



Key use cases for artificial intelligence to reduce the frequency of adverse drug events: a scoping review

Ania Syrowatka, Wenyu Song, Mary G Amato, Dinah Foer, Heba Edrees, Zoe Co, Masha Kuznetsova, Sevan Dulgarian, Diane L Seger, Aurélien Simona, Paul A Bain, Gretchen Purcell Jackson, Kyu Rhee, David W Bates

Adverse drug events (ADEs) represent one of the most prevalent types of health-care-related harm, and there is substantial room for improvement in the way that they are currently predicted and detected. We conducted a scoping review to identify key use cases in which artificial intelligence (AI) could be leveraged to reduce the frequency of ADEs. We focused on modern machine learning techniques and natural language processing. 78 articles were included in the scoping review. Studies were heterogeneous and applied various AI techniques covering a wide range of medications and ADEs. We identified several key use cases in which AI could contribute to reducing the frequency and consequences of ADEs, through prediction to prevent ADEs and early detection to mitigate the effects. Most studies (73 [94%] of 78) assessed technical algorithm performance, and few studies evaluated the use of AI in clinical settings. Most articles (58 [74%] of 78) were published within the past 5 years, highlighting an emerging area of study. Availability of new types of data, such as genetic information, and access to unstructured clinical notes might further advance the field.

Introduction

The US National Academy of Medicine has defined an adverse drug event (ADE) as “an injury resulting from medical intervention related to a drug”.¹ These events include non-preventable ADEs (also called adverse drug reactions), and adverse events resulting from medication errors. ADEs represent one of the most important types of health-care-related harm, both inside and outside the hospital, and there is substantial room for improvement in how we predict and detect these events.

The true incidence of ADEs is unknown; these events are often not identified and they are systematically under-reported.² An analysis of 28 US state inpatient databases showed that ADEs occurred during 2.1% of all inpatient stays and were present on admission in 5.1% of stays, and management of these ADEs has been estimated to cost US\$28 billion annually.³ However, this analysis was based on documented diagnostic codes, and undoubtedly underestimated true rates. A systematic review of potentially preventable ADEs showed that rates varied widely across inpatient populations, ranging from less than 0.1% to 13.3%, and depended on the approach for event detection, with more cases identified using prospective reporting methods than retrospective or voluntary reporting methods.⁴ The occurrence of ADEs in primary care is estimated to be higher than in inpatients. A scoping review showed that rates of ADEs in primary care varied widely according to the study population, setting, medications, and ADEs under study; estimates ranged from 6% in community-dwelling patients prescribed medications for dementia to 81% in patients treated for drug-resistant tuberculosis.⁵

These events are costly and morbid; patients with ADEs have longer hospital stays with greater associated costs and a higher likelihood of mortality than those who do not.⁶ About one in three ADEs are considered preventable.⁷

Algorithms and tools based on artificial intelligence (AI)—ie, computer applications that can perform tasks that normally require human intelligence⁸—have the potential to inform clinical decision making in real time to reduce the frequency, duration, and severity of ADEs. Advances in computing power, availability of large-scale patient databases, and machine learning algorithms—ie, algorithms and models that machines can use to learn without explicit instructions⁸—provide the capacity and capability to integrate various data sources and analyse complex inter-relationships between risk factors and outcomes at the point of care. For example, AI could provide timely and accurate predictions of which patients are likely to have ADEs before medications are prescribed. Identification of patients at risk could allow intervention to prevent ADEs; AI could also expand knowledge about which ADEs are preventable and identify new types of ADEs.

The objective of this scoping review was to identify the most promising areas (or key use cases) in which AI could be used to reduce the frequency of harm by providing patient-specific (ie, personalised) predictions to help prevent ADEs or by leading to early detection, mitigating the effects of ADEs. This scoping review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR).⁹

Methods

Search strategy and selection criteria

Two databases (PubMed [National Center for Biotechnology Information] and Embase [Elsevier]) were searched to identify relevant literature published between Jan 1, 1998, and Sept 9, 2020, to correspond with the release of the draft National Academy of Medicine report *To Err is Human: Building a Safer Health System*.¹ The main concepts of AI, prediction, early detection, and ADEs were mapped to the most relevant controlled

Lancet Digit Health 2021

Published Online

November 23, 2021

[https://doi.org/10.1016/](https://doi.org/10.1016/S2589-7500(21)00229-6)

S2589-7500(21)00229-6

Division of General Internal

Medicine (A Syrowatka PhD,

W Song PhD,

M G Amato PharmD, D Foer MD,

H Edrees PharmD, Z Co BS,

S Dulgarian BS, D L Seger RPh,

A Simona MD,

Prof D W Bates MD), and

Division of Allergy and Clinical

Immunology (D Foer), Brigham

and Women's Hospital, Boston,

MA, USA; Department of

Medicine (A Syrowatka, W Song,

D Foer, A Simona,

Prof D W Bates) and Countway

Library of Medicine

(P A Bain PhD), Harvard Medical

School, Boston, MA, USA;

Massachusetts College of

Pharmacy and Health Sciences,

Boston, MA, USA (M G Amato,

H Edrees); Harvard Business

School, Boston, MA, USA

(M Kuznetsova MPH); IBM

Watson Health, Cambridge,

MA, USA (G Purcell Jackson MD,

K Rhee MD); Department of

Pediatric Surgery, Vanderbilt

University Medical Center,

Nashville, TN, USA

(G Purcell Jackson); CVS Health,

Wellesley Hills, MA, USA

(K Rhee); Harvard T H Chan

School of Public Health,

Boston, MA, USA

(Prof D W Bates)

Correspondence to:

Dr Ania Syrowatka, Brigham and

Women's Hospital, Harvard

Medical School, Boston,

MA 02120, USA

asyrowatka@bwh.harvard.edu

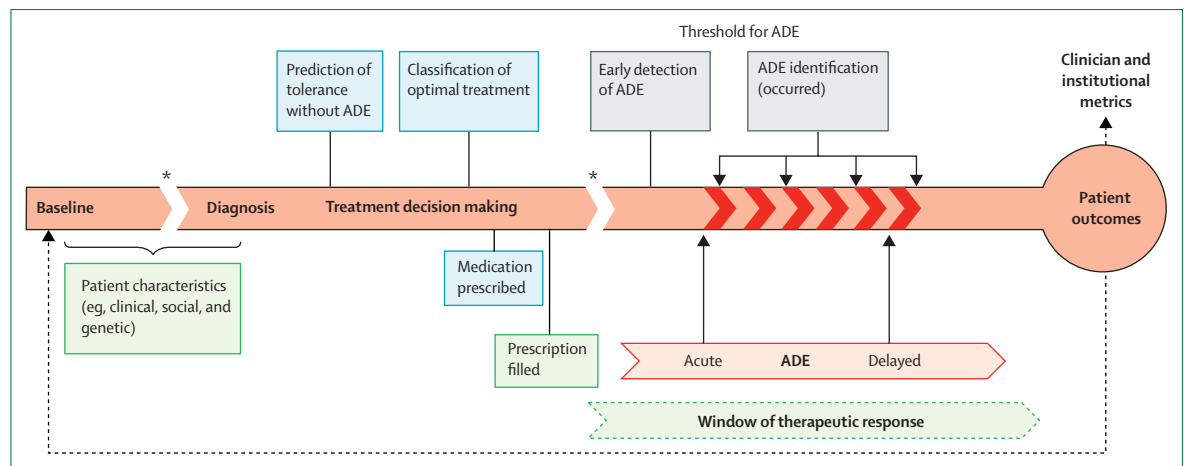


Figure: Timeline for prediction and early detection of ADEs

The green boxes represent patient-centred variables, the blue boxes represent provider-centred variables, and the black-grey boxes represent the threshold for ADEs. Asterisks indicate a discontinuity in time. ADE=adverse drug event.

vocabulary using Medical Subject Headings (MeSH) and free-text terms. An ADE was defined as “an injury resulting from medical intervention related to a drug”¹ and included adverse drug reactions and adverse events related to medication errors. Although the search strategy identified published literature on all ADEs, additional MeSH terms and keywords were added to capture important ADEs: medication errors, allergic reactions, and adverse effects on the blood (eg, thrombocytopenia), as well as drug-induced cardiotoxicity, neurotoxicity, hepatotoxicity, and nephrotoxicity.

The scoping review focused on modern AI techniques, such as neural networks, tree-based algorithms, support vector machines, and natural language processing. The full list of AI models is provided in the appendix (p 1). The review did not include traditional AI approaches, such as logistic or linear regression, due to the vast amount of literature and shift towards using more complex modelling approaches that can integrate large amounts of data from disparate sources to provide more accurate estimations or predictions. Full search strategies are provided in the appendix (pp 2–4).

The scoping review included studies that leveraged AI techniques to develop, validate, or evaluate prediction models to help prevent or manage ADEs, or early detection models to help identify existing ADEs and mitigate the effects, such as severity and duration. The figure depicts the timeline and delineates the difference between prediction and early detection models. Baseline patient characteristics can be integrated into both prediction and early detection models. Use cases for AI to reduce the frequency of ADEs are related to both patient and provider variables and span the full timeline. At the time of treatment decision making, clinical decision support can be provided to clinicians, such as predicting whether the patient is likely to have an ADE and whether there is a preferred treatment given the patient's risk

profile. This type of information can help prevent ADEs. Detection begins once the medication is prescribed, when medication errors can be identified even before medications are taken by the patient. The figure then shows the window of therapeutic response, which also corresponds with the window for occurrence of ADEs. These events can happen immediately, or patients can have delayed reactions. Early detection can help to reduce the severity or duration of ADEs. Both prevention and early detection of ADEs are expected to improve patient outcomes.

Articles were excluded if they were not published in the English language or did not report on original research or a structured review of the literature reported in accordance with PRISMA guidelines.^{9,10} Original research was excluded if the sample size was less than 200 patients, or if the article did not report standard model performance metrics (eg, accuracy or area under the receiver operating curve [AUC-ROC]) or comparisons with a control group for at least one AI model. Studies focused on ADE monitoring or post-marketing surveillance, child or youth populations (ie, aged <18 years), vaccines, dietary supplements, experimental medications not yet approved for use, or recreational use of medications were also excluded. Recreational use was defined as the use of medications that require a prescription but were not prescribed for the individual. Detailed inclusion and exclusion criteria are provided in the appendix (p 1).

Screening and data abstraction

Screening was completed in two stages using the Covidence systematic review management program. Articles were screened for relevance on the basis of information provided in the title and abstract and then evaluated for inclusion on the basis of the full text. Two of five reviewers (ASy, HE, ZC, MK, SD) independently screened articles at each stage. Disagreements were

See Online for appendix

For more on the Covidence systematic review management program see <https://www.covidence.org/>

Studies (n=78)	
Domain	
Prediction	67 (86%)
Early detection	11 (14%)
Publication year	
1998–2005	3 (4%)
2006–10	7 (9%)
2011–15	10 (13%)
2016–20	58 (74%)
Regions and countries	
North America	33 (42%)
USA	33 (42%)
Europe	16 (21%)
France	3 (4%)
Italy	3 (4%)
Netherlands	2 (3%)
Other	8 (10%)
Asia	21 (27%)
Taiwan	10 (13%)
Japan	4 (5%)
China	3 (4%)
South Korea	2 (3%)
Other	2 (3%)
Middle East	2 (3%)
Israel	1 (1%)
Turkey	1 (1%)
Oceania	1 (1%)
Australia	1 (1%)
Africa	1 (1%)
Nigeria	1 (1%)
Multiple countries	4 (5%)
Sample size	
200–500	22 (28%)
501–1000	13 (17%)
1001–10 000	19 (24%)
10 001–100 000	14 (18%)
100 001–1 000 000	7 (9%)
>1 000 000*	3 (4%)

(Table 1 continues in next column)

Studies (n=78)	
(Continued from previous column)	
Outcome†	
Adverse drug event	45 (58%)
Cardiovascular	7 (9%)
Renal	7 (9%)
Opioid overdose or opioid use disorder	6 (8%)
Metabolic or endocrine	3 (4%)
Abnormal blood count	3 (4%)
Allergic reaction	2 (3%)
Weight gain	2 (3%)
Nervous system	1 (1%)
Fall with injury	1 (1%)
Genitourinary	1 (1%)
Haemorrhage	1 (1%)
Multiple adverse drug events	3 (4%)
Not specified	8 (10%)
Treatment response	18 (23%)
Optimal dose	14 (18%)
Most appropriate treatment	3 (4%)
AI model‡	
Neural network	36 (46%)
Random forest	31 (40%)
Support vector machine	24 (31%)
Decision tree	19 (24%)
Bayesian	19 (24%)
K-nearest neighbours	12 (15%)
Gradient boosting machine	11 (14%)
Other‡	19 (24%)
Medication classification†	
Analgesics	13 (17%)
Narcotic	9 (12%)
Non-narcotic	4 (5%)
Antineoplastics	12 (15%)
Antibiotics	9 (12%)

(Table 1 continues in next column)

resolved by discussion and consensus between at least two reviewers or by a third independent reviewer.

The following information was abstracted for studies included in the review: citation information; use case domain (ie, prediction, early detection); population under study (ie, region, population description); sample size; AI models and number of variables; medication class; model outcome; type of ADE; performance metrics for the best performing AI model; model validation approach (eg, sample splitting, cross-validation); quality rating; clinical research phase equivalency; and data sources. Data were abstracted by one reviewer and then validated by a second reviewer (ASy, WS, MGA, DF, HE, ZC, MK, SD, DLS, ASi); sections were assigned on the basis of areas of expertise.

The accuracy or AUC-ROC was abstracted for the best performing AI model, since these metrics are most often reported in the medical literature. When this information was not available, other performance metrics were abstracted including sensitivity, specificity, mean error, and area under the precision-recall curve. If modern AI techniques were outperformed by traditional approaches, such as logistic regression, the information was also abstracted for comparison.

The quality of the studies was evaluated on the basis of the study design using a simplified version of the Oxford Centre for Evidence-Based Medicine levels of evidence.¹¹ The clinical research phase equivalency for each study was assessed using Park and colleagues' 2020 framework to describe the relatively early stages of this type of work, ranging from phase 0 (discovery and invention) to phase 5 (safety and effectiveness).¹² Common data sources were

Studies (n=78)	
(Continued from previous column)	
Anticoagulants	7 (9%)
Antivirals	6 (8%)
Cardiovascular	4 (5%)
Antipsychotics	4 (5%)
Anaesthetics	4 (5%)
Glucocorticoids	3 (4%)
Immunomodulators	3 (4%)
Anticonvulsants	2 (3%)
Immunosuppressants	2 (3%)
Antihyperglycaemics	2 (3%)
Multiple medication classes	6 (8%)
Not specified	5 (6%)
Other§	4 (5%)
Data source†	
Health records	46 (59%)
Electronic	23 (29%)
Unclear whether electronic	23 (29%)
Secondary use of research data	17 (22%)
Genetic data	13 (17%)
Publicly available dataset	12 (15%)
Administrative health data	10 (13%)
Biosensor data	1 (1%)
Quality assessment (scale: levels 1 to 5)¹¹	
Level 2: well designed controlled trial without randomisation or prospective comparative cohort trial	9 (12%)
Level 3: case-control study or retrospective cohort study	68 (87%)
Level 4: case series or cross-sectional study	1 (1%)
Equivalent clinical study phase (scale: phases 1 to 5)¹²	
Phase 0: discovery and invention	40 (51%)
Phase 1: technical performance and safety	33 (42%)
Phase 2: efficacy and side-effects	5 (6%)
Data are n (%), with all 78 studies included in the denominator in every case. AI=artificial intelligence. *Includes sample sizes of 1 247 722, 1 540 732, and 1 807 159 patients. †Percentages add to more than 100; some studies cover multiple categories. ‡Includes principal component analysis (n=3), k-means clustering (n=3), adaptive boosting (n=3), ensemble techniques (n=2), natural language processing (n=2), reinforcement learning (n=2), extremely randomised trees (n=1), simulated treatment learning (n=1), kernel machine learning (n=1), and bagging (n=1). §Includes urinary antispasmodic smooth muscle relaxants (n=1), contrast agents (n=1), thyroid hormones (n=1), and colony stimulating factors (n=1).	
Table 1: Characteristics of studies included in the scoping review	

identified and abstracted: health record data, genetic information, administrative health data, publicly available data, and secondary use of research data.

Data synthesis

Characteristics of the included studies were summarised. Key use cases for AI to reduce the frequency of ADEs were narratively synthesised. Use cases were identified according to the purpose of the model, either prediction or early detection, and the outcome being modelled. Commonly used AI techniques, main insights including

best performing models, and future directions were summarised.

Results

Study characteristics

From 7218 unique records, 78 articles met the target criteria and were included in the scoping review. A PRISMA flow diagram is presented in the appendix (p 5), and data abstracted from the articles are also provided in the appendix (pp 6–20). The scoping review did not identify any structured reviews focused on the use of AI to reduce the frequency of ADEs. A list of studies excluded at full-text screening is provided in the appendix (pp 21–34).

Characteristics of included studies are summarised in tables 1 and 2. Most studies were published within the past 5 years of our search (2016–20) and were conducted using patient data from North America, Asia, and Europe (table 1).

Studies developed and evaluated a wide range of AI algorithms. Half the studies focused on four medication classes: analgesics, antineoplastics, antibiotics, and anticoagulants. Table 3 shows the breakdown of medication and ADE classes by study sample size.

Most studies (73 [94%] of 78) reported on the development and validation of AI algorithms (equivalent to phases 0 or 1 of clinical trials), and five studies assessed the efficacy and unintended effects of AI solutions (equivalent to phase 2 of clinical trials).¹² 68 (87%) of these studies used case-control or retrospective cohort study designs corresponding with level 3 quality of evidence (table 1).

Prediction use cases

Most studies (67 [86%] of 78) developed, validated, or tested AI-based prediction models to help reduce the frequency of ADEs,^{13–79} and mapped onto four inter-related use cases (table 4).

