Evidence of Modeling Impact in Development of Policies for Controlling the Opioid Epidemic and Improving Public Health: A Scoping Review

Substance Abuse: Research and Treatment
Volume 13: 1–10
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DOI: 10.1177/1178221819866211

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ABSTRACT

BACKGROUND: Opioid addiction and overdose rates are reaching unprecedented levels in the U.S., with around 47,736 overdose deaths in 2017. Many stakeholders affect the opioid epidemic, including government entities, healthcare providers and policymakers, and opioid users. Simulation and conceptual modeling can help us understand the dynamics of the opioid epidemic by simplifying the real world and informing policymakers about different health interventions that could reduce the deaths caused by opioid overdose in the United States every year.

OBJECTIVES: To conduct a scoping review of simulation and conceptual models that propose policies capable of controlling the opioid epidemic. We demonstrate the strengths and limitations of these models and provide a framework for further improvement of future decision support tools.

METHODS: Using the methodology of a scoping review, we identified articles published after 2000 from eight electronic databases to map the literature that uses simulation and conceptual modeling in developing public health policies to address the opioid epidemic.

RESULTS: We reviewed 472 papers of which 14 were appropriate for inclusion. Each used either system dynamics simulation modeling, mathematical modeling, conceptual modeling, or agent-based modeling. All included studies tested and proposed strategies to improve health outcomes related to the opioid epidemic. Factors considered in the models included physicians prescribing opioids, trafficking, users recruiting new users, and doctor shopping; no model investigated the impact of age and spatial factors on the dynamics of the epidemic. Key findings from these studies were (1) prevention of opioid initiation is better than treatment of opioid addiction, (2) the analysis of an intervention's impact should include both benefits and harms, and (3) interventions with short-term benefits might have a counterproductive impact on the epidemic in long run.

CONCLUSIONS: While most studies examined the role of prescription opioids and trafficking on this epidemic, the transition of patients from prescription opioid use to nonprescription use including heroin and synthetic opioids such as fentanyl impacts the system significantly and results in an epidemic with quite different characteristics than what it had a decade ago. We recommend including the impact of age and geographic location on the opioid epidemic using modeling methods.

KEYWORDS: health policy, simulation and conceptual modeling, opioid, heroin, fentanyl

RECEIVED: July 1, 2019. **ACCEPTED:** July 5, 2019.

TYPE: Review

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Background

Opioid addiction and overdose rates are reaching unprecedented levels in the United States, with 47 736 overdose deaths in 2017,[1,2] and having the highest rates in West Virginia, Ohio, and Pennsylvania.[3] The United States faces three opioid epidemics—one from misuse of prescription opioids, one from synthetic opioids such as fentanyl, and the other due to illegally produced opioids such as heroin—all contributing to the high number of overdose deaths in this country.[4–6] Although the supply of prescription opioids has decreased, the use of heroin and synthetic opioids, which are more potent than prescription opioids,[7] continues to grow[8] and has raised the rate of opioid overdoses. While, opioid-related deaths driven by synthetic opioids have been on the rise in recent years and fentanyl has fueled the opioid epidemic,[9,10] less attention has been given to this line of drugs. Moreover, the supply of illicit and synthetic drugs and the interventions to suppress them have not been studied in detail. Additionally, current interventions, such as educational programs, lack comprehensive consideration of all factors contributing to opioid use trajectories and have not stemmed the epidemic.

The complexity of the opioid epidemic is multifactorial and includes poorly understood and unpredictable interactions among (1) stakeholders (e.g. patients (users), providers, and

policymakers); (2) demographic and spatial factors, such as providers' locations; and (3) transitions between health states of opioid users such as light and heavy users. For instance, regarding opioid diversion and recruitment of new users, opioid users have the tendency to recruit new users.[11] They may provide the pills to their friends and relatives, increasing the diversion of prescription opioids from intended use. Moreover, opioid users may acquire higher doses from physicians or illegally from drug traffickers, also increasing drug diversion. Patients with misuse/use disorders may "doctor shop," visiting several doctors to obtain opioids;[12] this phenomenon increases diversion,[13] as well as recruitment. These facts about this segment of the opioid epidemic—recruitment and diversion—are clearly indicating the complexity of this problem and because of this complexity, no one organization can solve the problem on its own. Moreover, this epidemic is dynamic as before 2010 most opioid-related deaths were among middle-aged people, largely among women and African Americans. Currently, however, the epidemic is affecting younger individuals; predominantly males and whites.[4] Also, the geographic patterns of opioid-related deaths vary in different states; heroin and synthetic-related deaths are higher in the northeastern United States.[4] Therefore, we need to adopt a multifaceted, holistic approach to address this dynamic, complex epidemic while considering all contributing factors.

