sam's Club pharmacies, and Rite Aid (85). PMP AWARxE is now in operation in 43 states and territories (83).	There is some evidence to suggest that the number of opioids dispensed is decreasing across Michigan (86,87).
NIC Inc (88,89).	US	2019 (88).	RxGov	Healthcare data-related intervention	RxGov, driven by machine learning, further enhances prescription drug monitoring programs (PDMP). For instance, RxGov supports interstate data sharing and provides improved data visualizations (88,90). Similar to Narx Care and PMP AWARxE, the primary intention of this intervention is to lessen inappropriate opioid prescribing, and to improve patient outcomes.	RxGov is now in operation in several states including Nebraska, Wisconsin and Utah. Recently selected as the PDMP for the state of Maine (90).	None found.
IBM Watson (91–93).	US	2018 (91).	Watson Care Manager	Healthcare data-related intervention	Watson Care Manager digitizes client's records allowing aftercare providers access to this data. The primary intention of this intervention is to aid in care continuity and to help reduce the risk of relapse (91).	Now available on the IBM website (94).	None found.

(*Continued*)

Table 1. (Continued).

Developer(s)	Setting	Year of publication	Intervention Name	Intervention Type	Intervention description/purpose	Stage of development	Preliminary findings in the context of OUD specifically
Olive (formerly known as CrossChx) (95,96).	US	2018 (95).	Olive	Healthcare data-related intervention	Olive is an AI powered-digital employee who automates many tasks including checking insurance eligibility and scheduling. The primary intention of this intervention is to help manage administrative tasks – saving time and money (95–97).	Now available on the Olive website (96).	None found.
Researchers at the Medical University of South Carolina (98).	US	2019 (98).	I2B2	Healthcare data-related intervention	I2B2 is currently being designed to help identify non-fatal opioid overdose in ED physicians' electronic health records (98,99). The primary intention of this intervention is to provide researchers with access to real-time data (98,99).	Appears in the development stage (98,99).	None found.
Biosensor-related interventions							
Carnegie Mellon University graduate students (100–102).	US	2018, 2019 (100–102).	HopeBand	Biosensor-related intervention	The HopeBand, a wrist-worn device, uses pulse oximetry to measure blood oxygen levels. Bluetooth technology links sensors on the band to a smartphone. If blood oxygen levels drop, emergency personnel receive a message with GPS location. The primary intention of this intervention is to detect opioid overdose.	Appears in the development stage (103,104).	None found.
Researchers at the University of Massachusetts (105,106).	US	2012 (105,106).	iHeal	Biosensor-related intervention	iHeal, a wrist-worn device, detects indicators of stress (e.g., skin temperature, heart rate) which may suggest cravings for opioids. This information is automatically transmitted to a smartphone which intervenes with patient-specific interventions. The primary intention of this intervention is to detect opioid cravings and to intervene – preventing opioid use (105,106).	Appears in the development stage (107).	None found.
Researchers at the University of Massachusetts (108).	US	2016 (108).	E4 Empatica	Biosensor-related intervention	E4 Empatica, a wrist-word device, measures heartbeat, motion, skin electrical conduct, and temperature. This information is then used to determine if relapse occurs (108). The primary intention of this intervention is to monitor abstinence.	Now available on the Empatica website (109).	Recent studies have reported a strong detection accuracy, one study quantified this as between 86.78% and 90.96% (22,110,111).

(*Continued*)

Table 1. (Continued).