The first use case was prediction of which patients were likely to have a future ADE, which should help to prevent or effectively manage ADEs.^{13–46} Most focused on prediction of specific types of ADEs associated with a class of medications; the most common types of ADEs studied were renal (seven [21%] of 34 studies) or cardiovascular (seven [21%]) adverse events, and opioid overdose or opioid use disorder (six [18%]). Notably, only two articles addressed prediction of allergic reactions and focused on prediction of β -lactam hypersensitivity.^{14,15}

15 (44%) of 34 studies assessed the performance of a single AI model.^{13,14,16,17,20,26,30–32,34,36,37,41,42,44} The other studies compared the performance of multiple models with neural networks and tree-based algorithms demonstrating the best performance based on accuracy and AUC-ROC, or other metrics reported in the studies. One study showed similar performance between federated learning (ie, training algorithms using multiple decentralised databases) and centralised approaches for development of AI-based ADE prediction models.²⁷

	Medication class (name)*	Studies (n=45)
Cardiovascular		
Venous thromboembolism	Antineoplastics (platinum compounds, fluoropyrimidines, anthracyclines, taxanes, paclitaxel, bevacizumab, gemcitabine, irinotecan, pemetrexed, herceptin, anti-tyrosine kinase, aromatase inhibitors)	2 (4%)
Hypotension	Anaesthetics and analgesics (sevoflurane, propofol, fentanyl, remifentanyl, midazolam, etomidate, bupivacaine)	3 (7%)
Cardiovascular diseases	Analgesics: non-narcotic (osteoarthritis medications including NSAIDs)	1 (2%)
Arrhythmia or dysrhythmia, heart failure	Antineoplastics (methotrexate, cyclophosphamide, carboplatin, others not specified)	1 (2%)
Renal		
Acute kidney injury	Antibiotics (vancomycin; n=4), antineoplastics (cisplatin; n=1), and multiple classes or not specified (n=1)	6 (13%)
Acute tubular necrosis	Contrast agents (medications not specified)	1 (2%)
Metabolic or endocrine		
Hepatotoxicity (jaundice, elevated liver function test)	Analgesics: non-narcotic (acetaminophen [paracetamol])	1 (2%)
Hypoglycaemia	Antihyperglycaemics (acarbose, acetohexamide, alogliptin, canagliflozin, chlorpropamide, colesevelam, dapagliflozin, glibenclamide, glimepiride, glipizide, linagliptin, miglitol, metformin, nateglinide, pioglitazone, repaglinide, rosiglitazone, saxagliptin, sitagliptin, tolazamide, voglibose)	1 (2%)
Metabolic syndrome	Antipsychotics (risperidone, olanzapine, clozapine)	1 (2%)
Opioid overdose or opioid use disorder		
Opioid abuse, overdose, poisoning, or dependence	Analgesics: narcotic (opioids)	6 (13%)
Abnormal blood count		
Low white blood count, neutropenia	Antineoplastics (platinum + taxanes, platinum + irinotecan; n=1) and antivirals (ganciclovir; n=1)	2 (4%)
Low platelets, heparin-induced thrombocytopenia	Anticoagulants (heparin)	1 (2%)
Allergic reaction		
Angioedema or anaphylaxis, urticaria, syncope, exanthema, unspecified	Antibiotics: penicillins, cephalosporins, other unspecified β -lactams (n=1), and benzylpenicillin, aminopenicillins, cephalosporins, other unspecified β -lactams (n=1)	2 (4%)
Nervous system		
Myopathy	Multiple classes or not specified	1 (2%)
Weight gain	Antipsychotics (amisulpride, aripiprazole, clozapine, medroxyprogesterone, flupentixol, fluphenazine decanoate, haloperidol, olanzapine, paliperidone, prochlorperazine, promazine, quetiapine, risperidone, trifluoperazine, sulpiride, zuclopenthixol; n=1) and medications not specified (n=1)	2 (4%)
Fall with injury		
Bone fracture	Glucocorticoids (inhaled corticosteroids)	1 (2%)
Genitourinary		
Post-operative urinary retention	Anaesthesia	1 (2%)
Haemorrhage		
Gastrointestinal haemorrhage	Anticoagulants and antiplatelets (warfarin, dabigatran, apixaban, rivaroxaban, clopidogrel, ticlopidine, aspirin, dipyridamole, cilostazol, ticagrelor)	1 (2%)
Multiple adverse drug events		
Adrenocortical insufficiency, aplastic anaemia, polyneuropathy, hypotension, generalised or localised skin eruption, osteoporosis, fetal damage, anaphylactic shock, allergy, vascular complications, infusion complications, cardiovascular related, other	Not specified (n=1), antineoplastics (platinum + gemcitabine, pemetrexed, paclitaxel, vinorelbine, or etoposide; n=1), and cardiovascular (benazepril, captopril, enalapril, lisinopril, labetalol, doxazosin, atenolol, metoprolol, pindolol, propranolol, clonidine, methyl dopa, minoxidil, bumetanide, furosemide, reserpine, spironolactone, triamterene, hydrochlorothiazide, metolazone; n=1)	3 (7%)
Not specified	Multiple classes or not specified	8 (18%)

NSAID=non-steroidal anti-inflammatory drug. *The number of studies is presented in parentheses following the medication class, unless the medication class applies to all studies in that row.

Table 2: Information about studies that focused on prediction or early detection of adverse drug events

The second use case was prediction of therapeutic response to medications. The scoping review identified many studies that developed or validated models to predict therapeutic response for which prevention of ADEs in patients not expected to benefit from treatment was stated as a motivation for model development. 18 (27%) of 67 studies addressed this use case^{45–62} and focused on antineoplastics to treat patients with cancer (four [22%] of 18 studies), or antivirals with or without immunomodulators to treat patients with HIV or hepatitis C (five [28%]). Eight (44%) of 18 studies

evaluated a single AI model.^{47,49,51,56–58,60,61} The remaining studies compared multiple models; use of support vector machines or tree-based algorithms generally resulted in the most favourable performance.

The third use case was prediction of optimal medication dosing to balance therapeutic benefit with ADE risk related to a specific medication. Several studies (14 [21%] of 67) covered this use case^{63–76} with a focus on anticoagulants (five [36%] of 14 studies), cardiovascular medications (two [14%]), and antineoplastics (two [14%]). Eight studies assessed the performance of a single AI

	Medication classes (78 studies)	ADE classes (45 studies)
200–500 participants	Analgesics (n=1); anaesthetics and analgesics (n=1); antibiotics (n=3); anticoagulants (n=2); antineoplastics (n=6); antipsychotics (n=3); antivirals (n=1); cardiovascular (n=2); immunomodulators and antivirals (n=1); thyroid hormones (n=1); multiple classes or not specified (n=1)	Abnormal blood count (n=2); cardiovascular (n=1); metabolic or endocrine (n=1); renal (n=3); weight gain (n=2); not specified (n=1)
501–1000 participants	Analgesics (n=1); antibiotics (n=2); anticoagulants (n=1); antineoplastics (n=3); antivirals (n=1); glucocorticoids (n=1); immunomodulators and antivirals (n=2); immunosuppressants (n=1); urinary antispasmodic smooth muscle relaxants (n=1)	Cardiovascular (n=1); renal (n=1); multiple ADEs (n=1)
1001–10 000 participants	Analgesics (n=2); anaesthetics (n=1); antibiotics (n=4); anticoagulants (n=3); anticonvulsants (n=2); antineoplastics (n=2); antivirals (n=1); cardiovascular (n=1); colony stimulating factors (n=1); contrast agents (n=1); multiple classes or not specified (n=1)	Abnormal blood count (n=1); allergic reaction (n=2); cardiovascular (n=3); metabolic or endocrine (n=1); renal (n=2); multiple ADEs (n=1); not specified (n=1)
10 001–100 000 participants	Analgesics (n=2); anaesthetics and analgesics (n=2); anticoagulants (n=1); antihyperglycaemics (n=2); antineoplastics (n=1); cardiovascular (n=1); glucocorticoids (n=1); glucocorticoids and immunosuppressants (n=1); multiple classes or not specified (n=3)	Cardiovascular (n=2); fall with injury (n=1); genitourinary (n=1); haemorrhage (n=1); metabolic or endocrine (n=1); opioid overdose or opioid use disorder (n=2); renal (n=1); multiple ADEs (n=1); not specified (n=1)
100 001–1 000 000 participants	Analgesics (n=3); multiple classes or not specified (n=4)	Opioid overdose or opioid use disorder (n=3); not specified (n=4)
>1 000 000 participants	Analgesics and antipsychotics (n=1); multiple classes or not specified (n=2)	Nervous system (n=1); opioid overdose or opioid use disorder (n=1); not specified (n=1)

ADE=adverse drug event.

Table 3: Medication and ADE classes by study sample size

model, with six of these studies using Bayesian estimation.^{63,66,67,71,73,75} Six studies tested multiple AI-based models, with random forests and ensemble models demonstrating the best performance.

The fourth prediction use case was prediction of the most appropriate treatment option to help guide selection of safe and effective pharmacological therapies. Only a small number of studies reported on this use case^{77–79} (three [4%] of 67 studies).

Overall, about a quarter of the prediction studies (16 [24%] of 67) developed algorithms using routinely collected, structured electronic health record (EHR) data including laboratory results, and an additional 21 studies (31%) developed algorithms using medical records, although it was not clear if the data were electronic. Eight studies (12%) used administrative health data and 17 studies (25%) relied on secondary use of research data; only one study integrated information from biosensors.¹⁸

Genetic information emerged as a potentially valuable data source. 13 (19%) of 67 studies included genetic variables to develop prediction models.^{41–45,47–50,74–77} Most studies including genetic information (nine [69%] of 13) were conducted using secondary research data and compared the performance of multiple AI algorithms. Genetic information was extracted from genetic variant genotyping data and expression profiles.

Integration of genetic and clinical data was one of the most important topics, in which one or several machine learning algorithms were applied to combine clinical and genetic risk factors to improve the performance of ADE prediction models.^{41,76} In eight studies, both genetic and clinical factors were combined as model input variables.^{42–45,47,74–76} In most cases, genetic factors were found to be associated with outcomes and

contributed to the model performance. In two studies, the value of adding genetic variables was evaluated.^{42,43} In a study predicting nephrotoxicity, adding genetic variables increased the AUC-ROC from 0.64 to 0.73.⁴² Although genetic features often improved model performance, non-significant results were also reported.⁴³

Multiple studies used machine learning methods to identify genetic factors associated with ADEs, including single nucleotide polymorphisms (SNPs) and related genes.^{41,47,50} Among them, a 12-gene signature was developed using mRNA expression data and a hybrid model to predict tumour recurrence in patients with lung adenocarcinoma.⁴⁹ In another lung cancer study, the association between both SNPs and genes with drug response and toxicity was estimated by logistic regression and neural network models.⁴⁵

One study developed a cancer (multiple myeloma) treatment learning system to predict patients' response to treatment using genetic similarities.⁴⁸ Better outcomes (ie, progression-free survival) for bortezomib and lenalidomide were shown, based on patients' gene expression signatures.

Early detection use cases

11 (14%) of 78 studies used AI-based models to identify ADEs (ten [91%] of 11)^{80–89} or medication errors (four [36%] of 11);^{87–90} three studies detected both. Data were obtained from health records for nine studies (noted as EHR data in seven studies) and pharmacy dispensing data for two studies.^{85,90} Two studies tested models in patient care settings and measured prescriber response after receiving clinical decision support alerts identifying potential ADEs.^{81,88} Most studies evaluated models that were designed to identify ADEs or errors in general, with

	Description	Studies, n	Common AI approaches*
Prediction		67†	
Predict which patients are likely to have an ADE	To prevent or manage ADEs	34	Neural network (n=17), random forest (n=17), decision tree (n=11), support vector machine (n=11), gradient boosting machine (n=7), k-nearest neighbours (n=6), Bayesian (n=5)
Predict therapeutic response (or non-response) to medications	To limit ADEs caused by medications that will not provide therapeutic benefit to the patient	18	Neural network (n=10), random forest (n=9), support vector machine (n=9), Bayesian (n=5)
Predict optimal medication dose or adaptive dosing	To balance therapeutic benefit with ADE risk	14	Bayesian (n=6), decision tree (n=5), k-nearest neighbours (n=5), neural network (n=5), random forest (n=4), support vector machine (n=4)
Predict most appropriate treatment options	To guide selection of safe and effective pharmacological therapies	3	No common models
Early detection		11†	
Detect ADEs	To reduce the duration or severity of harm	10	Neural network (n=6), random forest (n=3)
Detect medication prescribing errors	To prevent ADEs	4	Neural network (n=3)

ADE=adverse drug event. AI=artificial intelligence. *Applied in three or more studies. †Some studies addressed multiple use cases.

Table 4: Summary of prediction and early detection use cases with commonly used AI approaches

only three studies focused on identifying ADEs for specific medications.^{81–83} Most studies tested a single AI model, with only four studies evaluating multiple models.^{80,84,85,90}

Three studies used a software system (MedAware) that identified potential medication errors or ADEs in EHRs using several machine learning methods including neural networks.^{87–89} This software was designed to alert prescribers about clinical or medication dosage outliers, time-dependent irregularities occurring between medication use and patients' data, and potential drug duplication. It was found to more accurately identify potential ADEs (85% of alerts were considered clinically relevant *vs* 16% with a rule-based legacy system) and reduce alert burden (alerted on 0.4% *vs* 37.1% of orders).⁸⁸ Another study used natural language processing to analyse admission history and physical notes, along with medication lists and laboratory results, to alert providers about potential ADEs.⁸¹ Use of the algorithm also resulted in ordering of fewer potential adverse drug reaction-causing medications at any time during the hospital admission compared with a control group (47% *vs* 58%, $p<0.001$). Fewer adverse drug reaction-causing medications were also ordered within the first 24 h after admission in the intervention group (28% *vs* 39%, $p<0.001$). Other studies also reported successful detection of ADEs with the various models tested, but variability in study populations and performance of models between studies limited the ability to determine which type of AI model performed best for detecting ADEs.

Discussion

We performed this scoping review to summarise the published literature on the development, validation, and testing of AI-based algorithms and tools that provide patient-specific predictions to prevent ADEs and early detection to mitigate the harmful effects. The included studies were heterogeneous with regard to the types of

AI models used and medications and ADEs studied. Most articles only evaluated the technical performance of AI-based algorithms; there were only a few examples of studies describing the clinical evaluation of algorithms or tools. We identified key use cases to guide work in two areas: prediction and early detection.

Prediction use cases

The prediction literature identified various mechanisms to reduce the frequency of harm beyond simply predicting which patients are likely to have an ADE; there were four inter-related use cases (table 4). AI-based predictions could play an important role in reducing the overall frequency of ADEs. Identifying patients at higher risk of ADEs could inform dosing adjustments or additional interventions necessary to manage ADEs.⁹¹

Tree-based methods were widely used and performed well across the prediction use cases. These approaches are particularly well suited for clinical settings, given the relative interpretability compared with deep learning algorithms (a subset of machine learning that generally uses neural networks⁸).⁹² Most studies developed predictive models based on structured data routinely documented in health records or administrative health databases. Therefore, most of the necessary information, if not all, would be accessible through EHRs if these algorithms were implemented at the point of care. However, these findings also suggest that important information captured in clinical notes would be missed.

Natural language processing and newer deep learning approaches including transformer neural networks could be leveraged to access data contained in unstructured fields to improve the performance of predictive models.⁹³ Although considerably more complex than current methods, these types of extraction technologies are being developed by industry and academia, and these solutions are likely to become available to advance research and development of clinical decision support over the next few years. In addition, integration of additional

For more on MedAware see
<https://www.medaware.com/>

information (eg, clinical guidelines and comprehensive drug knowledge bases) as inputs into AI algorithms to complement data captured within the EHR could further serve to provide more appropriate recommendations at the point of care.

Genetics can play a pivotal role in patients' adverse and therapeutic responses to medications.⁹⁴ Many genome-wide association studies have been conducted to identify loci and genes associated with ADEs. For example, the P450 genes, a gene family with important implications for drug metabolism, have been assessed in multiple ADE studies.^{95,96}

In our scoping review, multiple studies showed the value of genetic data for ADE prediction. When machine learning-based algorithms were used, they were able to incorporate high-dimensional features to reflect complex patterns in large-scale datasets. Despite the promising potential of integrating genetic information with clinical information, substantial limitations were also noted. Few studies were purely based on genetic variables, suggesting a relatively small degree of variation explained by genetic factors compared with clinical factors.⁴³ Also, due to the shortage of patient-level genotyping data sources, only a small percentage of ADE studies included genetics.

Literature in the allergy domain was remarkably scarce and is an attractive target for future work. Our scoping review identified just two allergy studies,^{14,15} and both were published in the past 3 years, indicating that the allergy domain might be a developing area of focus for AI application. Antibiotics are the most common allergen in drug hypersensitivity, including in fatal anaphylaxis,⁹⁷ and the focus on β -lactam allergy aligns with a high volume of publications in the allergy literature focused on risk stratification of β -lactam allergy.⁹⁸ Machine learning applications in allergy remain an unmet need with the potential for substantial impact on patient outcomes. Drug allergy is an area with high patient morbidity motivating further work; it can be conceptualised as the severity of the drug allergy reaction itself—eg, death, anaphylaxis, or severe cutaneous ADEs. Alternatively, it could be viewed through the lens of far more common mild allergic reactions (eg, rashes, hives) for which avoidance of the associated medication (or drug class) can lead to selection of suboptimal or second-line drug choices, resulting in a high risk of morbidity—eg, the increased incidence of *Clostridium difficile* colitis with use of overly broad antibiotics when avoiding β -lactams.

Early detection use cases

Several types of AI models have been successful in detecting ADEs when tested using data from health records or pharmacy dispensing data. However, only a few of these systems have been tested in patient care settings. The models show promise in identifying ADEs that providers might otherwise miss and in reducing

alert burden seen with rule-based clinical decision support systems that provide alerts for all patients fitting a rule, but that might not be clinically useful in all patients (eg, a drug–drug interaction alert in all patients taking a combination of two medications, even for those that are often recommended to be used together, are being tolerated well by the patient, or are being monitored appropriately). Further testing of these models should be conducted to determine their performance in affecting providers' decision making when caring for patients.

There is a shortage of studies focused on identifying the best patient contact method, time and frequency, treatment setting, or patient population to screen for potential ADEs. It would be important to know, for example, whether using AI to identify patients to contact via patient portal, telephone call, or text when they are at home identifies ADEs sooner than limiting screening to visits or admissions in health-care settings. AI could also be used to identify the best time intervals to screen for ADEs after starting new medications or when continuing medications, or whether screening at some patient care locations (eg, inpatient, outpatient, or long-term care) is more successful for identification of ADEs than at other locations. More studies are needed to evaluate the added value of using natural language processing to access and integrate data from unstructured clinical notes.

Challenges of using AI to reduce the frequency of ADEs

Leveraging AI to reduce the frequency of ADEs is an emerging area of study, and further work is required to ensure that accurate, equitable, and meaningful tools are available at the point of care to inform clinical decision making. Most challenges relating to the implementation of AI solutions in health care apply here as well. High-performing models developed and validated at one or a small number of health-care sites might not translate well to different contexts and will require re-calibration to ensure efficacy and safety. Similarly, models need to be tested and calibrated for population subgroups to ensure that models perform well across all patient groups. To develop these equitable models, developers need access to data with high coverage of the underlying patient population. Prediction and detection of rare ADEs (eg, aplastic anaemia) poses additional challenges requiring careful consideration around the metrics used to evaluate model performance, applying sampling strategies to balance the data, and generating sufficiently large datasets to ensure enough cases for model development.

Overarching themes and recommendations

We present main insights and future directions for each domain (panel) and have identified several overarching themes. First, the application of AI to reduce the frequency of ADEs is an emerging area of study with most of the literature published within the past 5 years. Second, despite many AI-based algorithms showing promising performance, most studies were in early

phases of development with few evaluations beyond technical performance. As most AI algorithms that support or advise clinicians are not regulated, evaluations are often rudimentary, which is an ongoing limitation in other areas of health care.⁹⁹ It is crucial for high-performing algorithms to be systematically and comprehensively evaluated in prospective trials in clinical settings to show real-world impact and generate the evidence necessary for transparent, safe, and effective implementation. This research requires close collaboration between clinicians and informaticians to make the evaluation process efficient and successful. Third, genetic information was identified as a key data source that has the potential to substantially improve the performance of AI algorithms. With genotyping becoming more commonplace, this type of data should become more accessible over time for both model development and use at the point of care.

Limitations

This study had limitations. The search focused on the concepts of AI, prediction, early detection, and ADEs to identify key use cases for AI to reduce the frequency of ADEs. As such, the review summarised the literature in which ADEs were the focus of the study or in which reduction of ADEs was identified as a key motivation for model development. Related literature not included in this review might be available for some of the use cases.

Due to the large heterogeneity between studies with regard to the types of AI models used as well as the medications and ADEs studied, we were not able to do a formal assessment of the predictive validity of the different AI models. However, our work could inform systematic reviews aimed to answer more focused research questions about the use of AI for specific medications or ADEs and further delineate which AI techniques are most appropriate given different contexts and care settings.

In our study, AI model performance was generally evaluated using accuracy or AUC-ROC, which are most often reported in the medical literature. These metrics might not be the most informative, as they can overestimate performance of algorithms predicting rare ADEs and could account for the similar performances of AI models in studies that evaluated multiple techniques. Other metrics from the computer science literature are better able to account for unbalanced datasets than are accuracy or AUC-ROC, such as the area under the precision-recall curve (reported in a few studies included in this scoping review), and we expect that these metrics will become more widely reported in the medical literature over time.

