Artificial intelligence and opioid use: a narrative review

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APPENDIX 1.

Table S1: Search terms

Source	Date of search	Search terms
MEDLINE In-process and other non-indexed citations and MEDLINE	04/01/21	(((((opioid*).ti,ab OR (opiate*).ti,ab OR (narcotic*).ti,ab) **AND** (("artificial intelligence").ti,ab OR (AI).ti,ab OR ("machine learning").ti,ab OR ("natural language processing").ti,ab OR (nlp).ti,ab OR ("deep learning").ti,ab)) **OR** (exp *"ANALGESICS, OPIOID"/ **AND** (*"ARTIFICIAL INTELLIGENCE"/ OR *"COMPUTER HEURISTICS"/ OR *"EXPERT SYSTEMS"/ OR *"FUZZY LOGIC"/ OR *"KNOWLEDGE BASES"/ OR *"MACHINE LEARNING"/ OR *"NATURAL LANGUAGE PROCESSING"/ OR *"NEURAL NETWORKS, COMPUTER"/))) NOT (editorial).pt) [DT 2010-2021] [Languages English]"
EMBASE	04/01/21	"(((((opioid*).ti,ab OR (opiate*).ti,ab OR (narcotic*).ti,ab) **AND** (("artificial intelligence").ti,ab OR (AI).ti,ab OR ("machine learning").ti,ab OR ("natural language processing").ti,ab OR (nlp).ti,ab OR ("deep learning").ti,ab)) **OR** (exp *"NARCOTIC ANALGESIC AGENT"/ **AND** exp "ARTIFICIAL INTELLIGENCE"/)) NOT (editorial).pt) [DT 2010-2021] [English language]"
Cochrane Library – CENTRAL	25/11/20	(Exp Artificial intelligence and exp narcotics) or ("artificial intelligence" or AI or “natural language processing” or NLP or "deep learning" or "machine learning"):ti,ab,kw AND (opioid* or opiate* or narcotic*):ti,ab,kw Limited to 2010-2020.

APPENDIX 2.

Table S2: Summary of the 18 conference abstracts that were included in the review, ordered alphabetically by the domain to which AI was applied to assess the use of opioids, including surveillance and monitoring and risk prediction

Study ID (country)[ref]	Data source	Sample (n=)	AI Technology	Application	Outcome	Stage of development
Risk prediction						
Crosier 2017 (USA).[1]	Opioid users. Data from enrolled opioid users. (n = 260)	260	Random forest	Prediction of overdose frequency and identification of key predictive features	The model performed a binary classification to predict lifetime overdose status, with an error rate of 30.25%. Arrest history and the number of overdoses in a person's social network emerged as the most important predictors of overdose.	Preliminary research
Li 2018 (USA).[2]	Patients prescribed opioid medication. Data from the IMS LifeLink PharMetrics PlusTM database.	1,246,642	Boosted tree	Prediction of opioid overdoses among prescription opioid users	The boosted tree classifier outperformed other learning algorithms (c-statistic 0.77). The most significant prognostic features were, early refills, total days' supply, concomitant use of antidepressants, concomitant use of antipsychotics, and total opioid claims.	Preliminary research
Lo-Ciganic 2020B (USA).[3]	Medicaid beneficiaries who had made a medical claim. Integration of human services data, criminal justice records, and medical examiner's autopsy data with medical claims data.	79,086	Gradient boosting machine	Prediction of risk of opioid overdose.	The gradient boosting machine algorithm including comprehensive integrated data outperformed the model using medical claims only (c-statistic=0.920). Over 85% of individuals with overdoses were in the top two deciles having the highest overdose rates. Few individuals had overdose episodes in the bottom eight deciles.	Preliminary research
Lopez-Guzman 2019 (USA).[4]	Patients with OUD being treated in and outpatient setting.	74	LASSO logistic regression	Prediction of clinical outcomes for opioid use disorder using decision-making trajectories.	Most variables did not survive LASSA regression for relapse suggesting most of these personality factors, while useful for diagnosis, are not determinants of prognosis. The dynamics through time-in-treatment of decision-making parameters and symptom intensity (craving, anxiety, and withdrawal symptoms) were significant predictors of relapse.	Preliminary research
None 2019 (USA).[5]	Opioid naïve and non-naïve adults undergoing surgery. Data from claims data from the Clinformatics DataMart (OptumInsight).	199,423	Non-linear machine learning	Prediction of postoperative opioid prescription refills.	Compared with linear models, nonlinear models led to better performance AUROC = 0.754 vs 0.738. Medications commonly used to treat anxiety and insomnia were most predictive, especially among opioid-naive patients. These findings suggest that patient attributes, such as sleep disorders and anxiety, can be used to predict postoperative refill.	Preliminary research
Simon 2018 (USA).[6]	Patients with two years of continuous insurance eligibility selected from	23,371	Extreme gradient boosting	Prediction of whether a patient who does not currently have OUD will	The model was able to predict future OUD outcomes with a surprising level of fidelity in	Preliminary research