Developer(s)	Setting	Year of publication	Intervention Name	Intervention Type	Intervention description/purpose	Stage of development	Preliminary findings in the context of OUD specifically
Researchers at Purdue University (112,113).	US	2019 (112,113).	A2D2	Biosensor-related intervention	The A2D2 intervention consists of a magnetic field generator and an EKG skin-sensor. If an overdose is detected the magnetic field generator automatically heats up a naloxone-releasing device implanted in the body. The primary intention of this intervention is to detect opioid overdose and automatically administer naloxone (112,113).	Appears in the testing phase (114,115).	A recent bench evaluation conducted in mice found that the A2D2 intervention was successful in rapidly releasing a drug (within 10 seconds) using the magnetic field generator (114,115).
Researchers at UMass Medical School (116,117).	US	2015, 2017 (116,117).	eTectRX ID-CAP System	Biosensor-related intervention	eTectRX ID-CAP System is a digital pill which contains a sensor. Stomach acid then activates the sensor – which transmits medication ingestion information to a hip-mounted device. The primary intention of this intervention is to monitor opioid use or OAT concordance (116,117).	Now available on the eTectRX website (118).	A recent study has shown that this intervention was successful in monitoring opioid self-dosing (116,119).
Digital and virtual-related interventions							
Virtual Rehab (17,18,120).	US	2016 (17,18).	Virtual Rehab	Digital and virtual-related interventions	Virtual Rehab provides cognitive behavior and exposure therapy in a simulated environment (17,18). The primary intention of this intervention is to encourage behavior modification, and to curb opioid cravings (17,18).	Now available on the Virtual Rehab website (17).	Several studies have shown that digital and virtual-related interventions may play an important role in decreasing opioid use, providing opioid overdose training (e.g., naloxone training), and curbing the opioid epidemic (19–21).
Orexo and GAIA (121,122).	Sweden	2019 (121,122).	ODX-01	Digital and virtual-related interventions	ODX-01 is a digital therapy which provides simulated 1 to 1 interaction for those with OUD (121,122). The primary intention of this intervention is to treat OUD, and positively impact on patient outcomes (121,122).	Appears in the development phase (121,122).	None found.
Other interventions							
Lumina (123,124).	US	2018 (123).	Mission LISA (Learning Indicators of Substance Addiction).	Other	Mission LISA, an open source data mining initiative, seeks to provide real-time data to help inform policy decisions. The primary intention of this intervention is to inform policy decisions for how to best treat OUD and combat the opioid overdose epidemic (123,124).	Appears in use in the US (125,126).	None found.
Initially a White House initiative, now under the Laura and John Arnold Foundation (77,127).	US	2017, 2018 (77,127).	Open Lattice	Other	Open Lattice, a cloud-based platform, provides real-time information on service utilization, improves record linkage, and collaboration. The primary intention of this intervention is to improve continuity of OUD care, and to reduce opioid overdose (77,127).	Now available on the Open Lattice website (128).	None found.

(*Continued*)

Table 1. (Continued).

Developer(s)	Setting	Year of publication	Intervention Name	Intervention Type	Intervention description/purpose	Stage of development	Preliminary findings in the context of OUD specifically
The Defense Intelligence Agency (129–132).	US	2019 (129–132).	Sable Spear	Other	Sable Spear, a mass data analytics tool, uses publicly available information to pin-point suspicious activity associated with the unregulated opioid market (129–132). The primary intention of this intervention is to assist persons including law enforcement in abating the unregulated opioid market (129–132).	Appears in the scale-up phase (133).	One article reported a 900% increase in the identification of illegal activities since the inception of Sable Spear (130).

ACHESS: Addiction Comprehensive Health Enhancement Support System
A2D2: Automatic antidote delivery device
IBM: International Business Machines
I2B2: Informatics for integrating biology and the bedside
MIT: Massachusetts Institute of Technology
UMASS: University of Massachusetts

OUD (43), and was recently evaluated in a 12 week clinical trial involving 170 individuals living with OUD (138). The trial showed that participants who used the application were significantly more likely to remain engaged in OUD treatment, as compared to participants that did not use the application (138). Our analysis identified that a number of the applications are functionally similar to one another. For example, TryCycle and ACHESS both offer a digital version of recovery support. Some of the applications use novel subsets of AI (e.g., computer vison). For example, some use sonar and inaudible sound waves to detect decreased or absent breathing (from up to 3 feet away), and in the event that an overdose is suspected and the user fails to interact with the application, emergency services are automatically contacted. Second Chance was recently evaluated at a supervised injection site in Vancouver (InSite) (50). It was found that this application detected opioid-induced respiratory depression with 87% sensitivity and 89% specificity (50). Ai Cure, developed by Ai Cure Technologies, uses facial recognition software to confirm that the right medication (e.g., oral OAT) has been ingested at the right time (31,48). Additionally, Ai Cure has the capacity to link the user with a case manager who will reach out in the event of non-concordance. AiCure, along with Sober Grid and Addicaid are now available in commercial app stores (30).