Conclusion

We performed a scoping review, summarised the main insights, and identified several use cases in which AI could contribute to reducing the frequency and consequences of ADEs. Most studies only evaluated

Panel: Main insights and future directions for AI to reduce the frequency of ADEs

Prediction

Insights

Most studies developed predictive algorithms and applied a wide range of AI approaches, and focused on specific medication or ADE classes. Tree-based methods performed well across the prediction use cases. A limitation was that algorithms were generally developed using structured data. In many of the studies, genetic factors were applied to improve ADE clinical prediction models; both positive and negative results were reported. One of the remaining challenges is how to identify and select the most relevant genetic variables among large amounts of genetic profile information. Machine learning approaches showed promising progress to address this problem, but are still in the early stages of development.

Opportunities

- Integration of unstructured clinical notes and data from external sources as additional variables to complement structured EHR data to improve the performance of AI-based algorithms
- Inclusion of genetic components in ADE clinical predictions, given the rapid development of causal genetic variant models, such as fine mapping; large-scale clinical biobanks and machine learning algorithms will facilitate this process and make patient genetic information more applicable for clinical decisions to prevent ADEs than is currently possible
- More studies are needed in the fields of EHR-derived ADE genetic association models and machine learning-based clinical and genetic integration systems

Early detection

Insights

Several different AI approaches using data (mostly structured, some unstructured) from EHRs and pharmacy dispensing data showed success in identifying ADEs and prescribing errors. These models have the potential to detect ADEs earlier and more accurately than current methods, and could reduce alert fatigue resulting from too many alerts presented to prescribers using current rule-based alert systems.

Opportunities

- Additional studies of specific models to identify the best AI methods to detect ADEs and errors
- Prospective studies using AI models in patient care settings
- Attempts to identify the best patient population, treatment setting, patient contact method, and time and frequency to screen for ADEs
- Comparisons of benefits of safety outcomes between systems focused on detecting ADEs for high-risk medications, specific ADEs, or general ADE detection

ADE=adverse drug event. AI=artificial intelligence. EHR=electronic health record.

technical algorithm performance, and very few studies evaluated the use of AI in clinical settings. Research on predicting allergic reactions was scarce and only a small number of studies incorporated genetic data. Most studies were published in the past 5 years, highlighting an emerging area of study, and we expect many more studies in the next few years. Availability of new types of data and access to unstructured EHR notes might further advance the field.

Contributors

ASy, WS, MGA, DF, DLS, GPJ, KR, and DWB were responsible for study conception and design. ASy and PAB developed the literature searches. ASy, HE, ZC, MK, and SD reviewed the literature. ASy, WS, MGA, DF,

HE, ZC, SD, DLS, and ASi abstracted and verified the data. ASy, WS, MGA, and DF analysed and interpreted the data. All authors had full access to all the data in the study. ASy, WS, MGA, DF, and DWB drafted the original manuscript, and all co-authors reviewed the draft and provided critical feedback. All authors contributed to and approved the final manuscript.

Declaration of interests

ASy, WS, MGA, DF, HE, ZC, SD, and DWB received salary support from a grant funded by IBM Watson Health. DWB has received research support and consults for EarlySense, which makes patient safety monitoring systems. He receives cash compensation from CDI (Negev), which is a not-for-profit incubator for health IT startups. He receives equity from Valera Health, which makes software to help patients with chronic diseases. Clew, which makes software to support clinical decision making in intensive care, and MDClone, which takes clinical data and produces deidentified versions of it. He consults for and receives equity from AESOP, which makes software to reduce medication error rates, and FeelBetter. He has received research support from MedAware. GPJ is employed by IBM Watson Health, and her compensation includes salary and equity. KR was employed by IBM Watson Health, and is employed by CVS Health; his compensation from both IBM and CVS Health includes salary and equity. All other authors declare no competing interests.

Acknowledgments

ASy is supported by a Fellowship Award from the Canadian Institutes of Health Research. ASi is supported by a Fellowship Award from the Geneva University Hospitals. This work has been supported by IBM Watson Health (Cambridge, MA), which is not responsible for the content or recommendations made.

Editorial note: the *Lancet* Group takes a neutral position with respect to territorial claims in published tables.

References

- Kohn LT, Corrigan JM, Donaldson MS. To err is human: Building a safer health system. Washington, DC: Institute of Medicine of the National Academy of Sciences, 1999.
- Alatawi YM, Hansen RA. Empirical estimation of under-reporting in the US Food and Drug Administration ADVERSE EVENT REPORTING SYSTEM (FAERS). *Expert Opin Drug Saf* 2017; **16**: 761–67.
- Weiss AJ, Freeman WJ, Heslin KC, Barrett ML. Adverse drug events in US hospitals, 2010 versus 2014. HCUP statistical brief #234. Rockville, MD: Agency for Healthcare Research and Quality, 2018.
- Wolfe D, Yazdi F, Kanji S, et al. Incidence, causes, and consequences of preventable adverse drug reactions occurring in inpatients: a systematic review of systematic reviews. *PLoS One* 2018; **13**: e0205426.
- Khalil H, Huang C. Adverse drug reactions in primary care: a scoping review. *BMC Health Serv Res* 2020; **20**: 5.
- Poudel DR, Acharya P, Ghimire S, Dhital R, Bharati R. Burden of hospitalizations related to adverse drug events in the USA: a retrospective analysis from large inpatient database. *Pharmacoepidemiol Drug Saf* 2017; **26**: 635–41.
- Bates DW, Cullen DJ, Laird N, et al. Incidence of adverse drug events and potential adverse drug events. Implications for prevention. *JAMA* 1995; **274**: 29–34.
- Bates DW, Auerbach A, Schulam P, Wright A, Saria S. Reporting and implementing interventions involving machine learning and artificial intelligence. *Ann Intern Med* 2020; **172** (suppl): S137–44.
- Tricco AC, Lillie E, Zarin W, et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Ann Intern Med* 2018; **169**: 467–73.
- Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009; **6**: e1000097.
- Centre for Evidence-Based Medicine. Oxford Centre for Evidence-Based Medicine: levels of evidence (March 2009). 2009. <https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009> (accessed Nov 1, 2020).
- Park Y, Jackson GP, Foreman MA, Gruen D, Hu J, Das AK. Evaluating artificial intelligence in medicine: phases of clinical research. *JAMIA Open* 2020; **3**: 326–31.
- Imai S, Yamada T, Kasashi K, Ishiguro N, Kobayashi M, Iseki K. Construction of a flow chart-like risk prediction model of ganciclovir-induced neutropaenia including severity grade: a data mining approach using decision tree. *J Clin Pharm Ther* 2019; **44**: 726–34.
- Chiriac AM, Wang Y, Schrijvers R, et al. Designing predictive models for beta-lactam allergy using the drug allergy and hypersensitivity database. *J Allergy Clin Immunol Pract* 2018; **6**: 139–148.e2.
- Moreno EM, Moreno V, Laffond E, et al. usefulness of an artificial neural network in the prediction of β -lactam allergy. *J Allergy Clin Immunol Pract* 2020; **8**: 2974–82.e1.
- Ferroni P, Zanzotto FM, Scarpato N, Riondino S, Guadagni F, Roselli M. Validation of a machine learning approach for venous thromboembolism risk prediction in oncology. *Dis Markers* 2017; **2017**: 8781379.
- Ferroni P, Zanzotto FM, Scarpato N, et al. Risk assessment for venous thromboembolism in chemotherapy-treated ambulatory cancer patients: a machine learning approach. *Med Decis Making* 2017; **37**: 234–42.
- Kang AR, Lee J, Jung W, et al. Development of a prediction model for hypotension after induction of anesthesia using machine learning. *PLoS One* 2020; **15**: e0231172.
- Kendale S, Kulkarni P, Rosenberg AD, Wang J. Supervised machine-learning predictive analytics for prediction of postinduction hypotension. *Anesthesiology* 2018; **129**: 675–88.
- Lin CS, Chiu JS, Hsieh MH, Mok MS, Li YC, Chiu HW. Predicting hypotensive episodes during spinal anesthesia with the application of artificial neural networks. *Comput Methods Programs Biomed* 2008; **92**: 193–97.
- Liu L, Yu Y, Fei Z, et al. An interpretable boosting model to predict side effects of analgesics for osteoarthritis. *BMC Syst Biol* 2018; **12** (suppl 6): 105.
- Yang X, Gong Y, Waheed N, et al. Identifying cancer patients at risk for heart failure using machine learning methods. *AMIA Annu Symp Proc* 2020; **2019**: 933–41.
- Chen YF, Lin CS, Wang KA, et al. Design of a clinical decision support system for fracture prediction using imbalanced dataset. *J Healthc Eng* 2018; **2018**: 9621640.
- Hung CY, Lin CH, Chang CS, Li JL, Lee CC. Predicting gastrointestinal bleeding events from multimodal in-hospital electronic health records using deep fusion networks. *Annu Int Conf IEEE Eng Med Biol Soc* 2019; **2019**: 2447–50.
- Speiser JL, Karvellas CJ, Wolf BJ, Chung D, Koch DG, Durkalski VL. Predicting daily outcomes in acetaminophen-induced acute liver failure patients with machine learning techniques. *Comput Methods Programs Biomed* 2019; **175**: 111–20.
- Chiang WH, Shen L, Li L, Ning X. Drug-drug interaction prediction based on co-medication patterns and graph matching. *Int J Comput Biol Drug Des* 2020; **13**: 36–57.
- Choudhury O, Park Y, Salonidis T, Gkoulalas-Divanis A, Sylla I, Das AK. Predicting adverse drug reactions on distributed health data using federated learning. *AMIA Annu Symp Proc* 2020; **2019**: 313–22.
- Valeanu A, Damian C, Marinici CD, Negres S. The development of a scoring and ranking strategy for a patient-tailored adverse drug reaction prediction in polypharmacy. *Sci Rep* 2020; **10**: 9552.
- Cheng P, Waitman LR, Hu Y, Liu M. Predicting inpatient acute kidney injury over different time horizons: how early and accurate? *AMIA Annu Symp Proc* 2018; **2017**: 565–74.
- Imai S, Yamada T, Kasashi K, Kobayashi M, Iseki K. Usefulness of a decision tree model for the analysis of adverse drug reactions: evaluation of a risk prediction model of vancomycin-associated nephrotoxicity constructed using a data mining procedure. *J Eval Clin Pract* 2017; **23**: 1240–46.
- Yin WJ, Yi YH, Guan XF, et al. Preprocedural prediction model for contrast-induced nephropathy patients. *J Am Heart Assoc* 2017; **6**: e004498.
- Imai S, Yamada T, Kasashi K, Niinuma Y, Kobayashi M, Iseki K. Construction of a risk prediction model of vancomycin-associated nephrotoxicity to be used at the time of initial therapeutic drug monitoring: a data mining analysis using a decision tree model. *J Eval Clin Pract* 2019; **25**: 163–70.

- 33 Zasowski EJ, Murray KP, Trinh TD, et al. Identification of vancomycin exposure-toxicity thresholds in hospitalized patients receiving intravenous vancomycin. *Antimicrob Agents Chemother* 2017; **62**: 62.
- 34 Imai S, Takekuma Y, Kashiwagi H, et al. Validation of the usefulness of artificial neural networks for risk prediction of adverse drug reactions used for individual patients in clinical practice. *PLoS One* 2020; **15**: e0236789.
- 35 Dong X, Rashidian S, Wang Y, et al. Machine learning based opioid overdose prediction using electronic health records. *AMIA Annu Symp Proc* 2020; **2019**: 389–98.
- 36 Ellis RJ, Wang Z, Genes N, Ma'ayan A. Predicting opioid dependence from electronic health records with machine learning. *BioData Min* 2019; **12**: 3.
- 37 Hastings JS, Howison M, Inman SE. Predicting high-risk opioid prescriptions before they are given. *Proc Natl Acad Sci USA* 2020; **117**: 1917–23.
- 38 Lo-Ciganic WH, Huang JL, Zhang HH, et al. Evaluation of machine-learning algorithms for predicting opioid overdose risk among Medicare beneficiaries with opioid prescriptions. *JAMA Netw Open* 2019; **2**: e190968.
- 39 Lo-Ciganic WH, Huang JL, Zhang HH, et al. Using machine learning to predict risk of incident opioid use disorder among fee-for-service Medicare beneficiaries: a prognostic study. *PLoS One* 2020; **15**: e0235981.
- 40 Li X, Yu S, Zhang Z, et al. Predictive modeling of hypoglycemia for clinical decision support in evaluating outpatients with diabetes mellitus. *Curr Med Res Opin* 2019; **35**: 1885–91.
- 41 Huang K, Luo A, Li X, Li S, Wang S. Chemotherapy-induced neutropenia during adjuvant treatment for cervical cancer patients: development and validation of a prediction model. *Int J Clin Exp Med* 2015; **8**: 10835–44.
- 42 Garcia SL, Lauritsen J, Zhang Z, et al. Prediction of nephrotoxicity associated with cisplatin-based chemotherapy in testicular cancer patients. *JNCI Cancer Spectr* 2020; **4**: pkaa032.
- 43 Harrison RNS, Gaughran F, Murray RM, et al. Development of multivariable models to predict change in body mass index within a clinical trial population of psychotic individuals. *Sci Rep* 2017; **7**: 14738.
- 44 Lan TH, Loh EW, Wu MS, et al. Performance of a neuro-fuzzy model in predicting weight changes of chronic schizophrenic patients exposed to antipsychotics. *Mol Psychiatry* 2008; **13**: 1129–37.
- 45 Yin JY, Li X, Li XP, et al. Prediction models for platinum-based chemotherapy response and toxicity in advanced NSCLC patients. *Cancer Lett* 2016; **377**: 65–73.
- 46 Nickerson P, Tighe P, Shickel B, Rashidi P. Deep neural network architectures for forecasting analgesic response. *Annu Int Conf IEEE Eng Med Biol Soc* 2016; **2016**: 2966–69.
- 47 Ke WS, Hwang Y, Lin E. Pharmacogenomics of drug efficacy in the interferon treatment of chronic hepatitis C using classification algorithms. *Adv Appl Bioinform Chem* 2010; **3**: 39–44.
- 48 Ubels J, Sonneveld P, van Beers EH, Broijl A, van Vliet MH, de Ridder J. Predicting treatment benefit in multiple myeloma through simulation of alternative treatment effects. *Nat Commun* 2018; **9**: 2943.
- 49 Wan YW, Sabbagh E, Raese R, et al. Hybrid models identified a 12-gene signature for lung cancer prognosis and chemoresponse prediction. *PLoS One* 2010; **5**: e12222.
- 50 Lin E, Hwang Y. A support vector machine approach to assess drug efficacy of interferon- α and ribavirin combination therapy. *Mol Diagn Ther* 2008; **12**: 219–23.
- 51 Gudin J, Mavroudi S, Korfiati A, Theofilatos K, Dietze D, Hurwitz P. Reducing opioid prescriptions by identifying responders on topical analgesic treatment using an individualized medicine and predictive analytics approach. *J Pain Res* 2020; **13**: 1255–66.
- 52 Sauer CM, Sasson D, Paik KE, et al. Feature selection and prediction of treatment failure in tuberculosis. *PLoS One* 2018; **13**: e0207491.
- 53 Almas M, Parsons B, Whalen E. Prediction of therapeutic response to pregabalin in subjects with neuropathic pain. *Curr Med Res Opin* 2018; **34**: 2041–52.
- 54 Murphree DH, Arabmakki E, Ngufor C, Storlie CB, McCoy RG. Stacked classifiers for individualized prediction of glycemic control following initiation of metformin therapy in type 2 diabetes. *Comput Biol Med* 2018; **103**: 109–15.
- 55 Ng T, Chew L, Yap CW. A clinical decision support tool to predict survival in cancer patients beyond 120 days after palliative chemotherapy. *J Palliat Med* 2012; **15**: 863–69.
- 56 Ekpenyong ME, Etebong PI, Jackson TC. Fuzzy-multidimensional deep learning for efficient prediction of patient response to antiretroviral therapy. *Heliyon* 2019; **5**: e02080.
- 57 Hatzakis GE, Mathur M, Gilbert L, et al. Neural network-longitudinal assessment of the Electronic Anti-Retroviral Therapy (EARTH) cohort to follow response to HIV-treatment. *AMIA Annu Symp Proc* 2005; **2005**: 301–05.
- 58 Duan T, Rajpurkar P, Laird D, Ng AY, Basu S. Clinical value of predicting individual treatment effects for intensive blood pressure therapy. *Circ Cardiovasc Qual Outcomes* 2019; **12**: e005010.
- 59 Wu W, Bang S, Bleecker ER, et al. Multiview cluster analysis identifies variable corticosteroid response phenotypes in severe asthma. *Am J Respir Crit Care Med* 2019; **199**: 1358–67.
- 60 Waljee AK, Lipson R, Wiitala WL, et al. Predicting hospitalization and outpatient corticosteroid use in inflammatory bowel disease patients using machine learning. *Inflamm Bowel Dis* 2017; **24**: 45–53.
- 61 Maiellaro PA, Cozzolongo R, Marino P. Artificial neural networks for the prediction of response to interferon plus ribavirin treatment in patients with chronic hepatitis C. *Curr Pharm Des* 2004; **10**: 2101–09.
- 62 Sheyn D, Ju M, Zhang S, et al. Development and validation of a machine learning algorithm for predicting response to anticholinergic medications for overactive bladder syndrome. *Obstet Gynecol* 2019; **134**: 946–57.
- 63 Preston SL, Drusano GL, Berman AL, et al. Levofloxacin population pharmacokinetics and creation of a demographic model for prediction of individual drug clearance in patients with serious community-acquired infection. *Antimicrob Agents Chemother* 1998; **42**: 1098–104.
- 64 Hu YH, Wu F, Lo CL, Tai CT. Predicting warfarin dosage from clinical data: a supervised learning approach. *Artif Intell Med* 2012; **56**: 27–34.
- 65 Liu KE, Lo CL, Hu YH. Improvement of adequate use of warfarin for the elderly using decision tree-based approaches. *Methods Inf Med* 2014; **53**: 47–53.
- 66 Bondareva IB, Jelliffe RW, Andreeva OV, Bondareva KI. Predictability of individualized dosage regimens of carbamazepine and valproate mono- and combination therapy. *J Clin Pharm Ther* 2011; **36**: 625–36.
- 67 Kraff S, Lindauer A, Joerges M, Salamone SJ, Jaehde U. Excel-based tool for pharmacokinetically guided dose adjustment of paclitaxel. *Ther Drug Monit* 2015; **37**: 725–32.
- 68 Hu YH, Tai CT, Tsai CF, Huang MW. Improvement of adequate digoxin dosage: An application of machine learning approach. *J Healthc Eng* 2018; **2018**: 3948245.
- 69 Levy AE, Biswas M, Weber R, et al. Applications of machine learning in decision analysis for dose management for dofetilide. *PLoS One* 2019; **14**: e0227324.
- 70 Escandell-Montero P, Chermisi M, Martínez-Martínez JM, et al. Optimization of anemia treatment in hemodialysis patients via reinforcement learning. *Artif Intell Med* 2014; **62**: 47–60.
- 71 Marquet P, Bedu A, Monchaud C, et al. Pharmacokinetic therapeutic drug monitoring of Advagraf in more than 500 adult renal transplant patients, using an expert system online. *Ther Drug Monit* 2018; **40**: 285–91.
- 72 Chen SS, Zaborek NA, Doubleday AR, et al. Optimizing levothyroxine dose adjustment after thyroidectomy with a decision tree. *J Surg Res* 2019; **244**: 102–06.
- 73 Kraff S, Nieuweboer AJ, Mathijssen RH, et al. Pharmacokinetically based dosing of weekly paclitaxel to reduce drug-related neurotoxicity based on a single sample strategy. *Cancer Chemother Pharmacol* 2015; **75**: 975–83.
- 74 Ma Z, Wang P, Gao Z, Wang R, Khalighi K. Ensemble of machine learning algorithms using the stacked generalization approach to estimate the warfarin dose. *PLoS One* 2018; **13**: e0205872.
- 75 Öztaner SM, Temizel TT, Erdem SR, Özer M. A Bayesian estimation framework for pharmacogenomics driven warfarin dosing: a comparative study. *IEEE J Biomed Health Inform* 2015; **19**: 1724–33.