	commercial and government healthcare claims databases.			receive a diagnosis in the next 12 months.	individuals who did not have a prescription for opioids documented in administrative claims during the predictive period (AUROC = 0.837).	
Vassileva 2019A (USA).[7]	Mono-dependent opiate and stimulant users. Data from a larger study.	595	Elastic net	Prediction of addiction phenotypes in mono-dependent opiate and stimulant users.	For prediction of opiate dependence, the AUROC = 0.88. Reduced sensitivity to loss in opiate users was one of the most consistent findings across different tasks and cognitive models and could represent a potential biomarker for opiate addiction.	Preliminary research.
Vassileva 2019B (USA).[8]	Monosubstance-dependent substance users. Data from a larger study.	595	LASSO penalized regression models	Identification of behavioural markers that accurately classify alcohol dependence, nicotine dependence, cannabis dependence, opiate dependence, and stimulant dependence.	For classification accuracy for opiate dependence the AUROC = 0.91. Personality variables had higher predictive utility than neurocognitive variables. Psychopathy was the only common predictor of all drug classes	Preliminary research.
Wang 2019 (USA). [9]	Patients newly initiated on prescription opioids. Data from inpatient or emergency department claims of fee-for service Medicaid beneficiaries.	346	Machine learning, specifically, bi-kmeans clustering modelling	Identification of opioid-benzodiazepine (OPI-BZD) dose and duration trajectories and subsequent opioid overdose	Opioid overdose odds varied substantially across OPI-BZD use trajectories, with individuals having consistent high-dose OPI-BZD use having more than 10 times overdose odds.	Preliminary research.
Weiner 2019 (USA).[10]	Adult patients who had cough and received care in a medical institution. Data from EHR in a midwestern academic medical institution.	25,593	NLP	Identification and characterisation of opioid-containing cough suppressants among patients with chronic cough.	About one in five patients with chronic cough received an opioid-containing cough suppressant prescription, which was more likely in this cohort than in patients with non-chronic cough.	Preliminary research.
Workman et al. 2019(USA).[11]	Patients having outpatient visits for which one or more of eight opioid prescriptions were issued. Data from EHRs.	45,326	Deep learning	Prediction of opioid use disorder using prescription, patient, provider, and facility characteristics predictors.	The model was able to predict OUD with an AUROC= 0.87. Pain, mental health issues, traumatic brain injury, and male gender were identified as top features in the models. New potential risk factors include respiratory, as well as behavioural health and Social Service Providers.	Model development planned.
Surveillance and monitoring						
Carrell 2017 (USA).[12]	Patients receiving chronic opioid therapy through a staff model health care system. Data from EHR.	15,498	NLP and machine learning (a model based on NLP-extracted data from chart notes).	Identification of POU in large patient populations.	NLP-assisted manual review indicated that 1,453 (9.4%) patients had POU. In the validation set the algorithm achieved 56% sensitivity and 76% precision. EHR data useful for identifying with modest precision many patients experiencing POU.	Model development required.
Mahmud et al. 2018(USA).[13]	Patients admitted to hospital for a painful condition being treated with opioid analgesics.	30	Decision tree, K-Nearest Neighbor eXtreme Gradient Boosting	Automatic detection of opioid intake using electrodermal activity, skin temperature and triaxis acceleration data generated from a wrist worn biosensor.	Decision tree and eXtreme Gradient Boosting shows the best results. The detection the rate of the decision tree and extreme Gradient boosting is 99.3% and 99.8% respectively.	Model development planned.