Healthcare data-related interventions

Seven vastly different healthcare data-related interventions were identified: Hc1 Opioid Dashboard; Jiva Opioid AI; NarxCare and PMP AWARxE; RxGov; Watson Care Manager; "informatics for integrating biology and the bedside" (I2B2), and Olive (74–77,80,81,83,84,88,91,98,136). Two are prescription drug monitoring solutions designed to improve the identification and management of inappropriate opioid prescribing (NarxCare and PMP AWARxE, and RxGov) (83,84). Together, NarxCare and PMP AWARxE, synthesizes and analyzes prescription information, providing machine learning risk scores and analytic insights (84). This information has the capacity to improve identification and management of inappropriate prescribing – with the goal of improving patient safety and outcomes (84). Our review yielded notably wide dissemination of NarxCare and PMP AWARxE – which are currently active across 42 US states (83,84). RxGov, a similar prescription drug monitoring solution, is currently active across Maryland and Nebraska. Two are cloud-based solutions which leverage machine learning – one analyzes healthcare data of opioid misuse, and addiction at a population level (Hc1 Opioid Dashboard) (74,75,136), whereas the other digitizes patient records to provide a centralized data aggregation solution for collaborative care teams (Watson Care Manager) (91).

With regards to the other healthcare data-related interventions, one identifies cases of opioid misuse in claims and other data including social determinants of health data such as social support and access to nutritious food, which are sourced from assessments, claims, and US governmental data sources (Jiva Opioid AI) (139). Another is an AI-powered digital employee who can be deployed in a hospital's electronic medical record system (Olive). Olive can conduct many tasks including checking insurance eligibility, prior authorizations, and cross-checking the patient with enormous amounts of data (140). Finally, this review identified that Researchers at the Medical University of South Carolina are working to enhance an existing informatics tool which will use natural language processing to retrospectively identify nonfatal opioid overdoses in Emergency Department Physicians' electronic records (I2B2) (98). This real-time information could help researchers to better understand what configuration of traits predict opioid overdose, while helping to improve clinical trial design and recruitment (98).

Biosensor-related interventions

Five biosensor-related interventions were identified: the HopeBand; iHeal; E4 Empatica; the Automatic Antidote Delivery Device (A2D2); and eTectRx ID-CAP System (100,105,106,108,112,113,116,141–143). Perhaps the most novel intervention identified was the A2D2 (112,113). Currently under development by a team of Researchers at Purdue University, the A2D2 intervention consists of an armband, a magnetic field generator, an EKG skin-sensor, and a heat-activated naloxone drug capsule. The device automatically converts EKG heart rate signals to a measure of respiration rate, and in the event that an overdose is detected the magnetic field generator heats up the naloxone drug capsule implanted in the body – automatically releasing the drug within seconds (113). With regards to the other biosensor-related interventions, the HopeBand, iHeal and E4 Empatica are functionally similar to one another – each is a wrist-worn device which uses measures such as pulse oximetry, skin temperature, motion, and heartbeat to track trigger points for opioid use, relapse or overdose. Finally, our review identified the eTectRX ID-CAP System, designed to monitor medication concordance. To store pill ingestion data, each pill in the system includes a radiofrequency emitter, and the patient wears a patch on their abdomen which is attached to a cable reader the size of an iPod (143). In the pilot study, researchers monitored the concordance of oxycodone following an extremity fracture (143). This information has the potential to aid in the identification of escalating opioid use patterns – which may suggest development of physical dependence or addiction (116).

Digital and virtual related interventions

Two digital and virtual related interventions were identified including Virtual Rehab and ODX-01 (17,18,121,122). An old intervention with new utility, Virtual Rehab uses virtual simulations, cognitive behavior and exposure therapy to trigger, and to help cope with opioid cravings (17). Currently in the development stage, ODX-01 is a digital therapy which will be used to engage users in an individualized, simulated one to one interaction – guiding the user toward specific goals including therapeutic targets (121,122).

Other interventions

Finally, three interventions were identified which did not fit into the other categories: Mission LISA; Open Lattice; and Sable Spear (77,95,123,129,130,140,144). Mission LISA and Sable Spear both examine publicly available information and open source data including websites, social media feeds, etc. However, the primary objective of Mission LISA is to help drive solutions for how to best treat OUD and combat the opioid overdose epidemic by providing stakeholders with real-time information to help foster evidence-based prevention and treatment (123), whereas the primary objective of Sable Spear is to examine indicators of illegal or suspicious activity associated with the illicit opioid market, and notifies diplomatic, law enforcement, or military personnel, as appropriate (123,144). Open Lattice is a cloud-based platform designed to improve record linkage and cross-agency collaboration (including medical providers and law enforcement), and provides real-time information on how resources such as detox centers, peer recovery centers, and housing and employment providers are being used (127).