- 76 Pavani A, Naushad SM, Kumar RM, Srinath M, Malempati AR, Kutala VK. Artificial neural network-based pharmacogenomic algorithm for warfarin dose optimization. *Pharmacogenomics* 2016; **17**: 121–31.
- 77 Blangero Y, Rabilloud M, Ecochard R, Subtil F. A Bayesian method to estimate the optimal threshold of a marker used to select patients' treatment. *Stat Methods Med Res* 2020; **29**: 29–43.
- 78 König R, Cao X, Oswald M, et al. Macrolide combination therapy for patients hospitalised with community-acquired pneumonia? An individualised approach supported by machine learning. *Eur Respir J* 2019; **54**: 54.
- 79 Desrochers J, Wojciechowski J, Klein-Schwartz W, Gobburu JVS, Gopalakrishnan M. Bayesian forecasting tool to predict the need for antidote in acute acetaminophen overdose. *Pharmacotherapy* 2017; **37**: 916–26.
- 80 Taft LM, Evans RS, Shyu CR, et al. Countering imbalanced datasets to improve adverse drug event predictive models in labor and delivery. *J Biomed Inform* 2009; **42**: 356–64.
- 81 Smith JC, Chen Q, Denny JC, Roden DM, Johnson KB, Miller RA. Evaluation of a novel system to enhance clinicians' recognition of preadmission adverse drug reactions. *Appl Clin Inform* 2018; **9**: 313–25.
- 82 Marchetti M, Barelli S, Zermatten MG, et al. Rapid and accurate Bayesian diagnosis of heparin-induced thrombocytopenia. *Blood* 2020; **135**: 1171–84.
- 83 Lin CC, Bai YM, Chen JY, et al. Easy and low-cost identification of metabolic syndrome in patients treated with second-generation antipsychotics: artificial neural network and logistic regression models. *J Clin Psychiatry* 2010; **71**: 225–34.
- 84 Jeong E, Park N, Choi Y, Park RW, Yoon D. Machine learning model combining features from algorithms with different analytical methodologies to detect laboratory-event-related adverse drug reaction signals. *PLoS One* 2018; **13**: e0207749.
- 85 Hoang T, Liu J, Roughead E, Pratt N, Li J. Supervised signal detection for adverse drug reactions in medication dispensing data. *Comput Methods Programs Biomed* 2018; **161**: 25–38.
- 86 Bagattini F, Karlsson I, Rebane J, Papapetrou P. A classification framework for exploiting sparse multi-variate temporal features with application to adverse drug event detection in medical records. *BMC Med Inform Decis Mak* 2019; **19**: 7.
- 87 Schiff GD, Volk LA, Volodarskaya M, et al. Screening for medication errors using an outlier detection system. *J Am Med Inform Assoc* 2017; **24**: 281–87.
- 88 Segal G, Segev A, Brom A, Lifshitz Y, Wasserstrum Y, Zimlichman E. Reducing drug prescription errors and adverse drug events by application of a probabilistic, machine-learning based clinical decision support system in an inpatient setting. *J Am Med Inform Assoc* 2019; **26**: 1560–65.
- 89 Rozenblum R, Rodriguez-Monguió R, Volk LA, et al. Using a machine learning system to identify and prevent medication prescribing errors: a clinical and cost analysis evaluation. *Jt Comm J Qual Patient Saf* 2020; **46**: 3–10.
- 90 Hasan S, Duncan GT, Neill DB, Padman R. Automatic detection of omissions in medication lists. *J Am Med Inform Assoc* 2011; **18**: 449–58.
- 91 Coleman JJ, Pontefract SK. Adverse drug reactions. *Clin Med (Lond)* 2016; **16**: 481–85.
- 92 Elshawi R, Al-Mallah MH, Sakr S. On the interpretability of machine learning-based model for predicting hypertension. *BMC Med Inform Decis Mak* 2019; **19**: 146.
- 93 Huang K, Altosaar J, Ranganath R. ClinicalBERT: modeling clinical notes and predicting hospital readmission. *arXiv* 2019; published online April 10. <https://arxiv.org/abs/1904.05342> (preprint).
- 94 Pirmohamed M. Pharmacogenetics and pharmacogenomics. *Br J Clin Pharmacol* 2001; **52**: 345–47.
- 95 Dean L. Amitriptyline therapy and CYP2D6 and CYP2C19 genotype. In: Pratt VM, Scott SA, Pirmohamed M, et al, eds. Medical genetics summaries. Bethesda, MD: National Center for Biotechnology Information; March 23, 2017.
- 96 Zanger UM, Schwab M. Cytochrome P450 enzymes in drug metabolism: regulation of gene expression, enzyme activities, and impact of genetic variation. *Pharmacol Ther* 2013; **138**: 103–41.
- 97 Pawankar R, Canonica GW, Holgate ST, Lockey RF, Blaiss M. World Allergy Organization (WAO) white book on allergy. Milwaukee, WI: World Allergy Organization, 2011.
- 98 Blumenthal KG, Shenoy ES, Varughese CA, Hurwitz S, Hooper DC, Banerji A. Impact of a clinical guideline for prescribing antibiotics to inpatients reporting penicillin or cephalosporin allergy. *Ann Allergy Asthma Immunol* 2015; **115**: 294–300.e2.
- 99 Siontis GC, Tzoulaki I, Castaldi PJ, Ioannidis JP. External validation of new risk prediction models is infrequent and reveals worse prognostic discrimination. *J Clin Epidemiol* 2015; **68**: 25–34.

Copyright © 2021 The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY 4.0 license.

THE LANCET

Digital Health

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed.
We post it as supplied by the authors.

Supplement to: Syrowatka A, Song W, Amato MG, et al. Key use cases for artificial intelligence to reduce the frequency of adverse drug events: a scoping review. *Lancet Digit Health* 2021; published online Nov 23. [https://doi.org/10.1016/S2589-7500\(21\)00229-6](https://doi.org/10.1016/S2589-7500(21)00229-6).

APPENDIX for

“Key Use Cases for Artificial Intelligence to Reduce the Frequency of Adverse Drug Events:

A Scoping Review”

Appendix Table 1. Inclusion and exclusion criteria

Include	Exclude
Articles describing the application of AI for prediction or early detection to reduce the frequency of ADEs - An ADE was defined as “an injury resulting from medical intervention related to a drug” and included: adverse drug reactions and adverse events related to medication errors	Articles reporting on ADEs related to: - Vaccines - Dietary supplements - Experimental drugs not yet approved for use - Recreational use of medications, defined as the use of medications that require a prescription but that were not prescribed for the individual
Modern artificial intelligence techniques: Adaptive boosting, Bayesian, decision trees, fuzzy logic, gradient boosting, k-means clustering, natural language processing, nearest neighbors, neural networks, principal component analysis, random forests, reinforcement learning, simulated treatment learning, support vector machines	Traditional artificial intelligence approaches, such as: - Rule-based systems - Logistic and linear regression
	Sample size less than 200 patients
Inpatient, outpatient, community, and home settings	Studies focused on ADE monitoring or post-marketing surveillance
Adult populations (18 years and older)	Child and youth populations (under the age of 18 years)
Peer-reviewed articles describing: - Original research - Structured reviews of the literature reported in accordance with PRISMA guidelines	Not published in the English language
	Did not report standard performance metrics (e.g., accuracy or AUC) or comparisons with a control group for at least one modern AI model

Appendix Note 1. PubMed (NCBI) Search Strategy

((("Drug Therapy"[Mesh] OR "drug therapy"[Subheading] OR "Pharmacology"[Mesh] OR "Pharmaceutical Preparations"[Mesh] OR "Drug Monitoring"[Mesh] OR medication*[tiab] OR drug*[tiab] OR pharmaceutic*[tiab] OR pharmaco*[tiab])) AND ("adverse effects"[Subheading] OR "Long Term Adverse Effects"[Mesh] OR adverse effect*[tiab] OR adverse event*[tiab] OR side effect*[tiab] OR adverse reaction*[tiab] OR complication*[tiab] OR contraindication*[tiab] OR poison*[tiab] OR toxicit*[tiab] OR overdose*[tiab])) OR ("chemically induced"[Subheading] OR "Drug Overdose"[Mesh] OR "Drug-Related Side Effects and Adverse Reactions"[Mesh] OR "Adverse Drug Reaction Reporting Systems"[Mesh] OR "Drug Eruptions"[Mesh] OR "Drug Hypersensitivity"[Mesh] OR "Drug Hypersensitivity Syndrome"[Mesh] OR "Drug Interactions"[Mesh] OR "Contraindications, Drug"[Mesh] OR "Medication Errors"[Mesh] OR "Medication Reconciliation"[Mesh] OR "Pharmacovigilance"[Mesh] OR drug reaction*[tiab] OR adverse drug*[tiab] OR drug hypersensitivit*[tiab] OR medication error*[tiab] OR pharmacovigilance[tiab] OR Stevens Johnson[tiab] OR Lyell*[tiab] OR "Stevens-Johnson Syndrome"[MeSH] OR epidermal necrolysis*[tiab] OR "Anemia, Hemolytic"[MeSH] OR "Thrombocytopenia"[MeSH] OR "Neutropenia"[MeSH] OR "Eosinophilia"[MeSH] OR Thrombocytopeni*[tiab] OR Neutropeni*[tiab] OR Eosinophili*[tiab] OR "Cardiotoxicity"[Mesh] OR cardiotoxic*[tiab] OR "Neurotoxicity Syndromes"[Mesh] OR neurotoxic*[tiab] OR hepatotoxic*[tiab] OR nephrotoxic*[tiab])) AND ("Artificial Intelligence"[mesh] OR artificial intelligence*[tiab] OR ai model*[tiab] OR "Pattern Recognition, Automated"[mesh] OR pattern recognition[tiab] OR pattern identification[tiab] OR computational intelligence*[tiab] OR machine intelligence*[tiab] OR intelligent system*[tiab] OR computer reasoning[tiab] OR expert system*[tiab] OR machine learning[tiab] OR supervised learning[tiab] OR unsupervised learning[tiab] OR deep learning[tiab] OR decision tree*[tiab] OR random forest*[tiab] OR neural network*[tiab] OR perceptron*[tiab] OR connectionist*[tiab] OR adversarial

network*[tiab] OR graph convolutional network*[tiab] OR support vector*[tiab] OR multiple kernel[tiab]
 OR multi kernel[tiab] OR multikernel[tiab] OR structured kernel[tiab] OR knn[tiab] OR rnn[tiab] OR
 nearest neighb*[tiab] OR kmeans[tiab] OR k-means[tiab] OR k means[tiab] OR ensemble learning[tiab]
 OR ensemble model*[tiab] OR transfer learning[tiab] OR reinforcement learning[tiab] OR language
 processing[tiab] OR language processor*[tiab] OR bayes*[tiab] OR fuzzy logic[tiab])
 AND ("Risk Factors"[Mesh] OR "Forecasting"[Mesh] OR predict*[tiab] OR prevent*[tiab] or detect*[tiab]
 OR identif*[tiab] OR risk*[tiab])
 NOT ("Animals"[mesh] NOT "Humans"[mesh])
 Restricted to ENGLISH LANGUAGE and PUBLISHED January 1, 1998 to September 9, 2020.

Appendix Note 2. EMBASE (Elsevier) Search Strategy

((('drug therapy'/exp OR 'pharmacology'/exp OR 'pharmaceutics'/exp OR 'drug'/exp OR 'drug
 monitoring'/exp OR 'medication*':ab,ti OR 'drug*':ab,ti OR 'pharmaceutic*':ab,ti OR 'pharmaco*':ab,ti)
 AND ('adverse event'/exp OR 'side effect'/exp OR 'toxicity'/exp OR 'adverse effect*':ab,ti OR 'adverse
 event*':ab,ti OR 'side effect*':ab,ti OR 'adverse reaction*':ab,ti OR 'complication*':ab,ti OR
 'contraindication*':ab,ti OR 'poison*':ab,ti OR 'toxicit*':ab,ti OR 'overdose*':ab,ti)
 OR 'chemically induced'/exp OR 'drug overdose'/exp OR 'adverse drug reaction'/exp OR
 'pharmacovigilance'/exp OR 'drug interaction'/exp OR 'drug contraindication'/exp OR 'medication
 error'/exp OR 'medication therapy management'/exp OR 'drug intoxication'/exp OR 'drug toxicity'/exp
 OR 'drug reaction*':ab,ti OR 'adverse drug*':ab,ti OR 'drug hypersensitivit*':ab,ti OR 'medication
 error*':ab,ti OR 'pharmacovigilance*':ab,ti OR 'stevens johnson*':ab,ti OR 'lyell*':ab,ti OR 'stevens
 johnson syndrome'/exp OR 'epidermal necrolysis*':ab,ti OR 'hemolytic anemia'/exp OR
 'thrombocytopenia'/exp OR 'neutropenia'/exp OR 'eosinophilia'/exp OR 'thrombocytopeni*':ab,ti OR
 'neutropeni*':ab,ti OR 'eosinophili*':ab,ti OR 'cardiotoxicity'/exp OR 'cardiotoxic*':ab,ti OR

'neurotoxicity'/exp OR 'neurotoxic*':ab,ti OR 'liver toxicity'/exp OR 'hepatotoxic*':ab,ti OR
'nephrotoxicity'/exp OR 'nephrotoxic*':ab,ti)

AND ('artificial intelligence'/exp OR 'artificial intelligence*':ab,ti OR 'ai model*':ab,ti OR 'pattern
recognition':ab,ti OR 'pattern identification':ab,ti OR 'computational intelligence*':ab,ti OR 'machine
intelligence*':ab,ti OR 'intelligent system*':ab,ti OR 'computer reasoning':ab,ti OR 'expert system*':ab,ti
OR 'machine learning'/exp OR 'machine learning':ab,ti OR 'supervised learning':ab,ti OR 'unsupervised
learning':ab,ti OR 'deep learning':ab,ti OR 'decision tree*':ab,ti OR 'random forest':ab,ti OR 'neural
network*':ab,ti OR 'perceptron*':ab,ti OR 'connectionist*':ab,ti OR 'adversarial network*':ab,ti OR
'graph convolutional network*':ab,ti OR 'support vector*':ab,ti OR 'multiple kernel':ab,ti OR 'multi
kernel':ab,ti OR 'multikernel':ab,ti OR 'structured kernel':ab,ti OR 'knn':ab,ti OR 'rnn':ab,ti OR 'nearest
neighb*':ab,ti OR 'kmeans':ab,ti OR 'k-means':ab,ti OR 'k means':ab,ti OR 'ensemble learning':ab,ti OR
'ensemble model*':ab,ti OR 'transfer learning':ab,ti OR 'reinforcement learning':ab,ti OR 'language
processing':ab,ti OR 'language processor*':ab,ti OR 'bayes*':ab,ti OR 'fuzzy logic':ab,ti)

AND ('risk factor'/exp OR 'prediction and forecasting'/exp OR 'predict*':ab,ti OR 'prevent*':ab,ti OR
'detect*':ab,ti OR 'identif*':ab,ti OR 'risk*':ab,ti)