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Mazer-Amirshahi 2017 (USA).[14]	Patients exposed to a patient safety event reported by frontline staff. Data from Patient safety event (PSE) data in an academic healthcare system.	282	NLP	Analysis of patient safety events related to look-alike/sound-alike medication errors that occurred involving opioid analgesics.	Look-alike/sound-alike errors involving opioid analgesics were more frequently associated with oxycodone products, particularly immediate release/extended release formulations and most occurred in the ordering stage of the medication process. Severe adverse effects were rare, but potentially life threatening.	Preliminary research
Rifat 2019 (Bangladesh).[15]	Tweets containing keywords, primarily generic names of 17 opioid drugs.	166,723	NLP, recurrent Neural Networks, convolution neural network	Identification of opioid abuse from social media to reduce harm from opioid overdoses.	Convolutional recurrent neural network performed the best with an F1 score of 0.71. Out of 98 ADRs found from tweets, 50 could be mapped to Lowest Level Terms and 48 to Preferred Terms. Most adverse drug reactions related to codeine, fentanyl and tylenol.	Preliminary research.
Sarker 2019A (USA).[16]	Tweets using prescription and illicit opioid keywords.	5,979	NLP Random Forest	Automatic characterisation of opioid-related chatter to improve the current state of opioid toxicosurveillance.	The classifier obtained an accuracy of 68.7%. The automatic classification experiments produced promising results, despite the small amount of annotated data, suggesting that automated, real-time opioid toxicosurveillance may be a possibility with more annotated data.	Preliminary research
Sarker 2020 (USA). [17]	Reddit messages from 5 users who had mentioned opioid keywords (prescription or illicit) in their posts.	4,288 posts	NLP	Analysis of opioid content in longitudinal data posted in a social media forum.	Longitudinal timelines revealed a variety of information including: their use of illicit and non-medical; use of prescription drugs; all five reported opioid addiction; social impacts of their drug use e.g. loss of employment; clinical consequences of addiction e.g., suicidality; challenges of opioid addiction and reoccurrence of use	Preliminary research
Vonkorff 2014 (USA).[18]	Chronic non-cancer pain patients receiving COT. Data from electronic medical records from Group Health.	22,143	NLP	Prevalence of prescription opioid abuse/overuse among COT patients.	Among 3663 NLP positive records, 77 % were manually validated as indicating opioid addiction, abuse or overuse. The prevalence rates for prescription opioid addiction, abuse or overuse were common among COT patients, with the highest rates observed among patients aged between 18-44. (12.3%)	Preliminary research.

AUROC: area under the receiver operating characteristic curve; COT: chronic opioid therapy; EHR: electronic health records; NLP: Natural language processing; OUD: opioid use disorder; POU: problem opioid use

APPENDIX 3. Detailed summary of the four areas of AI application in opioid research

1: Risk prediction

Most of the studies reviewed focused on developing AI technology to support identification of factors that could predict the increased risk of developing an adverse opioid related outcome. The aim of this research being either to identify risks early and prevent resultant issues or, as a method of classification for opioid-dependent and long-term users. In this category, most of the AI tools researched focused on the development of prolonged opioid use following surgery. A range of factors were found to be predictive of prolonged use following surgery and included age; marital status; preoperative opioid use, medication, and haemoglobin; tobacco use; comorbidity of depression or diabetes and instrumentation. Other adverse outcomes explored were the risk of dependence, abuse, and overdose.

Some of the AI technology developed in this category was at a more advanced level of development with several researchers publishing their tools online as open access. However, to progress the validation and deployment of these at pace and scale within individual healthcare settings requires facilitation and guidance at a national level.

2: Surveillance and monitoring

Studies in this category investigated AI technology to improve surveillance and monitoring of misuse and illegal selling and to detect consequences that could result from opioid misuse. Most of the AI models in this category used natural language processing technology. The models ranged in their stage of development from preliminary research through to being available online as open access.

The purpose of the AI technology was to gather intelligence to support public health surveillance and prevent adverse consequences of opioid use. Adverse clinical consequences studied included HIV outbreaks triggered by opioid abuse and transition to injection drug use, suicidality, opioid overdose in opioid users from their social media posts, opioid-induced respiratory depression, and opioid induced constipation. In some of these studies the clinical consequence of opioid use had resulted in avoidable utilisation of healthcare resources, for example misdiagnosis of the cause of abdominal pain resulting in unnecessary surgery.[19]

Some studies in this category researched AI technology to classify different subgroups, estimate prevalence and identify the scale and location of illegal online selling. Illegal use of opioids, both selling and individual use, is a difficult area to tackle.

3: Pain management

Studies in this category explored pain management in various patient cohorts including adolescents from minority backgrounds and patients with depression concomitantly prescribed an antidepressant. Research also focused on patient characteristics that could determine opioid requirements post-surgery. AI models in this category ranged in their stage of development with some being at the preliminary stages of research, others required external validation, and some were available online as open access.

4: Patient support technology

This was the group with the least number of studies. Both studies in this category used smart phone technology. One study used a random forest algorithm to predict opioid craving or stress in the user through their movement as assessed by GPS.[20] The other study tested an AI enabled peer support platform that patients with OUD could use to support their recovery.[21] In both cases, further development of the model was being planned.

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