Adopting a more comprehensive approach and predictive analysis toward policy and evaluation could prevent many of the tens of thousands of deaths caused by opioid overdose in the United States every year. Providing a comprehensive list of interventions and key findings of previous modeling works to researchers and modelers would facilitate the development of future models for this crisis and other drug epidemics.

We conducted a scoping review of articles that address the complexities of the opioid epidemic through modeling and provide policymakers decision support tools for choosing the best policy options. We sought to answer the following questions: (1) What segments and factors of the opioid epidemic have been considered in *simulation and conceptual modeling*? (2) What are the key findings of these modeling articles that contribute to controlling this crisis and improving public health in the United States? (3) What are the main gaps/areas that need to be studied further?

Methods

We used the methodology of a scoping review as outlined by Arksey and O'Malley[14] and Peters et al[15] to map the literature that uses simulation and conceptual modeling in developing public health policies to address the opioid epidemic. Scoping review is an appropriate technique for the goals of this project since it aims to rapidly extract the underlying concepts of a research area and the resources available.[14] Unlike systematic reviews that follow highly focused research questions,[16] it defines broader research aims. In accordance with the scoping review methodology, we did not perform a quality assessment of the selected articles and followed these five steps: (1) identifying research objectives; (2) finding relevant studies; (3) selecting final studies for data extraction; (4) charting the data in selected studies; and (5) summarizing and reporting results.

We analyzed studies that use modeling to evaluate or propose policies capable of controlling the opioid epidemic and positively improving public health. The reason we considered conceptual models is that they help modelers to develop simulation, computerized models.[17,18] In addition, we demonstrate the limitations of these models and provide a theoretical framework including factors and areas that need to be included in the models for further improvement of these decision support tools.

Eligibility criteria

We included opioid simulation and conceptual models that replicated historical data such as opioid overdoses, modeled different segments of the epidemic, and proposed scenarios and strategies in controlling the epidemic. These studies used a variety of simulation modeling techniques including system dynamics, agent-based models, mathematical models, discrete event simulation, and dynamical systems. We did not include interventions conducted solely in health care facilities, such as clinical settings or providers' offices, because this kind of interventions lack consideration of important mechanisms of the epidemic and are only effective for that particular settings. Moreover, they will not provide us with a big-picture overview of the system.

Besides simulation models, conceptual models included a nonsoftware description of a real-world problem and contained concise structural and behavioral features of this problem. From a conceptual model, a future detailed simulation model can be developed to answer specific research questions.[19]

In addition, we excluded nonhuman studies, conference abstracts, cost-effectiveness or econometric models, regression models, and data mining approaches in this review.

Search strategy

In collaboration with an information specialist/librarian (MM), we developed strategies for and searched eight databases: Medline (Ovid), Embase (Ovid), CINAHL (Ebscohost), Dissertations & Theses Global (ProQuest), Web of Science (Clarivate Analytics), PsycINFO (Ebscohost), Scopus (scopus.com), and Archive.org from 2000 to July 2018. (See Supplemental material 1 for search strategies.) The Medline strategy, which was translated for the other database searches, was peer-reviewed by a librarian at the same institution.

Screening methods

The search strategy yielded 581 references. After duplicates were removed using EndNote (Clarivate Analytics),