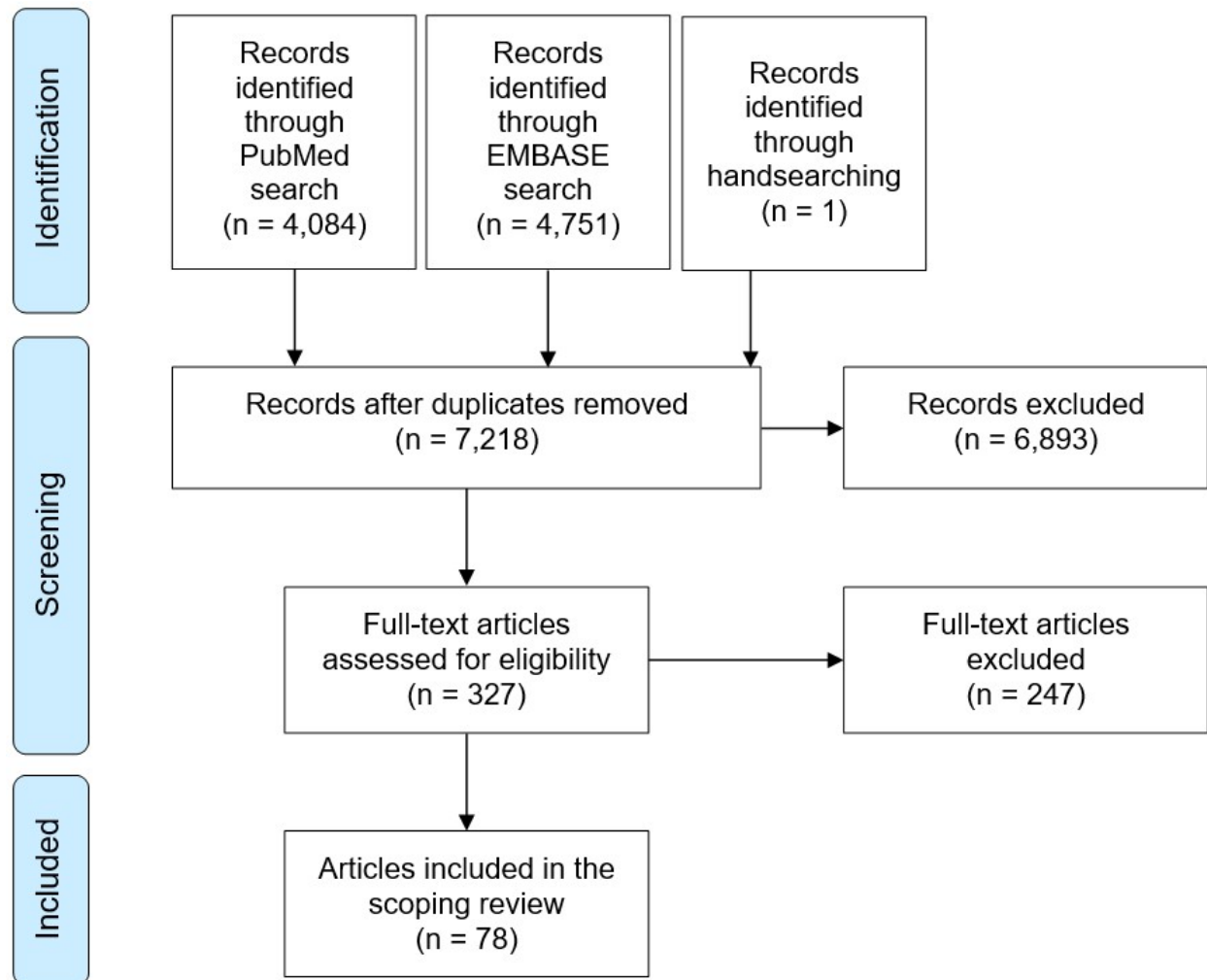
AND 'human'/exp

NOT 'conference abstract'/it

AND [english]/lim

AND [1-1-1998]/sd NOT [10-9-2020]/sd

AND [embase]/lim



Appendix Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flow

Diagram showing disposition of articles

Appendix Table 2. Data Abstraction of Study Characteristics

First Author Name	Year	Article Title	Relevant Domains	Country or Region	Study Population	Sample Size	Medication Classification	Outcome	Description of ADE	PMID or DOI
Almas M	2018	Prediction of therapeutic response to pregabalin in subjects with neuropathic pain	Prediction	USA	Cohort of patients with neuropathic pain on pregabalin	4,227	Anticonvulsants	Treatment Response	N/A	30183410
Bagattini F	2019	A classification framework for exploiting sparse multi-variate temporal features with application to adverse drug event detection in medical records	Detection	Sweden	Case-control study of inpatients	13,757	Multiple Classes or Not Specified	ADE	Multiple ADEs	30630486
Blangero Y	2020	A Bayesian method to estimate the optimal threshold of a marker used to select patients' treatment	Prediction	France	Cohort of patients on chemotherapy with stage III colon adenocarcinoma	1,068	Antineoplastics	Most Appropriate Treatment	N/A	10.1177/0962280218821394
Bondareva IB	2011	Predictability of individualized dosage regimens of carbamazepine and valproate mono- and combination therapy	Prediction	Russia	Cohort of patients with epilepsy on mono or combination therapy of carbamazepine and valproate	2,050	Anticonvulsants	Optimal Dose	N/A	21062333
Chen SS	2019	Optimizing Levothyroxine Dose Adjustment After Thyroidectomy With a Decision Tree	Prediction	USA	Retrospective cohort of patients who received thyroidectomy and were prescribed levothyroxine	320	Thyroid Hormones	Optimal Dose	N/A	31279993
Chen YF	2018	Design of a Clinical Decision Support System for Fracture Prediction Using Imbalanced Dataset	Prediction	Taiwan	Retrospective cohort of patients with asthma, COPD, or bronchiectasis on inhaled corticosteroids	11,645	Glucocorticoids	ADE	Fall with Injury	29765586
Cheng P	2017	Predicting Inpatient Acute Kidney Injury over Different Time Horizons: How Early and Accurate?	Prediction	USA	Retrospective cohort of patients with acute kidney disease	33,703	Multiple Classes or Not Specified	ADE	Renal	29854121
Chiang WH	2020	Drug-drug interaction prediction based on co-medication patterns and graph matching	Prediction	USA	Case reports of patients who experienced an adverse drug reaction	1,540,732	Multiple Classes or Not Specified	ADE	Nervous System	10.1504/IJCBDD.2020.105093
Chiriac AM	2018	Designing Predictive Models for Beta-Lactam Allergy Using the Drug Allergy and Hypersensitivity Database	Prediction	France	Cohort of patients with suspected beta-lactam allergy	2,191	Antibiotics	ADE	Allergic Reaction	28739365
Choudhury O	2019	Predicting Adverse Drug Reactions on Distributed Health Data using Federated Learning	Prediction	USA	Cohort of patients prescribed opioids or antipsychotic medications	1,247,722	Analgesics and Antipsychotics	ADE	Opioid Overdose or Opioid Use Disorder	32308824
Desrochers J	2017	Bayesian Forecasting Tool to Predict the Need for Antidote in Acute Acetaminophen Overdose	Prediction	USA	Retrospective cohort of patients with acute acetaminophen overdose	432	Analgesics	Most Appropriate Treatment	N/A	28609563
Dong X	2019	Machine Learning Based Opioid Overdose Prediction Using Electronic Health Records	Prediction	USA	Retrospective cohort of inpatients at risk of opioid overdose	550,000	Analgesics	ADE	Opioid Overdose or Opioid Use Disorder	32308832
Duan T	2019	Clinical Value of Predicting Individual Treatment Effects for Intensive Blood Pressure Therapy	Prediction	USA	Cohort of patients with cardiovascular disease	14,094	Cardiovascular	Treatment Response	N/A	30857410

First Author Name	Year	Article Title	Relevant Domains	Country or Region	Study Population	Sample Size	Medication Classification	Outcome	Description of ADE	PMID or DOI
Ekpenyong ME	2019	Fuzzy-multidimensional deep learning for efficient prediction of patient response to antiretroviral therapy	Prediction	Nigeria	Retrospective cohort of patients with HIV on antiretroviral therapy	2,822	Antivirals	Treatment Response	N/A	31372545
Ellis RJ	2019	Predicting opioid dependence from electronic health records with machine learning	Prediction	USA	Case-control study of patients with opioid dependence and individuals without opioid dependence	51,040	Analgesics	ADE	Opioid Overdose or Opioid Use Disorder	30728857
Escandell-Montero P	2014	Optimization of anemia treatment in hemodialysis patients via reinforcement learning	Prediction	Multiple Countries (Spain, Germany, Austria)	Cohort of simulated hemodialysis patients treated with darbepoetin alfa	5,060	Colony Stimulating Factors	Optimal Dose	N/A	25091172
Ferroni P [a]	2017	Validation of a Machine Learning Approach for Venous Thromboembolism Risk Prediction in Oncology	Prediction	Italy	Cohort of outpatients with cancer at risk for venous thromboembolism	608	Antineoplastics	ADE	Cardiovascular	29104344
Ferroni P [b]	2017	Risk Assessment for Venous Thromboembolism in Chemotherapy-Treated Ambulatory Cancer Patients	Prediction	Italy	Cohort of ambulatory cancer patients with primary or relapsing/recurrent solid cancers	1,179	Antineoplastics	ADE	Cardiovascular	27491558
Garcia SL	2020	Prediction of Nephrotoxicity Associated With Cisplatin-Based Chemotherapy in Testicular Cancer Patients	Prediction	Denmark	Cohort of patients with testicular cancer on cisplatin-based chemotherapy	433	Antineoplastics	ADE	Renal	32617516
Gudin J	2020	Reducing Opioid Prescriptions by Identifying Responders on Topical Analgesic Treatment Using an Individualized Medicine and Predictive Analytics Approach	Prediction	USA	Retrospective cohort of patients with chronic pain on topical analgesics	631	Analgesics	Treatment Response	N/A	32547186
Harrison RNS	2017	Development of multivariable models to predict change in Body Mass Index within a clinical trial population of psychotic individuals	Prediction	United Kingdom	Clinical trial participants with a psychotic disorder	284	Antipsychotics	ADE	Weight Gain	29116126
Hasan S	2011	Automatic detection of omissions in medication lists	Detection	USA	Retrospective cohort of patients prescribed medications at long-term care clinics	419	Multiple Classes or Not Specified	ADE	Not Specified	21447497
Hastings JS	2020	Predicting high-risk opioid prescriptions before they are given	Prediction	USA	Retrospective cohort of patients prescribed opioids	80,768	Analgesics	ADE	Opioid Overdose or Opioid Use Disorder	31937665
Hatzakis GE	2005	Neural Network-longitudinal assessment of the Electronic Anti-Retroviral Therapy (EARTH) Cohort to follow response to HIV-treatment	Prediction	Multiple Countries (Canada, Greece, Cyprus, Martinique, India)	Retrospective cohort of patients with HIV on anti-retroviral therapy	595	Antivirals	Treatment Response	N/A	16779050

First Author Name	Year	Article Title	Relevant Domains	Country or Region	Study Population	Sample Size	Medication Classification	Outcome	Description of ADE	PMID or DOI
Hoang T	2018	Supervised signal detection for adverse drug reactions in medication dispensing data	Detection	Australia	Cohort of patients dispensed prescription medications	1,807,159	Multiple Classes or Not Specified	ADE	Not Specified	29852965
Hu YH [a]	2012	Predicting warfarin dosage from clinical data: a supervised learning approach	Prediction	Taiwan	Retrospective cohort of inpatients prescribed warfarin	587	Anticoagulants	Optimal Dose	N/A	22537823
Hu YH [b]	2018	Improvement of Adequate Digoxin Dosage: An Application of Machine Learning Approach	Prediction	Taiwan	Retrospective cohort of inpatients prescribed digoxin	307	Cardiovascular	Optimal Dose	N/A	30210752
Huang K	2015	Chemotherapy-induced neutropenia during adjuvant treatment for cervical cancer patients: development and validation of a prediction model	Prediction	China	Case-control study of patients with cervical cancer and chemotherapy-induced neutropenia	335	Antineoplastics	ADE	Abnormal Blood Count	26379877
Hung CY	2019	Predicting Gastrointestinal Bleeding Events from Multimodal In-Hospital Electronic Health Records Using Deep Fusion Networks	Prediction	Taiwan	Cohort of inpatients and outpatients prescribed anticoagulants or antiplatelets	16,757	Anticoagulants	ADE	Hemorrhage	31946393
Imai S [a]	2017	Usefulness of a decision tree model for the analysis of adverse drug reactions: Evaluation of a risk prediction model of vancomycin-associated nephrotoxicity constructed using a data mining procedure	Prediction	Japan	Retrospective cohort of patients who received intravenous vancomycin	592	Antibiotics	ADE	Renal	28544476
Imai S [b]	2019	Construction of a flow chart-like risk prediction model of ganciclovir-induced neutropaenia including severity grade: A data mining approach using decision tree	Prediction	Japan	Retrospective cohort of patients who received intravenous ganciclovir	396	Antivirals	ADE	Abnormal Blood Count	31148201
Imai S [c]	2019	Construction of a risk prediction model of vancomycin-associated nephrotoxicity to be used at the time of initial therapeutic drug monitoring: A data mining analysis using a decision tree model	Prediction	Japan	Retrospective cohort of patients who received intravenous vancomycin	402	Antibiotics	ADE	Renal	30280456
Imai S [d]	2020	Validation of the usefulness of artificial neural networks for risk prediction of adverse drug reactions used for individual patients in clinical practice	Prediction	Japan	Retrospective cohort of patients who received intravenous vancomycin	1,141	Antibiotics	ADE	Renal	32726360
Jeong E	2018	Machine learning model combining features from algorithms with different analytical methodologies to detect laboratory-event-related adverse drug reaction signals	Detection	South Korea	Cohort of inpatients	475,417	Multiple Classes or Not Specified	ADE	Not Specified	30462745
Kang AR	2020	Development of a prediction model for hypotension after induction of anesthesia using machine learning	Prediction	South Korea	Retrospective cohort of inpatients who underwent laparoscopic cholecystectomy and were induced with anesthesia	222	Anesthetics and Analgesics	ADE	Cardiovascular	32298292
Ke WS	2010	Pharmacogenomics of drug efficacy in the interferon treatment of chronic hepatitis C using classification algorithms	Prediction	Taiwan	Cohort of patients with chronic hepatitis C	523	Immunomodulators and Antivirals	Treatment Response	N/A	21918625
Kendale S	2018	Supervised Machine-learning Predictive Analytics for Prediction of Postinduction Hypotension	Prediction	USA	Retrospective cohort of patients who underwent any procedure that required general anesthesia	13,323	Anesthetics and Analgesics	ADE	Cardiovascular	30074930

First Author Name	Year	Article Title	Relevant Domains	Country or Region	Study Population	Sample Size	Medication Classification	Outcome	Description of ADE	PMID or DOI
König R	2019	Macrolide combination therapy for patients hospitalised with community-acquired pneumonia? An individualised approach supported by machine learning	Prediction	Germany	Cohort of patients with community-acquired pneumonia	4,898	Antibiotics	Most Appropriate Treatment	N/A	31537702
Kraff S [a]	2015	Pharmacokinetically based dosing of weekly paclitaxel to reduce drug-related neurotoxicity based on a single sample strategy	Prediction	The Netherlands	Retrospective cohort of patients with solid tumors on paclitaxel	200	Antineoplastics	Optimal Dose	N/A	25761456
Kraff S [b]	2015	Excel-Based Tool for Pharmacokinetically Guided Dose Adjustment of Paclitaxel	Prediction	Multiple Countries (Europe, Canada)	Retrospective cohort of patients receiving paclitaxel	250	Antineoplastics	Optimal Dose	N/A	25774704
Lan TH	2008	Performance of a neuro-fuzzy model in predicting weight changes of chronic schizophrenic patients exposed to antipsychotics	Prediction	Taiwan	Cohort of inpatients meeting DSM-IV diagnosis of schizophrenia, treated with antipsychotics, either typical or atypical, for more than 2 years	220	Antipsychotics	ADE	Weight Gain	10.1038/sj.mp.4002128
Levy AE	2019	Applications of machine learning in decision analysis for dose management for dofetilide	Prediction	USA	Retrospective cohort of patients initiating dofetilide	354	Cardiovascular	Optimal Dose	N/A	31891645
Li X	2019	Predictive modeling of hypoglycemia for clinical decision support in evaluating outpatients with diabetes mellitus	Prediction	USA	Retrospective cohort of patients with hypoglycemia	38,780	Antihyperglycemics	ADE	Metabolic or Endocrine	31234649
Lin CC	2010	Easy and low-cost identification of metabolic syndrome in patients treated with second-generation antipsychotics: artificial neural network and logistic regression models	Detection	Taiwan	Cohort of inpatients with a diagnosis of schizophrenia or schizoaffective disorder treated with second-generation antipsychotics for at least 6 months	452	Antipsychotics	ADE	Metabolic or Endocrine	19814949
Lin CS	2008	Predicting hypotensive episodes during spinal anesthesia with the application of artificial neural networks	Prediction	Taiwan	Retrospective cohort of surgical inpatients who received spinal anesthesia	1,501	Anesthetics	ADE	Cardiovascular	18760495
Lin E	2008	A Support Vector Machine Approach to Assess Drug Efficacy of Interferon- α and Ribavirin Combination Therapy	Prediction	Taiwan	Retrospective cohort of patients with hepatitis C on Interferon- α and Ribavirin	523	Immunomodulators and Antivirals	Treatment Response	N/A	10.1007/BF03256287
Liu KE	2014	Improvement of Adequate Use of Warfarin for the Elderly Using Decision Tree-based Approaches	Prediction	Taiwan	Retrospective cohort of inpatients who received warfarin	377	Anticoagulants	Optimal Dose	N/A	24136011
Liu L	2018	An interpretable boosting model to predict side effects of analgesics for osteoarthritis	Prediction	USA	Retrospective cohort of patients with osteoarthritis	4,350	Analgesics	ADE	Cardiovascular	30463545
Lo-Ciganic WH [a]	2019	Evaluation of Machine-Learning Algorithms for Predicting Opioid Overdose Risk Among Medicare Beneficiaries With Opioid Prescriptions	Prediction	USA	Cohort of Medicare beneficiaries without cancer who filled at least one opioid prescription	560,057	Analgesics	ADE	Opioid Overdose or Opioid Use Disorder	30901048

First Author Name	Year	Article Title	Relevant Domains	Country or Region	Study Population	Sample Size	Medication Classification	Outcome	Description of ADE	PMID or DOI
Lo-Ciganic WH [b]	2020	Using machine learning to predict risk of incident opioid use disorder among fee-for-service Medicare beneficiaries: A prognostic study	Prediction	USA	Cohort of Medicare beneficiaries without cancer who filled at least one opioid prescription	361,527	Analgesics	ADE	Opioid Overdose or Opioid Use Disorder	32678860
Ma Z	2018	Ensemble of machine learning algorithms using the stacked generalization approach to estimate the warfarin dose	Prediction	USA	Cohort of chronic warfarin users	5,743	Anticoagulants	Optimal Dose	N/A	30339708
Maiellaro PA	2004	Artificial Neural Networks for the Prediction of Response to Interferon Plus Ribavirin Treatment in Patients with Chronic Hepatitis C	Prediction	Italy	Retrospective cohort of patients with chronic hepatitis C	300	Immunomodulators and Antivirals	Treatment Response	N/A	15279549
Marchetti M	2020	Rapid and accurate Bayesian diagnosis of heparin-induced thrombocytopenia	Detection	Switzerland	3 cohorts (retrospective derivation cohort, prospective derivation cohort, and prospective validation cohort) of patients with suspected heparin-induced thrombocytopenia	1,213	Anticoagulants	ADE	Abnormal Blood Count	31945147
Marquet P	2018	Pharmacokinetic Therapeutic Drug Monitoring of Advagraf in More Than 500 Adult Renal Transplant Patients, Using an Expert System Online	Prediction	France	Retrospective cohort study of renal transplant patients who received Advagraf	530	Immunosuppressants	Optimal Dose	N/A	29505493
Moreno EM	2020	Usefulness of an Artificial Neural Network in the Prediction of β -Lactam Allergy	Prediction	Spain	Cohort of patients with suspected beta-lactam allergy	1,271	Antibiotics	ADE	Allergic Reaction	32702519
Murphree DH	2018	Stacked Classifiers for Individualized Prediction of Glycemic Control Following Initiation of Metformin Therapy in Type 2 Diabetes	Prediction	USA	Retrospective cohort of patients with type 2 diabetes	12,147	Antihyperglycemics	Treatment Response	N/A	30347342
Ng T	2012	A Clinical Decision Support Tool To Predict Survival in Cancer Patients beyond 120 Days after Palliative Chemotherapy	Prediction	Singapore	Retrospective cohort of terminally ill cancer patients on chemotherapy	325	Antineoplastics	Treatment Response	N/A	22690950
Nickerson P	2016	Deep Neural Network Architectures for Forecasting Analgesic Response	Prediction	USA	Retrospective cohort of patients who received non-ambulatory/non-obstetric surgery	26,090	Anesthetics and Analgesics	ADE and Treatment Response	Genitourinary	28268935
Öztaner SM	2015	A Bayesian Estimation Framework for Pharmacogenomics Driven Warfarin Dosing: A Comparative Study	Prediction	Turkey	Retrospective cohort of patients prescribed warfarin chronically	4,580	Anticoagulants	Optimal Dose	N/A	25020183
Pavani A	2016	Artificial neural network-based pharmacogenomic algorithm for warfarin dose optimization	Prediction	India	Cohort of patients prescribed warfarin	447	Anticoagulants	Optimal Dose	N/A	26666467
Preston SL	1998	Levofloxacin Population Pharmacokinetics and Creation of a Demographic Model for Prediction of Individual Drug Clearance in Patients with Serious Community-Acquired Infection	Prediction	USA	Retrospective cohort of patients treated with levofloxacin for community-acquired infection of the skin, respiratory tract, or urinary tract	272	Antibiotics	Optimal Dose	N/A	9593134

First Author Name	Year	Article Title	Relevant Domains	Country or Region	Study Population	Sample Size	Medication Classification	Outcome	Description of ADE	PMID or DOI
Rozenblum R	2020	Using a Machine Learning System to Identify and Prevent Medication Prescribing Errors: A Clinical and Cost Analysis Evaluation	Detection	USA	Cohort of outpatients	747,985 (sub-sample of 300 charts)	Multiple Classes or Not Specified	ADE	Not Specified	31786147
Sauer CM	2018	Feature selection and prediction of treatment failure in tuberculosis	Prediction	Multiple Countries (Azerbaijan, Belarus, Moldova, Georgia, Romania)	Retrospective cohort of patients with tuberculosis	587	Antibiotics	Treatment Response	N/A	30458029
Schiff GD	2017	Screening for medication errors using an outlier detection system	Detection	USA	Cohort of outpatients	747,985 (sub-sample of 300 charts)	Multiple Classes or Not Specified	ADE	Not Specified	28104826
Segal G	2019	Reducing drug prescription errors and adverse drug events by application of a probabilistic, machine-learning based clinical decision support system in an inpatient setting	Detection	Israel	Prospective cohort of inpatients	3,160	Multiple Classes or Not Specified	ADE	Not Specified	31390471
Sheyn D	2019	Development and Validation of a Machine Learning Algorithm for Predicting Response to Anticholinergic Medications for Overactive Bladder Syndrome	Prediction	USA	Retrospective cohort of female patients with overactive bladder syndrome treated with anticholinergics	641	Urinary Antispasmodic - Smooth Muscle Relaxants	Treatment Response	N/A	31599833
Smith JC	2018	Evaluation of a Novel System to Enhance Clinicians' Recognition of Preadmission Adverse Drug Reactions	Detection	USA	Cohort of inpatients on antihypertensives at admission	4,401	Cardiovascular	ADE	Multiple ADEs	29742757
Speiser JL	2019	Predicting daily outcomes in acetaminophen-induced acute liver failure patients with machine learning techniques	Prediction	USA	Retrospective cohort of patients with acetaminophen-induced acute liver failure	1,042	Analgesics	ADE	Metabolic or Endocrine	31104700
Taft LM	2009	Countering Imbalanced Datasets to Improve Adverse Drug Event Predictive Models in Labor and Delivery	Detection	USA	Retrospective cohort of inpatients admitted for labor and delivery	106,480	Multiple Classes or Not Specified	ADE	Not Specified	18824133
Ubels J	2018	Predicting treatment benefit in multiple myeloma through simulation of alternative treatment effects	Prediction	The Netherlands	Cohort of patients with multiple myeloma treated with thalidomide and melphalan or only melphalan	910	Antineoplastics	Treatment Response	N/A	10.1038/s41467-018-05348-5
Valeanu A	2020	The development of a scoring and ranking strategy for a patient-tailored adverse drug reaction prediction in polypharmacy	Prediction	Romania	Case reports of patients who experienced an adverse drug reaction	82,681	Multiple Classes or Not Specified	ADE	Not Specified	32533040
Waljee AK	2017	Predicting Hospitalization and Outpatient Corticosteroid Use in Inflammatory Bowel Disease Patients Using Machine Learning	Prediction	USA	Retrospective cohort study of inpatients and outpatients with inflammatory bowel disease	20,368	Glucocorticoids and Immunosuppressants	Treatment Response	N/A	29272474
Wan YW	2010	Hybrid Models Identified a 12-Gene Signature for Lung Cancer Prognosis and Chemoresponse Prediction	Prediction	USA	Retrospective cohort of patients with lung adenocarcinoma	442	Antineoplastics	Treatment Response	N/A	20808922