Discussion

This review draws attention to several novel AI interventions focused on OUD, the majority of which are now in use by governing bodies or available through commercial app stores and company websites (68.97%), despite a lack of rigorous scientific evidence to support their use in this context. Few empirical evaluations of these interventions to date have shown promise in terms of usability, in helping to aid OUD diagnosis and care, in the identification of opioid overdose risk, and in the reversal of opioid overdose. There are, of course, several limitations to these evaluations, including a lack of randomized controlled trials involving humans, short follow-up durations, and heterogeneous samples, to draw definitive conclusions from.

Although not explicitly searched for, there appeared to be little discussion pertaining to the usability, utility, and acceptability of these interventions. For many AI interventions that involved smartphones, there was a lack of discussion about access to these types of technologies among this population. Further to this point, a study recently conducted in Vancouver found that of the 443 people who use drugs (PWUD) involved in the study, less than half (48%) owned a mobile phone. Of those interested in using an app to mitigate opioid overdose deaths, participants were far more willing to use an app that provides drug supply alerts (n = 92), as compared with an app that monitors breathing (n = 63) (145).

Other issues rarely discussed include the myriad of privacy, ethical, legal, and human rights issues potentially associated with the use of OUD-specific AI interventions (146–149). Specifically, concerns have been expressed that machine learning algorithms and natural language processing methods could potentially mirror human biases in their decision making processes (148,150,151). This is because these forms of AI draw from historical data which may contain preexisting biases (148,150,151). For example, existing evidence has shown that AI algorithms which seek to identify illegal activity (such as Sable Spear) are commonly biased against people of color (151,152). This phenomenon has been shown to perpetuate racial stigma and discrimination, which can in turn lead to higher risk of legal action for many of these individuals (151,152). As many of the intricate questions posed by algorithmic decision making continue to fall outside of current anti-discrimination laws and policies, reexamination of these laws and policies and its integration with technology will be critical to ensuring that AI interventions are designed in an equitable way (152,153). Another ongoing challenge relates to the protection of personal health data (134,148). With numerous issues of data confidentiality and transparency yet to be resolved, users of these interventions may worry about cyber-crimes and data hacking, or storing their data on smartphones or wearable devices which could be lost or stolen (134,145). As with all forms of new technology, the crucial question is how law and regulation remain 'connected' and avoid constantly playing catch up. A notable question arises about legal liability (155), for example, which law(s) would apply in the case of a malfunctioning intervention, or in the event of a false-positives or a false-negative, and to whom might they apply? Should health care professionals and providers be held responsible for decisions made or informed by 'black box' algorithms which they cannot fully understand? (156) Can robots be regarded as legal entities and thus be subject to legal actions or will liability always revert to back to humans who use such technology? Clearly, the very idea of 'robot law' raises highly contentious philosophical, ethical and legal questions for society (157). The need for clarity is pressing given concern that the lack of a clear framework for liability will mean that businesses and the public will be reluctant to rely on AI applications (158). In short, AI significantly challenges existing models of regulation and will require some fresh thinking about how best to manage the human-machine relationship (159). The development and implementation of ethical guidelines (160–162) are urgently needed in consideration of this paradigm shift (163). Also seldom mentioned are the challenges associated with cross-sectoral collaboration (e.g., insufficient collaborative data networks in place to share data) (164,165), and cost-effectiveness (134,148).

This review has a number of limitations. First, it is possible that relevant works were missed given the search strategy and the exclusion criteria imposed upon the yielded published work. Second, the AI interventions identified in this review are overwhelmingly being developed and tested in the US, and the extent to which these interventions and findings may be generalizable in other settings is unknown. Finally, gray literature is known to be associated with a high risk of bias and questions of quality remain (166,167).

Although more research is needed to establish definitive conclusions on the effectiveness of these interventions, this review draws attention to several AI interventions which show promise in helping to aid the diagnosis and treatment of OUD, the identification of opioid overdose risk, and the reversal of opioid overdose. There remains a particularly urgent need for research which examines the usability, utility, and acceptability of these interventions. Understanding the legal, ethical, and social implications of these AI interventions is both fundamental and crucial to future research and delivery of care in this area.

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ORCID

Rod Knight http://orcid.org/0000-0002-1464-1584

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