First Author Name	Year	Article Title	Relevant Domains	Country or Region	Study Population	Sample Size	Medication Classification	Outcome	Description of ADE	PMID or DOI
Wu W	2019	Multiview Cluster Analysis Identifies Variable Corticosteroid Response Phenotypes in Severe Asthma	Prediction	USA	Retrospective cohort of patients with severe asthma on corticosteroids	528	Glucocorticoids	Treatment Response	N/A	30682261
Yang X	2019	Identifying Cancer Patients at Risk for Heart Failure Using Machine Learning Methods	Prediction	USA	Case-control study of patients with cancer	17,446	Antineoplastics	ADE	Cardiovascular	32308890
Yin JY	2016	Prediction models for platinum-based chemotherapy response and toxicity in advanced NSCLC patients	Prediction	China	Cohort of patients with advanced non-small cell lung cancer on platinum-based chemotherapy	525	Antineoplastics	ADE and Treatment Response	Multiple ADEs	27126360
Yin WJ	2017	Preprocedural Prediction Model for Contrast-Induced Nephropathy Patients	Prediction	China	Case-control study of inpatients who received contrast media for coronary angiography, percutaneous coronary intervention, computerized tomography scan or endovascular procedures	8,800	Contrast Agents	ADE	Renal	28159819
Zasowski EJ	2018	Identification of Vancomycin Exposure-Toxicity Thresholds in Hospitalized Patients Receiving Intravenous Vancomycin	Prediction	USA	Retrospective cohort of patients with suspected bacteremia or pneumonia who received intravenous vancomycin	323	Antibiotics	ADE	Renal	29084753

Appendix Table 3. Data Abstraction of AI Models, Study Ratings, and Data Sources

First Author Name	AI Model Types	Number of Variables	AI Model Performance	Validation Approach	Quality Assessment	Study Phase	Health Record Data	Genetic Data	Administrative Health Data	Publicly Available Data	Secondary Use of Research Data	Other Data Sources
Almas M	Bayesian, Random Forest	17	Week 5: Pain response: Random forest, partial least squares, logistic regression: AUC=0.91 Week 8: Pain response: Partial least squares, logistic regression: AUC=0.88 Week 12: Pain response: Partial least squares: AUC=0.87 Pain-related sleep interference: Random forest: AUC=0.93 Patient global impression of change: Logistic regression: AUC=0.77	Cross-validation (10-fold) Sample splitting (33% validation)	3	0	No	No	No	No	Yes	
Bagattini F	Random Forest	Exact number unknown	AUCs ranged from 0.59 to 0.87 depending on adverse drug event	Cross-validation (10-fold)	3	0	Yes, EHR	No	No	No	No	
Blangero Y	Bayesian	Exact number unknown	Coverage probability=95%	N/A	3	1	No	Yes	No	No	Yes	
Bondareva IB	Bayesian	Exact number unknown	Mean absolute prediction error (MAPE%): CBZ monotherapy=17.4% VPA monotherapy=17.7% CBZ with VPA=18.3% VPA with CBZ=21.7%	Validation study	3	1	Yes	No	No	No	No	
Chen SS	Decision Tree	1	Accuracy=75%	Cross-validation (10-fold) Sample splitting (33% validation)	3	0	Yes, EHR	No	No	No	No	
Chen YF	K-Nearest Neighbors, Support Vector Machine	20	Accuracy=63-68%, AUC=0.75-0.76	Cross-validation (10-fold) Sample splitting (50% validation)	3	2	No	No	Yes	No	No	
Cheng P	Adaptive Boosting, Random Forest	2,048 (considered)	Random forest: AUC=0.77	Cross-validation (10-fold)	3	0	Yes, EHR	No	Yes	No	No	
Chiang WH	Support Vector Machine	1,210	Accuracy=0.84, AUC=0.91	Cross-validation (5-fold)	3	0	No	No	No	Yes	No	
Chiriak AM	Decision Tree	4	AUC=0.73	External validation	2	1	Yes	No	No	No	No	

First Author Name	AI Model Types	Number of Variables	AI Model Performance	Validation Approach	Quality Assessment	Study Phase	Health Record Data	Genetic Data	Administrative Health Data	Publicly Available Data	Secondary Use of Research Data	Other Data Sources
Choudhury O	Neural Network, Support Vector Machine	Exact number unknown	Opioid data: neural network: Accuracy=74% Antipsychotic data: neural network: Accuracy=71%	Cross-validation (5-fold) Sample splitting (30% validation)	3	1	Yes, EHR	No	Yes	No	No	
Desrochers J	Bayesian	Exact number unknown	Accuracy=42%	Independent validation cohort	3	0	Yes	No	No	No	No	
Dong X	Decision Tree, Neural Network, Random Forest	12,407	SPARCS: Random forest: Accuracy=96%, AUC=95% Neural network: Accuracy=97%, AUC=94% Health Facts: Random forest: Accuracy=99%, AUC=95% Neural network: Accuracy=98%, AUC=95%	Sample splitting (10% validation)	3	0	Yes, EHR	No	Yes	No	No	
Duan T	Random Forest	17	AUC=0.60	RF base learners with out-of-sample participant for prediction Correction for "optimism"	3	0	No	No	No	No	Yes	
Ekpenyong ME	Neural Network	24	Stanford database: Accuracy=97% Akwa-Ibom database: Accuracy=99%	Sample splitting (10% validation)	3	0	No	No	No	Yes	No	
Ellis RJ	Random Forest	95	AUC=92%	Cross-validation (10-fold)	3	0	Yes, EHR	No	No	No	No	
Escandell-Montero P	Decision Tree, K-Means Clustering, Reinforcement Learning	11 (considered)	Fitted Q-iteration increased the proportion of patients that were within the targeted range of hemoglobin by 28% Reduced the amount of drug used by 5%	Cross-validation Simulated validation	3	0	No	No	No	No	No	
Ferroni P [a]	Kernel Machine Learning	66	AUC=0.72	Validation study	3	1	Yes	No	No	No	No	
Ferroni P [b]	Support Vector Machine	23	AUCPR=0.21	Cross-validation (3-fold) Sample splitting (30% validation)	3	1	Yes	No	No	No	No	
Garcia SL	Random Forest	17	AUC=0.69	Nested cross-validation Sample splitting	3	1	Yes	Yes	No	No	No	
Gudin J	Support Vector Machine	49	Total drugs change: AUC=0.89 Total interference change: AUC=0.79 Total severity change: AUC=0.74 Total complaints change: AUC=0.83	Cross-validation (5-fold) Sample splitting (20% validation)	3	2	No	No	No	No	Yes	

First Author Name	AI Model Types	Number of Variables	AI Model Performance	Validation Approach	Quality Assessment	Study Phase	Health Record Data	Genetic Data	Administrative Health Data	Publicly Available Data	Secondary Use of Research Data	Other Data Sources
Harrison RNS	Gradient Boosting Machine, K-Nearest Neighbors, Random Forest, Support Vector Machine	8 to 12	K-nearest neighbours: Accuracy=58% Generalised linear model (best overall): Accuracy=60%	Cross-validation (10-fold) Sample splitting (25% validation)	3	0	No	Yes	No	No	Yes	
Hasan S	K-Nearest Neighbors, Principal Component Analysis	Exact number unknown	Identified missing medication in the top-10 list=40-50% Identified therapeutic class of missing medication in the top-10 list=50-65%	Cross-validation	3	0	No	No	Yes	No	No	
Hastings JS	Neural Network	1,301	Neural network: AUC=0.80	Sample splitting (25% validation)	3	1	No	No	Yes	No	No	
Hatzakis GE	Neural Network	Exact number unknown	Prediction of treatment response in never-treated patients: AUC=0.87 Prediction of change in treatment response: AUC=0.63 Prediction of subsequent change in treatment response: AUC=0.72	Cross-validation Sample splitting (5% validation)	3	0	No	No	No	No	Yes	
Hoang T	Decision Tree, Gradient Boosting Machine, Neural Network, Random Forest, Support Vector Machine	728	Gradient boosting machine: AUC=0.82	Cross-validation Sample splitting (25% validation)	3	0	No	No	Yes	Yes	No	
Hu YH [a]	Decision Tree, K-Nearest Neighbors, Neural Network, Support Vector Machine	Exact number unknown	Bagged support vector regression: MAE=0.21 Bagged voting with 4 classifiers: MAE=0.21	Cross-validation (10-fold)	3	1	Yes	No	No	No	No	
Hu YH [b]	Decision Tree, K-Nearest Neighbors, Neural Network, Random Forest	10	Non-DDI group: Random forest: Accuracy=0.84%, AUC=0.91 DDI group: Random forest: Accuracy=81%, AUC=0.89	Cross-validation (10-fold)	3	1	Yes	No	No	No	No	
Huang K	Neural Network	28	Internal validation: Accuracy=89%; AUC=0.90 External validation: Accuracy=82%; AUC=0.78	Internal and external validation	3	1	No	Yes	No	No	Yes	Primary data collection
Hung CY	Gradient Boosting Machine, Neural Network, Random Forest	8 to 64	Neural network: AUC=0.88	Cross-validation (5-fold) Sample splitting	3	1	Yes, EHR	No	No	No	No	
Imai S [a]	Decision Tree	4	Decision tree and logistic regression: Accuracy=87%	Cross-validation (10-fold)	3	1	Yes	No	No	No	No	
Imai S [b]	Decision Tree	3	Decision tree and logistic regression: Accuracy=85%	Cross-validation (10-fold)	3	1	Yes, EHR	No	No	No	No	
Imai S [c]	Decision Tree	4	Accuracy=87%	Cross-validation (10-fold)	3	1	Yes	No	No	No	No	

First Author Name	AI Model Types	Number of Variables	AI Model Performance	Validation Approach	Quality Assessment	Study Phase	Health Record Data	Genetic Data	Administrative Health Data	Publicly Available Data	Secondary Use of Research Data	Other Data Sources
Imai S [d]	Neural Network	8	Accuracy=86%, AUC=0.82	Cross-validation (10-fold)	3	1	Yes, EHR	No	No	No	No	
Jeong E	Neural Network, Random Forest, Support Vector Machine	48	Random forest: AUC=0.82	Cross-validation (10-fold)	3	1	Yes, EHR	No	No	No	No	
Kang AR	Bayesian, Neural Network, Random Forest	89	Random forest: Accuracy=79%, AUC=0.84	Cross-validation (4-fold) Sample splitting (25% validation)	3	1	Yes, EHR	No	No	No	No	Biosensor data
Ke WS	Neural Network	24	Accuracy=80%, AUC=0.72	Cross-validation (10-fold)	3	0	No	Yes	No	No	Yes	
Kendale S	Bayesian, Gradient Boosting Machine, K-Nearest Neighbors, Neural Network, Random Forest, Support Vector Machine	58	Gradient boosting machine: AUC=0.74	Cross-validation (10-fold) Sample splitting (30% validation)	3	1	Yes, EHR	No	No	No	No	
König R	Decision Tree	3	Patients treated according to decision tree recommendations had a lower mortality rate of 27% (OR: 1.83)	Cross-validation (100-fold)	3	0	No	No	No	No	Yes	
Kraff S [a]	Bayesian	5	Potential reduction of grade 2 chemotherapy-induced peripheral neuropathy from 10 to 4%	N/A	3	1	No	No	No	Yes	No	
Kraff S [b]	Bayesian	6	Paclitaxel Tc > 0.05 umol/L: NONMEM: Median RPE (bias)=0.07%; Median RUPE (precision)=10.14% Excel: Median RPE (bias)=2.81%; Median RUPE (precision)=11.44% Paclitaxel Conc (18-30h): NONMEM: Median RPE (bias)=1.08%; Median RUPE (precision)=3.51% Excel: Median RPE (bias)=0.27%; Median RUPE (precision)=1.09%	Cross-validation	3	0	No	No	No	Yes	No	
Lan TH	Neural Network	13	Subjects with weight gain accurately identified=93%	Sample splitting	3	0	Yes	Yes	No	No	No	
Levy AE	Gradient Boosting Machine, K-Means Clustering, K-Nearest Neighbors, Principal Component Analysis, Random Forest, Reinforcement Learning, Support Vector Machine	25	Accuracy=96%	Sample splitting (20% validation)	3	0	Yes	No	No	No	No	

First Author Name	AI Model Types	Number of Variables	AI Model Performance	Validation Approach	Quality Assessment	Study Phase	Health Record Data	Genetic Data	Administrative Health Data	Publicly Available Data	Secondary Use of Research Data	Other Data Sources
Li X	Decision Tree, Natural Language Processing, Random Forest	20	Random forest: AUC=90%	Cross-validation (10-fold) Sample splitting (33% validation)	3	0	Yes, EHR	No	No	No	No	
Lin CC	Neural Network	12	Internal validation: Accuracy=88%; AUC=0.93 External validation: Accuracy=81%; AUC=0.91	Sample splitting (33% validation) Internal and external validation	2	0	Yes	No	No	No	No	
Lin CS	Neural Network	14	Neural network: Accuracy=78%, AUC=0.80	Sample splitting (25% validation)	3	0	Yes	No	No	No	No	
Lin E	Neural Network, Support Vector Machine	25	Support vector machine with Gaussian radial basis function kernel: AUC=0.74	Cross-validation (5-fold)	3	0	No	Yes	No	No	Yes	
Liu KE	Adaptive Boosting, Decision Tree, K-Nearest Neighbours, Neural Network, Random Forest, Support Vector Machine	7	No drug-drug interaction group: Random forest (without AdaBoost): Accuracy=80%, AUC=0.87 C4.5 decision tree (with AdaBoost): Accuracy=82%, AUC=0.87 Drug-drug interaction group: Random forest (without AdaBoost): Accuracy=81%, AUC=0.89 Classification and regression tree (with AdaBoost): Accuracy=81%, AUC=0.87	Cross-validation (10-fold)	3	0	Yes	No	No	No	No	
Liu L	Decision Tree, Gradient Boosting Machine, Support Vector Machine	324	Gradient boosting machine: AUC=0.92	Cross-validation (10-fold)	3	0	No	No	No	Yes	Yes	
Lo-Ciganic WH [a]	Gradient Boosting Machine, Neural Network, Random Forest	268	Neural network: AUC=0.91 Gradient boosting machine: AUC=0.90	Sample splitting (33% validation)	3	1	No	No	Yes	No	No	
Lo-Ciganic WH [b]	Gradient Boosting Machine, Neural Network, Random Forest	269	Gradient Boosting Machine: AUC=0.88 Neural Network: AUC=0.88 Random Forest: AUC=0.87 Elastic-net penalized logistic regression: AUC=0.88	Sample splitting (33% validation)	3	1	No	No	Yes	No	No	
Ma Z	Extremely Randomized Trees, Gradient Boosting Machine, K-Nearest Neighbors, Neural Network, Random Forest, Support Vector Machine, and ensembles of multiple machine learning algorithms	35	Stack 1 (Gradient boosting trees, support vector machine, neural network): Mean absolute error=8.3; Percentage of patients whose predicted dose of warfarin was within 20% of the therapeutic dose)=48%	Cross-validation Sample splitting (20% validation)	3	1	No	Yes	No	Yes	Yes	

First Author Name	AI Model Types	Number of Variables	AI Model Performance	Validation Approach	Quality Assessment	Study Phase	Health Record Data	Genetic Data	Administrative Health Data	Publicly Available Data	Secondary Use of Research Data	Other Data Sources
Maiellaro PA	Neural Network	10	Accuracy=70%	Sample splitting (limited information)	3	0	No	No	No	No	Yes	
Marchetti M	Bayesian	Exact number unknown	Accuracy>95%	Prospective validation cohort	2	1	Yes	No	No	No	No	
Marquet P	Bayesian	Exact number unknown	Requests with a recommendation of “dose modification”: next AUC was more often within proposed target ranges when adjusted dose was within the proposed target (95.7%) than not (68.3%) Requests with recommendation of “no dose modification”: new AUC more often within the target when the dose was continued within (95.4%) than outside (50%) the proposed ranges	N/A	3	0	No	No	No	Yes	No	
Moreno EM	Decision Tree, Neural Network	42	Training sample: AUC=0.94 Test sample: sensitivity=81%, specificity=98%, positive predictive value=91%, negative predictive value=95%	Cross-validation (5-fold) Prospective validation cohort Model construction in retrospective cohort	2	1	Yes	No	No	No	No	
Murphree DH	Gradient Boosting Machine, Neural Network, Random Forest, and ensemble techniques	58	Gradient boosting machine (gbm) and gbmStack: AUC=0.75	Cross-validation (5-fold) Sample splitting (20% validation)	3	0	No	No	Yes	No	No	
Ng T	Bayesian, Neural Network, Principal Component Analysis, Support Vector Machine	69	Neural network: Accuracy=78%, AUC=0.86	Cross-validation (5-fold) Sample splitting (31% validation)	3	1	Yes	No	No	No	No	
Nickerson P	Neural Network, Random Forest, Support Vector Machine	200	Post-operative urinary retention: Support vector machine: Accuracy=66% Pain response to analgesic: Support vector regression: MSE=5.14; Elastic-net logistic regression (best overall) MSE=4.96	Sample splitting: 20% validation (outcome: predicting POUR) 33% validation (outcome: forecasting pain levels)	3	0	Yes, EHR	No	No	No	No	
Öztaner SM	Bayesian	10	Variation explained=45% and 51%	Sample splitting (33% validation)	3	0	No	Yes	No	Yes	Yes	

First Author Name	AI Model Types	Number of Variables	AI Model Performance	Validation Approach	Quality Assessment	Study Phase	Health Record Data	Genetic Data	Administrative Health Data	Publicly Available Data	Secondary Use of Research Data	Other Data Sources
Pavani A	Neural Network	15	Internal validation: Accuracy=75% (patients with INR<2.0); Accuracy=83% (patients with INR>3.5) External validation: Reduced out-of-range INRs (OR: 0.49), rate of adverse drug reactions (OR: 0.00), and time to reach first therapeutic INR (OR: 6.73)	Sample splitting and independent validation cohort	2	1	Yes	Yes	No	No	No	
Preston SL	Bayesian	3 to 8	Clearance from plasma: median bias=0.5%; median precision=18.3% Peak concentration in plasma: median bias=3.3%; median precision=21.8%	Sample splitting (37% validation)	3	0	Yes	No	No	No	No	
Rozenblum R	Neural Network	Exact number unknown	Accurate alerts=92% Clinically valid alerts=80%	Sample splitting: 50% used for algorithms refinement 50% used for alerts evaluation	3	1	Yes, EHR	No	No	No	No	
Sauer CM	Random Forest, Support Vector Machine	27	Random forest: AUC=0.70 Forward stepwise selection (best overall): AUC=0.74	Cross-validation Sample splitting (30% validation)	3	0	No	No	No	Yes	No	
Schiff GD	Neural Network	Exact number unknown	Valid alerts=76%	Rating system not formally validated	3	1	Yes, EHR	No	No	No	No	
Segal G	Neural Network	Exact number unknown	Clinically valid alerts=85% Clinically useful alerts=80%	Alerts system validation by "clinical champion"	2	2	Yes, EHR	No	No	No	No	
Sheyn D	Bayesian, Neural Network, Random Forest, Support Vector Machine	41	External validation: Random forest: Accuracy=81%, AUC=0.78	Cross-validation External validation (second tertiary medical center)	2	2	Yes, EHR	No	No	No	No	
Smith JC	Natural Language Processing	Exact number unknown	Accurate alert=86% Intervention group ordered fewer suspected ADR-causing preadmission medications compared with the control group (47% vs. 58%)	None, comparison between intervention and control group	2	2	Yes, EHR	No	No	No	No	
Speiser JL	Bayesian, Decision Tree, K-Nearest Neighbors, Neural Network, Random Forest, Support Vector Machine	14	BiMM tree: AUC=0.70 (original dataset) BiMM forest and standard random forest: AUC=0.75 (imputed dataset)	Sample splitting (50% validation)	3	1	No	No	No	No	Yes	

First Author Name	AI Model Types	Number of Variables	AI Model Performance	Validation Approach	Quality Assessment	Study Phase	Health Record Data	Genetic Data	Administrative Health Data	Publicly Available Data	Secondary Use of Research Data	Other Data Sources
Taft LM	Bayesian, Decision Tree	Exact number unknown	Bayesian: AUC=0.92-0.95	Cross-validation (10-fold)	3	1	Yes, EHR	No	No	No	No	
Ubels J	Random Forest, Simulated Treatment Learning, Support Vector Machine	Exact number unknown	Two-fold progression free survival benefit observed for bortezomib in 19.8% of the patients Three-fold progression free survival benefit observed for lenalidomide in 31.1% of the patients	Cross-validation	3	0	No	Yes	No	Yes	Yes	
Valeanu A	K-Nearest Neighbors, Neural Network, Random Forest	22	Neural network: Hospitalization class prediction: Accuracy=72% Hospitalization probability prediction: AUC=79% Mortality class prediction: Accuracy=77% Mortality probability prediction: AUC=85%	Sample splitting (21% validation)	4	1	No	No	No	Yes	No	
Waljee AK	Random Forest	Exact number unknown	AUC=0.87	Sample splitting (30% validation)	3	0	Yes	No	No	No	No	
Wan YW	Bayesian	12	Memorial Sloan-Kettering Cancer Center: sensitivity=87%, specificity=58% Dana-Farber Cancer Institute: sensitivity=68%, specificity=76%	External validation	3	0	No	Yes	No	No	Yes	
Wu W	K-Means Clustering, Support Vector Machine	100	Support vector machine: Accuracy=81%	Cross-validation (10-fold) Independent test set	3	0	Yes	No	No	No	No	
Yang X	Gradient Boosting Machine, Random Forest, Support Vector Machine	Exact number unknown	Gradient boosting machine: AUC=0.91	Cross-validation (5-fold) Sample splitting (20% validation)	3	0	Yes, EHR	No	No	No	No	
Yin JY	Adaptive Boosting, Bagging, Bayesian, Decision Tree, K-Nearest Neighbors, Neural Network, Random Forest, Support Vector Machine	26	Bayesian: Response prediction: Accuracy=71%, AUC=0.78 Overall toxicity prediction: Accuracy=62%, AUC=0.63	Independent validation cohort	2	1	Yes	Yes	No	No	No	
Yin WJ	Random Forest	13	Accuracy=82%, AUC=0.91	Cross-validation (5-fold) Sample splitting (20% validation)	3	0	Yes, EHR	No	No	No	No	
Zasowski EJ	Bayesian, Decision Tree	37 (considered)	AUCs ranged from 0.48 to 0.67 depending on threshold	N/A	3	0	Yes, EHR	No	No	No	No	

Appendix Table 4. Articles excluded at the full-text screen (N=247)

First Author Name	Year	Article Title	PMID, DOI or Reference
Abdollahi H	2018	Cochlea CT radiomics predicts chemoradiotherapy induced sensorineural hearing loss in head and neck cancer patients: A machine learning and multi-variable modelling study.	29329660
Adam TJ	2019	Big Data Cohort Extraction for Personalized Statin Treatment and Machine Learning.	30848466
Alberts M	2020	Risks of Stroke and Mortality in Atrial Fibrillation Patients Treated with Rivaroxaban and Warfarin.	31888412
Albrecht W	2019	Prediction of human drug-induced liver injury (DILI) in relation to oral doses and blood concentrations.	31250071
Ali SF	2018	Using Temporal Covariance of Motion and Geometric Features via Boosting for Human Fall Detection.	29895812
Andreu F	2015	Development of a population PK model of tacrolimus for adaptive dosage control in stable kidney transplant patients.	25254416
Antignac M	2011	Prediction tacrolimus blood levels based on the Bayesian method in adult kidney transplant patients.	21347736
Aquilante CL	2007	Development of a warfarin-dosing algorithm in Asian patients: A pharmacogenomic approach.	10.2217/17410541.4.1.83
Bartova L	2019	Results of the European Group for the Study of Resistant Depression (GSRD) - basis for further research and clinical practice.	31340696
Bekele BN	2010	Risk-group-specific dose finding based on an average toxicity score.	19645698
Ben Guebila M	2019	Predicting gastrointestinal drug effects using contextualized metabolic models.	31242176
Bjelogrić M	2020	Emerging Concepts and Applied Machine Learning Research in Patients with Drug-Induced Repolarization Disorders.	32570374
Blumenthal KG	2017	Adverse and Hypersensitivity Reactions to Prescription Nonsteroidal Anti-Inflammatory Agents in a Large Health Care System.	28110055
Bouzillé G	2019	An Automated Detection System of Drug-Drug Interactions from Electronic Patient Records Using Big Data Analytics.	31437882
Brettingham-Moore KH	2011	Pretreatment transcriptional profiling for predicting response to neoadjuvant chemoradiotherapy in rectal adenocarcinoma.	21224373
Brier ME	2011	Predictive modeling for improved anemia management in dialysis patients.	21941178
Brown D	2018	Temporal case-based reasoning for type 1 diabetes mellitus bolus insulin decision support.	28986108
Burden AM	2019	Pharmacoepidemiology and Big Data Analytics: Challenges and Opportunities when Moving towards Precision Medicine.	31883553

First Author Name	Year	Article Title	PMID, DOI or Reference
Burgmann H	2003	The influence of comorbidity on the effect of levofloxacin treatment success of ambulatory respiratory tract infections.	12764869
Caldés AP	2014	Optimal sparse sampling for estimating ganciclovir/valganciclovir AUC in solid organ transplant patients using NONMEN.	24305626
Campagne O	2019	The impact of tacrolimus exposure on extrarenal adverse effects in adult renal transplant recipients.	30414331
Carenini M	2009	ReMINE: an ontology-based risk management platform.	19745233
Castellan AC	2013	Quantitative prediction of the impact of drug interactions and genetic polymorphisms on cytochrome P450 2C9 substrate exposure.	23344982
Chan E	2001	Population pharmacokinetics of carbamazepine in Singapore epileptic patients.	11422016
Chavada R	2017	Establishment of an AUC(0-24) Threshold for Nephrotoxicity Is a Step towards Individualized Vancomycin Dosing for Methicillin-Resistant Staphylococcus aureus Bacteremia.	28242672
Chelaru MI	2010	Levodopa-induced dyskinesias detection based on the complexity of involuntary movements.	19878692
Chen VC	2019	Predicting chemo-brain in breast cancer survivors using multiple MRI features and machine-learning.	30417933
Chen X	2019	Prediction of Disease Comorbidity Using HeteSim Scores based on Multiple Heterogeneous Networks.	31530261
Chester Wasko M	2016	Prednisone Use and Risk of Mortality in Patients with Rheumatoid Arthritis: Moderation by Use of Disease-Modifying Antirheumatic Drugs.	26415107
Chisaki Y	2016	Population Pharmacodynamic Model for Bayesian Prediction of Myelosuppression Profiles Based on Routine Clinical Data after Gemcitabine and Carboplatin Treatment.	27606802
Chung KF	2019	Predicting response to triamcinolone in severe asthma by machine learning.	10.1164/rccm.201902-0320ED
Claisse G	2019	Predicting the dose of vancomycin in ICU patients receiving different types of RRT therapy: a model-based meta-analytic approach.	30768726
Costello JC	2014	A community effort to assess and improve drug sensitivity prediction algorithms.	24880487
Cronin MT	2003	Computer-aided prediction of drug toxicity and metabolism.	12613181
Csajka C	2004	Population pharmacokinetics of indinavir in patients infected with human immunodeficiency virus.	15328077
Csajka C	2003	Population pharmacokinetics and effects of efavirenz in patients with human immunodeficiency virus infection.	12545140
Cuplov V	2020	Machine Learning Approach to Forecast Chemotherapy-Induced Haematological Toxicities in Patients with Rhabdomyosarcoma.	32709121

First Author Name	Year	Article Title	PMID, DOI or Reference
Dave MB	2020	Optimization of infliximab therapy in inflammatory bowel disease using a dashboard approach-an Indian experience.	10.1007/s00228-020-02975-0
de Jonge ME	2004	Bayesian pharmacokinetically guided dosing of paclitaxel in patients with non-small cell lung cancer.	15073098
De Ramón Fernández A	2019	A decision support system for predicting the treatment of ectopic pregnancies.	31445255
Deist TM	2018	Machine learning algorithms for outcome prediction in (chemo)radiotherapy: An empirical comparison of classifiers.	29763967
Del Fiol G	2000	Design, implementation and evaluation of a clinical decision support system to prevent adverse drug events.	11187651
Delaney JA	2010	Associations of antiretroviral drug use and HIV-specific risk factors with carotid intima-media thickness.	20671544
Devitt EJ	2011	Early proteomic analysis may allow noninvasive identification of hepatitis C response to treatment with pegylated interferon α -2b and ribavirin.	21164346
Dharmasaroja P	2012	Prediction of intracerebral hemorrhage following thrombolytic therapy for acute ischemic stroke using multiple artificial neural networks.	22333462
Domine D	1998	Nonlinear neural mapping analysis of the adverse effects of drugs.	9517012
Donagher J	2018	Therapeutic drug monitoring: using Bayesian methods to evaluate hospital practice.	10.1002/jppr.1432
Dong J	2019	Evaluation of the predictive performance of Bayesian dosing for warfarin in Chinese patients.	30777785
Dong M	2017	Opportunities for model-based precision dosing in the treatment of sickle cell anemia.	28807656
Dong Z	2015	Anticancer drug sensitivity prediction in cell lines from baseline gene expression through recursive feature selection.	26121976
Du X	2020	Predicting in-hospital mortality of patients with febrile neutropenia using machine learning models.	32325370
Duconge J	2016	A novel admixture-based pharmacogenetic approach to refine warfarin dosing in Caribbean Hispanics.	10.1371/journal.pone.0145480
Duke JD	2011	A successful model and visual design for creating context-aware drug-drug interaction alerts.	22195086
Dykstra MA	2017	Urine metabolomics as a predictor of patient tolerance and response to adjuvant chemotherapy in colorectal cancer.	10.3892/mco.2017.1407
Edwards RA	2018	Predicting Responses to Pregabalin for Painful Diabetic Peripheral Neuropathy Based on Trajectory-Focused Patient Profiles Derived from the First 4 Weeks of Treatment.	30206821
El Adoui M	2020	Multi-input deep learning architecture for predicting breast tumor response to chemotherapy using quantitative MR images	10.1007/s11548-020-02209-9

First Author Name	Year	Article Title	PMID, DOI or Reference
Eljebari H	2012	Population pharmacokinetics and Bayesian estimation of cyclosporine in a Tunisian population of hematopoietic stem cell transplant recipient.	22527344
Erekson DM	2018	Assessing risk of opioid misuse in the treatment of chronic pain: Building a practical actuarial approach.	30387861
Ermer SC	2020	An Automated Algorithm Incorporating Poincaré Analysis Can Quantify the Severity of Opioid-Induced Ataxic Breathing.	32287122
Fan J	2018	Prediction of Central Nervous System Side Effects Through Drug Permeability to Blood-Brain Barrier and Recommendation Algorithm.	29058464
Fayet-Mello A	2013	Free and total plasma levels of lopinavir during pregnancy, at delivery and postpartum: implications for dosage adjustments in pregnant women.	22914504
Fernandez de Canete J	2012	Artificial neural networks for closed loop control of in silico and ad hoc type 1 diabetes.	22178070
Fleck DE	2017	Prediction of lithium response in first-episode mania using the LITHium Intelligent Agent (LITHIA): Pilot data and proof-of-concept.	28574156
Friberg LE	2006	Pharmacokinetic-pharmacodynamic modelling of QT interval prolongation following citalopram overdoses.	16433872
Gambús PL	2011	Modeling the effect of propofol and remifentanyl combinations for sedation-analgesia in endoscopic procedures using an Adaptive Neuro Fuzzy Inference System (ANFIS).	21131550
Gauvin A	2002	A limited-sampling strategy to estimate individual pharmacokinetic parameters of vinorelbine in elderly patients with advanced metastatic cancer.	12045458
Gauvin A	2000	Bayesian estimate of vinorelbine pharmacokinetic parameters in elderly patients with advanced metastatic cancer.	10914711
Ghoraani B	2020	Multilevel Features for Sensor-Based Assessment of Motor Fluctuation in Parkinson's Disease Subjects.	31562114
Ghoshal UC	2020	Prediction of outcome of treatment of acute severe ulcerative colitis using principal component analysis and artificial intelligence.	10.1002/jgh3.12342
Gibson RJ	2015	What are the predictive factors in the risk and severity of chemotherapy-induced gastrointestinal toxicity?	10.2217/fon.15.138
Giri S	2019	Increased Plasma Nitrite and von Willebrand Factor Indicates Early Diagnosis of Vascular Diseases in Chemotherapy Treated Cancer Patients.	29974375
Gomes A	2017	Pharmacokinetic modeling of gentamicin in treatment of infective endocarditis: Model development and validation of existing models.	28475651
Gong CS	2014	Predicting postoperative vomiting for orthopedic patients receiving patient-controlled epidural analgesia with the application of an artificial neural network.	25162027

First Author Name	Year	Article Title	PMID, DOI or Reference
Gram M	2017	Prediction of postoperative opioid analgesia using clinical-experimental parameters and electroencephalography.	27470494
Guo B	2018	Using Naive Bayes Algorithm to Estimate the Response to Drug in Lung Cancer Patients.	30686250
Hack CE	2010	A Bayesian network model for biomarker-based dose response.	20412521
Haeseker MB	2014	Vancomycin dosing in neutropenic patients.	25390637
Han M	2012	Support vector machines coupled with proteomics approaches for detecting biomarkers predicting chemotherapy resistance in small cell lung cancer.	10.3892/or.2012.2037
Hénin E	2009	A dynamic model of hand-and-foot syndrome in patients receiving capecitabine.	19078948
Henneghan AM	2018	Identifying cytokine predictors of cognitive functioning in breast cancer survivors up to 10 years post chemotherapy using machine learning.	29759139
Herz DM	2015	Abnormal dopaminergic modulation of striato-cortical networks underlies levodopa-induced dyskinesias in humans.	25882651
Herz DM	2016	Resting-state connectivity predicts levodopa-induced dyskinesias in Parkinson's disease.	26954295
Hiramatsu N	2011	Pretreatment prediction of anemia progression by pegylated interferon alpha-2b plus ribavirin combination therapy in chronic hepatitis C infection: decision-tree analysis.	21681410
Hong JC	2018	Predicting Emergency Visits and Hospital Admissions During Radiation and Chemoradiation: An Internally Validated Pretreatment Machine Learning Algorithm.	30652595
Hsu KC	2017	Model-based optimization approaches for precision medicine: A case study in presynaptic dopamine overactivity.	28614410
Hu F	2020	Predicting Lipid-Lowering Medication Persistence after the First Cardiovascular Disease Hospitalization.	32726811
Huang EX	2017	Independent test of a model to predict severe acute esophagitis.	10.1016/j.adro.2016.11.003
Huang J	2010	Genomic indicators in the blood predict drug-induced liver injury.	20676066
Hui EP	2011	Prediction of outcome in cancer patients with febrile neutropenia: a prospective validation of the Multinational Association for Supportive Care in Cancer risk index in a Chinese population and comparison with the Talcott model and artificial neural network.	20820815
Huitema AD	2001	Validation of a therapeutic drug monitoring strategy for thiotepea in a high-dose chemotherapy regimen.	11802099
Hutchinson TA	2000	Bayesian assessment of adverse drug reactions.	11192652
Hylan TR	2015	Automated prediction of risk for problem opioid use in a primary care setting.	25640294

First Author Name	Year	Article Title	PMID, DOI or Reference
Imanishi M	2019	Efficacy of adjuvant chemotherapy after resection of pulmonary metastasis from colorectal cancer: a propensity score-matched analysis.	30471650
Jalloul N	2015	Detection of Levodopa Induced Dyskinesia in Parkinson's Disease patients based on activity classification.	26737447
Jochems A	2016	Distributed learning: Developing a predictive model based on data from multiple hospitals without data leaving the hospital - A real life proof of concept.	10.1016/j.radonc.2016.10.002
Jose A	2019	Anticoagulation in pulmonary arterial hypertension: a decision analysis.	10.1177/2045894019895451
Jovanović M	2015	Application of Counter-propagation Artificial Neural Networks in Prediction of Topiramate Concentration in Patients with Epilepsy.	26670371
Jungquist CR	2019	Identifying Patients Experiencing Opioid-Induced Respiratory Depression During Recovery from Anesthesia: The Application of Electronic Monitoring Devices.	31050151
Kalantarian H	2016	A wearable sensor system for medication adherence prediction.	27068873
Karhade AV	2019	Machine learning for prediction of sustained opioid prescription after anterior cervical discectomy and fusion.	30710731
Kashkooli K	2020	Improved tracking of sevoflurane anesthetic states with drug-specific machine learning models.	32485685
Kashkooli K	2019	Drug-Specific Models Improve the Performance of an EEG-based Automated Brain-State Prediction System.	31947172
Kaufmann GR	1998	Safety and efficacy of a two-compartment Bayesian feedback program for therapeutic tobramycin monitoring in the daily clinical use and comparison with a non-Bayesian one-compartment model.	9558131
Keijsers NL	2000	Detection and assessment of the severity of levodopa-induced dyskinesia in patients with Parkinson's disease by neural networks.	11104192
Keijsers NL	2003	Movement parameters that distinguish between voluntary movements and levodopa-induced dyskinesia in Parkinson's disease.	12623181
Keine D	2019	Polypharmacy in an Elderly Population: Enhancing Medication Management Through the Use of Clinical Decision Support Software Platforms.	30900186
Khayl F	2019	Prediction of docetaxel toxicity in older cancer patients: a Bayesian network approach.	31038767
Kim DW	2020	Wearable technology and systems modeling for personalized chronotherapy.	10.1016/j.coisb.2020.07.007
Kim DW	2018	Machine learning to predict the occurrence of bisphosphonate-related osteonecrosis of the jaw associated with dental extraction: A preliminary report.	29698784
Kimmel SE	2013	A pharmacogenetic versus a clinical algorithm for warfarin dosing.	10.1056/NEJMoa1310669

First Author Name	Year	Article Title	PMID, DOI or Reference
Kimura H	2005	Plasma MIP-1beta levels and skin toxicity in Japanese non-small cell lung cancer patients treated with the EGFR-targeted tyrosine kinase inhibitor, gefitinib.	16153743
Kopylev L	2007	Towards quantitative uncertainty assessment for cancer risks: central estimates and probability distributions of risk in dose-response modeling.	17905499
Koutkias V	2009	A knowledge engineering framework towards clinical support for adverse drug event prevention: the PSIP approach.	19745243
Kulldorff M	2013	Drug safety data mining with a tree-based scan statistic.	10.1002/pds.3423
Kuo KM	2019	Predicting hospital-acquired pneumonia among schizophrenic patients: a machine learning approach.	30866913
Laffey JG	2003	Assessment of a simple artificial neural network for predicting residual neuromuscular block.	12488378
Lai NH	2020	Comparison of the predictive outcomes for anti-tuberculosis drug-induced hepatotoxicity by different machine learning techniques.	31911332
Laínez JM	2014	Comparison of an assumption-free Bayesian approach with Optimal Sampling Schedule to a maximum a posteriori Approach for Personalizing Cyclophosphamide Dosing.	24038448
Lakshmi KS	2019	A comparative analysis of adverse drug reaction prediction techniques.	Lakshmi KS, Vadivu G. International Journal of Pharmaceutical Sciences Review & Research. 2019;55(1):1-5.
Lancaster MC	2016	Improved Prediction of Drug-Induced Torsades de Pointes Through Simulations of Dynamics and Machine Learning Algorithms.	26950176
Langers P	2014	Limited sampling model for advanced mycophenolic acid therapeutic drug monitoring after liver transplantation.	24081208
Larios Delgado N	2019	Fast and accurate medication identification.	31304359
Lawal S	2014	Predicting neutropenia risk in breast cancer patients from pre-chemotherapy characteristics.	10.2174/1875036201408010016
Le Meur Y	2007	Individualized mycophenolate mofetil dosing based on drug exposure significantly improves patient outcomes after renal transplantation.	17908276
Li MH	2018	Automated assessment of levodopa-induced dyskinesia: Evaluating the responsiveness of video-based features.	29748112
Li MH	2018	Vision-based assessment of parkinsonism and levodopa-induced dyskinesia with pose estimation.	30400914
Li Q	2007	Bayesian modelling of the dynamics of hepatotoxicity.	17252524
Liang Z	2018	Fast Screening Technology for Drug Emergency Management: Predicting Suspicious SNPs for ADR with Information Theory-based Models.	29336255

First Author Name	Year	Article Title	PMID, DOI or Reference
Liang Z	2016	DL-ADR: a novel deep learning model for classifying genomic variants into adverse drug reactions.	27510822
Lin E	2008	A support vector machine approach to assess drug efficacy of interferon-alpha and ribavirin combination therapy.	18652518
Lin R	2018	A Deep Deterministic Policy Gradient Approach to Medication Dosing and Surveillance in the ICU.	30441448
Loke PY	2011	Pilot study on developing a decision support tool for guiding re-administration of chemotherapeutic agent after a serious adverse drug reaction.	21794175
Lopez-Martinez D	2019	Deep Reinforcement Learning for Optimal Critical Care Pain Management with Morphine using Dueling Double-Deep Q Networks.	31946739
Luong ML	2012	Risk factors for voriconazole hepatotoxicity at 12 weeks in lung transplant recipients.	22486950
Ma Y	2006	Predicting cancer drug response by proteomic profiling.	16899605
Machireddy A	2018	Analysis of DCE-MRI for Early Prediction of Breast Cancer Therapy Response.	30440488
Mahmoud AA	2020	Pharmacokinetic Assessment of Pre- and Post-Oxygenator Vancomycin Concentrations in Extracorporeal Membrane Oxygenation: A Prospective Observational Study.	32468446
Maier C	2020	Bayesian Data Assimilation to Support Informed Decision Making in Individualized Chemotherapy.	31905420
Manuel O	2010	Ganciclovir exposure under a 450 mg daily dosage of valganciclovir for cytomegalovirus prevention in kidney transplantation: A prospective study.	10.1111/j.1399-0012.2009.01205.x
Mao JJ	2018	External evaluation of population pharmacokinetic models for ciclosporin in adult renal transplant recipients.	28891596
Martinelli EF	2003	Rapid I.V. loading with phenytoin with subsequent dose adaptation using non-steady-state serum levels and a Bayesian forecasting computer program to predict maintenance doses.	10.1046/j.0269-4727.2003.00506.x
Martinez-Balibrea E	2010	UGT1A and TYMS genetic variants predict toxicity and response of colorectal cancer patients treated with first-line irinotecan and fluorouracil combination therapy.	10.1038/sj.bjc.6605776
Martín-Guerrero JD	2003	Dosage individualization of erythropoietin using a profile-dependent support vector regression.	14560766
McDougall DAJ	2016	The Impact of Model-Misspecification on Model Based Personalised Dosing.	10.1208/s12248-016-9943-9
Ménard T	2019	Enabling Data-Driven Clinical Quality Assurance: Predicting Adverse Event Reporting in Clinical Trials Using Machine Learning.	10.1007/s40264-019-00831-4
Menke A	2018	Precision pharmacotherapy: psychiatry's future direction in preventing, diagnosing, and treating mental disorders.	30510440

First Author Name	Year	Article Title	PMID, DOI or Reference
Mera TO	2012	Quantitative assessment of levodopa-induced dyskinesia using automated motion sensing technology.	23365855
Miller JE	1999	Notification of real-time clinical alerts generated by pharmacy expert systems.	10566374
Miñarro-Giménez JA	2014	An ontology-based, mobile-optimized system for pharmacogenomic decision support at the point-of-care.	24787444
Modongo C	2015	Amikacin Concentrations Predictive of Ototoxicity in Multidrug-Resistant Tuberculosis Patients.	26248372
Molassiotis A	2012	An exploratory study to clarify the cluster of symptoms predictive of chemotherapy-related nausea using random forest modeling.	22672920
Monjanel-Mouterde S	2002	Bayesian population model of methotrexate to guide dosage adjustments for folate rescue in patients with breast cancer.	12081632
Monjanel-Mouterde S	1998	Bayesian calculation of methotrexate clearance after low dose intramuscular administration in patients with rheumatoid arthritis.	9676756
Moon H	2018	Subgroup analysis based on prognostic and predictive gene signatures for adjuvant chemotherapy in early-stage non-small-cell lung cancer patients.	29157115
Moreno E	2016	Predictive models in drug allergy: An appropriate patient selection is needed.	10.1016/j.jaip.2016.05.020
Motykie GD	1999	The use of a Bayesian forecasting model in the management of warfarin therapy after total hip arthroplasty	10.1016/S0883-5403(99)90015-3
Mull HJ	2008	Informatics tools for the development of action-oriented triggers for outpatient adverse drug events.	18999297
Nakamura T	2001	Factors influencing the prediction of steady state concentrations of digoxin.	10.1248/bpb.24.403
Nakano T	2016	Change of teicoplanin loading dose requirement for incremental increases of systemic inflammatory response syndrome score in the setting of sepsis.	27125378
Negri L	2014	Tuberculosis: Relevance of isoniazid dosage in prevention of liver side effects.	10.2515/therapie/2014202
Nováček V	2020	Predicting Polypharmacy Side-effects Using Knowledge Graph Embeddings.	32477666
Oda K	2020	Reduced nephrotoxicity with vancomycin therapeutic drug monitoring guided by area under the concentration-time curve against a trough 15-20 µg/mL concentration.	32721597
Ouchi K	2018	Machine Learning to Predict, Detect, and Intervene Older Adults Vulnerable for Adverse Drug Events in the Emergency Department.	29858745
Oyaga-Iriarte E	2019	Prediction of irinotecan toxicity in metastatic colorectal cancer patients based on machine learning models with pharmacokinetic parameters.	31105026

First Author Name	Year	Article Title	PMID, DOI or Reference
Padar S	1999	Transformation of an acetaminophen toxicity nomogram to an artificial neural network.	10507243
Padullés A	2016	Contribution of Population Pharmacokinetics to Dose Optimization of Ganciclovir-Valganciclovir in Solid-Organ Transplant Patients.	26824942
Parkinson J	2012	Application of data mining and visualization techniques for the prediction of drug-induced nausea in man.	22157355
Pastor ML	2015	Model-based approach to early predict prolonged high grade neutropenia in carboplatin-treated patients and guide G-CSF prophylactic treatment	10.1007/s11095-014-1493-1
Paule I	2012	Dose adaptation of capecitabine based on individual prediction of limiting toxicity grade: evaluation by clinical trial simulation.	21809035
Payne TH	2016	Examination of medication clinical decision support using Bayes' theorem.	10.2146/ajhp150964
Pea F	2000	High vancomycin dosage regimens required by intensive care unit patients cotreated with drugs to improve haemodynamics following cardiac surgical procedures.	10702552
Pea F	2000	Optimisation of vancomycin regimen in neutropenic haematological patients with normal renal function. Multiple daily doses may be preferable.	10.2165/00044011-200019030-00006
Potruch A	2020	The role of chronobiology in drug-resistance epilepsy: The potential use of a variability and chronotherapy-based individualized platform for improving the response to anti-seizure drugs.	32629327
Qiu R	2004	Diminishing the risk of nonrelapse mortality in hematopoietic stem cell transplantation: Prediction of exposure to the cyclophosphamide metabolite carboxyethylphosphoramidate mustard.	10.1016/j.clpt.2004.05.006
Qu G	2012	Local analgesia adverse effects prediction using multi-label classification.	10.1016/j.neucom.2011.08.038
Ramella S	2018	A radiomic approach for adaptive radiotherapy in non-small cell lung cancer patients.	30462705
Rappelsberger AD	2017	Adverse Drug Event Monitoring with Clinical and Laboratory Data Using Arden Syntax.	29295277
Raschke RA	2017	Clinical effectiveness of a Bayesian algorithm for the diagnosis and management of heparin-induced thrombocytopenia.	28622439
Ray JE	2006	Decision support tool to individualize cyclosporine dose in stable, long-term heart transplant recipients receiving metabolic inhibitors: overcoming limitations of cyclosporine C2 monitoring.	17045935
Rhodes NJ	2016	An exploratory analysis of the ability of a cefepime trough concentration greater than 22 mg/L to predict neurotoxicity.	26712584
Rousseau A	2000	Adaptive control methods for the dose individualisation of anticancer agents.	10803455

First Author Name	Year	Article Title	PMID, DOI or Reference
Sadikov A	2017	Feasibility of spirometry features for objective assessment of motor function in Parkinson's disease.	28416144
Saito K	2012	Predictive factors of response to intravenous ciclosporin in severe ulcerative colitis: The development of a novel prediction formula.	10.1111/apt.12033
Saito M	2010	Population pharmacokinetics of R- and S-carvedilol in Japanese patients with chronic heart failure.	20686235
Salas S	2006	Therapeutic drug monitoring for dose individualization of Cisplatin in testicular cancer patients based upon total platinum measurement in plasma.	16885721
Salinger DH	2006	Real-time dose adjustment of cyclophosphamide in a preparative regimen for hematopoietic cell transplant: a Bayesian pharmacokinetic approach.	16914577
Salmasian H	2013	An automated tool for detecting medication overuse based on the electronic health records.	23233423
Saludes V	2013	Relevance of baseline viral genetic heterogeneity and host factors for treatment outcome prediction in hepatitis C virus 1b-infected patients.	24015264
Samwald M	2015	Pharmacogenomic knowledge representation, reasoning and genome-based clinical decision support based on OWL 2 DL ontologies.	25880555
Scholten EM	2005	AUC-guided dosing of tacrolimus prevents progressive systemic overexposure in renal transplant recipients.	15882290
Seeling W	2012	Knowledge-based tacrolimus therapy for kidney transplant patients.	22874202
Senapati S	2014	Genome-wide analysis of methotrexate pharmacogenomics in rheumatoid arthritis shows multiple novel risk variants and leads for TYMS regulation.	24583629
Serretti A	2007	A neural network model for combining clinical predictors of antidepressant response in mood disorders.	16970992
Serretti A	2007	Clinical prediction of antidepressant response in mood disorders: Linear multivariate vs. neural network models.	10.1016/j.psychres.2006.07.009
Seyednasrollah F	2017	A DREAM Challenge to Build Prediction Models for Short-Term Discontinuation of Docetaxel in Metastatic Castration-Resistant Prostate Cancer.	30657384
Shah AA	2019	Development of a machine learning algorithm for prediction of failure of nonoperative management in spinal epidural abscess.	31059819
Shibahara T	2018	Machine-Learning Approach for Modeling Myelosuppression Attributed to Nimustine Hydrochloride.	30652567
Shifrin M	2020	Near-optimal insulin treatment for diabetes patients: A machine learning approach.	10.1016/j.artmed.2020.101917
Siebert U	2004	Systematic assessment of decision models in Parkinson's disease.	15367256

First Author Name	Year	Article Title	PMID, DOI or Reference
Spyridonos P	2013	Gray Hausdorff distance measure for medical image comparison in dermatology: Evaluation of treatment effectiveness by image similarity.	23020792
Stassen HH	2020	Inflammatory processes linked to major depression and schizophrenic disorders and the effects of polypharmacy in psychiatry: evidence from a longitudinal study of 279 patients under therapy.	32696276
Su R	2019	Developing a Multi-Dose Computational Model for Drug-Induced Hepatotoxicity Prediction Based on Toxicogenomics Data.	30040651
Sugimoto M	2014	Development of Web tools to predict axillary lymph node metastasis and pathological response to neoadjuvant chemotherapy in breast cancer patients.	25096734
Sullivan K	2019	Machine Learning Could Facilitate Optimal Titration of Guideline-Directed Medical Therapy in Heart Failure.	10.1016/j.jacc.2019.06.063
Sutton AJ	2005	A Bayesian approach to evaluating net clinical benefit allowed for parameter uncertainty.	15649668
Teramachi H	2002	Evaluation of predictability for vancomycin dosage regimens by the Bayesian method with Japanese population pharmacokinetic parameters.	12392090
Thygesen H	2010	Estimation strategies for reacting to the identification of an association between the genome and adverse drug reactions.	10.1080/10543401003602615
Tippenhauer K	2020	Integrating Pharmacogenetic Decision Support into a Clinical Information System.	32570457
Tod M	2005	Pharmacokinetic/pharmacodynamic and time-to-event models of ribavirin-induced anaemia in chronic hepatitis C.	15828854
Tran A	2006	Pharmacokinetics and toxicity of docetaxel: role of CYP3A, MDR1, and GST polymorphisms.	16765145
Tsipouras MG	2011	On automated assessment of Levodopa-induced dyskinesia in Parkinson's disease.	22254893
Turki T	2016	Learning approaches to improve prediction of drug sensitivity in breast cancer patients.	28269014
Tyler NS	2020	An artificial intelligence decision support system for the management of type 1 diabetes.	32694787
Tyrak KE	2020	Artificial neural network identifies nonsteroidal anti-inflammatory drugs exacerbated respiratory disease (N-ERD) cohort.	10.1111/all.14214
Urquidi-Macdonald M	2004	Abciximab pharmacodynamic model with neural networks used to integrate sources of patient variability.	14749692
Valafar H	2000	Predicting the effectiveness of hydroxyurea in individual sickle cell anemia patients.	10648847
Van Der Bol JM	2010	A CYP3A4 phenotype-based dosing algorithm for individualized treatment of irinotecan.	10.1158/1078-0432.CCR-09-1526
van Gorp F	2012	Population pharmacokinetics and pharmacodynamics of escitalopram in overdose and the effect of activated charcoal.	21883384

First Author Name	Year	Article Title	PMID, DOI or Reference
Van Looy S	2007	A novel approach for prediction of tacrolimus blood concentration in liver transplantation patients in the intensive care unit through support vector regression.	17655766
Wallin ÅK	2011	Galantamine treatment in Alzheimer's disease: Response and long-term outcome in a routine clinical setting.	10.2147/NDT.S24196
Wallin JE	2009	A tool for neutrophil guided dose adaptation in chemotherapy.	19084287
Wang P	2010	Using genetic and clinical factors to predict tacrolimus dose in renal transplant recipients.	10.2217/pgs.10.105
Warkentin TE	2011	Impact of laboratory testing for heparin-induced antibodies: Using Bayes' rule to prevent overdiagnosis of heparin-induced thrombocytopenia.	10.1515/JLM.2010.019
Warren LL	2007	Use of pairwise marker combination and recursive partitioning in a pharmacogenetic genome-wide scan.	10.2515/therapie/2014202
Watanabe M	2014	Developing population pharmacokinetic parameters for high-dose methotrexate therapy: implication of correlations among developed parameters for individual parameter estimation using the Bayesian least-squares method.	24882404
Watanabe T	2011	Gene expression signature and response to the use of leucovorin, fluorouracil and oxaliplatin in colorectal cancer patients.	21680303
Wen MS	2008	Prospective study of warfarin dosage requirements based on CYP2C9 and VKORC1 genotypes.	10.1038/sj.clpt.6100453
Wing K	2014	Development of predictive genetic tests for improving the safety of new medicines: The utilization of routinely collected electronic health records.	10.1016/j.drudis.2013.11.003
Wright A	2010	An automated technique for identifying associations between medications, laboratory results and problems.	10.1016/j.jbi.2010.09.009
Wright DF	2013	A Bayesian dose-individualization method for warfarin.	23329393
Wu CT	2020	Applying Data Mining Techniques for Predicting Prognosis in Patients with Rheumatoid Arthritis.	32260259
Wu H	2005	Modeling long-term HIV dynamics and antiretroviral response: Effects of drug potency, pharmacokinetics, adherence, and drug resistance.	10.1097/01.qai.0000165907.04710.da
Xu Y	2019	Bayesian non-parametric survival regression for optimizing precision dosing of intravenous busulfan in allogeneic stem cell transplantation.	31467455
Xu Y	2015	Deep Learning for Drug-Induced Liver Injury.	26437739
Yang J	2007	Efficacy of interferon treatment for chronic hepatitis C predicted by feature subset selection and support vector machine.	17489504

First Author Name	Year	Article Title	PMID, DOI or Reference
Yap KY	2012	Computational prediction of state anxiety in Asian patients with cancer susceptible to chemotherapy-induced nausea and vomiting.	22367655
Ying H	2007	A self-learning fuzzy discrete event system for HIV/AIDS treatment regimen selection.	17702293
Zeng P	2019	Characterizing the Structural Pattern Predicting Medication Response in Herpes Zoster Patients Using Multivoxel Pattern Analysis.	31191228
Zhang HX	2019	Systematic external evaluation of published population pharmacokinetic models of mycophenolate mofetil in adult kidney transplant recipients co-administered with tacrolimus.	30597603
Zhang Y	2020	Therapeutic Drug Monitoring Coupled with Bayesian Forecasting Could Prevent Vancomycin-Associated Nephrotoxicity in Renal Insufficiency Patients: A Prospective Study and Pharmacoeconomic Analysis.	32097248
Zhao S	2018	Bevacizumab in combination with different platinum-based doublets in the first-line treatment for advanced nonsquamous non-small-cell lung cancer: A network meta-analysis.	29171009
Zheng B	2019	Predictors of the therapeutic effect of corticosteroids on radiation-induced optic neuropathy following nasopharyngeal carcinoma.	30834973
Zheng WL	2020	Adaptive sedation monitoring from EEG in ICU patients with online learning.	10.1109/TBME.2019.2943062
Zhu L	2014	Predicting response to preoperative chemotherapy agents by identifying drug action on modeled microRNA regulation networks.	10.1371/journal.pone.0098140
Zhu S	2018	Prediction of Drug-Gene Interaction by Using Metapath2vec.	30108606
Zitnik M	2018	Modeling polypharmacy side effects with graph convolutional networks.	29949996
Zurlinden TJ	2016	A novel approach for estimating ingested dose associated with paracetamol overdose.	26441245