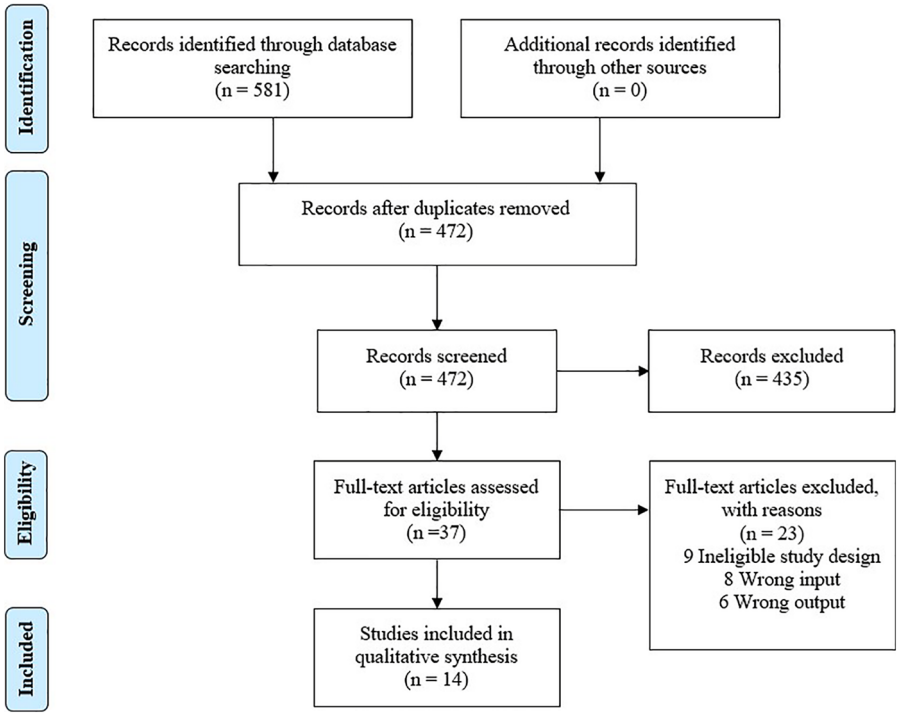

Figure 1. PRISMA diagram, including the inclusion and exclusion process.

472 references were imported into Covidence (Covidence.org), an online systematic review platform. Two reviewers (NS and SS) screened studies for inclusion. When consensus was not reached, a third person (RH) reviewed the study and served as the tie-breaker. Title and abstract screening excluded 435 studies, resulting in 37 studies for full-text review. Twenty-three were excluded because of ineligible study design (not a simulation or conceptual model), wrong input (not related to any opioids), and wrong output (not providing policy analyses). This left 14 studies for data extraction. Figure 1 shows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram, which illustrates the inclusion and exclusion process.

Results

The extracted data from the 14 selected studies include author–year, modeling method, research area/main outcome, key factors included, tested or proposed scenario/strategy, and key findings through modeling or literature review by the selected articles (see Table 1). Of these 14 articles, five used system dynamics modeling, three used mathematical modeling, five used conceptual modeling, and one used agent-based modeling.

We should mention that three of these articles were derived from one simulation model.[23,27,29] They were based on either a segment of that simulation model or an updated version of it. They tested different interventions using the model or considered a more comprehensive set of variables in the updated model. In addition, although Schmidt et al[25] developed their research paper using the Wakeland et al[27] simulation model, we considered it as a conceptual modeling work as it reveals data requirements, which will help modelers to define the scope of their simulation model.

We summarized the results of Table 1 into simulation and conceptual models and then provided a list of the investigated interventions below.

Simulation modeling

The simulation studies found that (1) preventing opioid initiation has a greater impact on opioid-use health outcomes than treatment strategies; (2) interventions have both benefits and harms and comprehensive analyses must consider both; (3) an intervention might have a positive impact if other factors are controlled in the system; and (4) interventions, such as educational program or prescription drug monitoring program (PDMP), can have a counterproductive impact on the overdoses in the long run. PDMP is a state-run program that is used by pharmacies, law enforcement, and providers to track prescription medications and control the opioid epidemic.[20] The use of PDMP would only impact opioid prescribing behavior, doctor shopping, and diversion of prescription opioids. On the other hand, it has a negligible impact on the use of nonmedical opioids such as heroin or on the ultimate number of opioid overdoses, and might even increase the transmission to heroin and synthetic opioids as it halts access to prescription opioids.[20,23] Furthermore, to see the positive impact of an intervention, we need to control other factors in the system, as Wakeland et al[26,29] express that the success of tamper-resistant drug formulation intervention is dependent on controlling the prescribing of opioids and diversion of leftover medicine.

Table 1. Summary of studies of modeling impact in development of policies to control the opioid epidemic.

AUTHOR (REFERENCE)	MODELING METHOD	RESEARCH AREA/ MAIN OUTCOME	KEY FACTORS INCLUDED	TESTED OR PROPOSED SCENARIO/STRATEGY	KEY FINDINGS THROUGH MODELING OR LITERATURE REVIEW
Gatley[20]	System dynamics modeling	Opioid abuse through diversion and doctor shopping "visiting several doctors to obtain opioids"	Providers' prescription of opioids, patients on short- or long-acting opioids, opioid diversion, doctor shopping, heroin users	Prescription drug monitoring program (PDMP)	1. Opioid diversion is a major contributor to the opioid death rate. 2. PDMP will slow opioid proliferation but will not stop the epidemic. 3. PDMP will only control the behavior of conspicuous doctor shoppers. High price and less availability of prescription opioids associated with heroin use.
Battista et al[21]	Mathematical modeling	Number of people addicted to prescription opioids or in rehabilitation/ treatment	Medical and nonmedical opioid use and addiction, opioid diversion, relapse	Stopping the diversion of prescribed opioids. Increasing the rate of addiction treatment	1. To have an addiction-free community we need to stop prescribing opioids and diversion of prescription opioids; however, due to the availability of illicit drugs, we always face the threat of an endemic addiction. Increasing the motivation of opioid addicts to start treatment will help to combat the epidemic.
Finley et al[22]	Conceptual modeling	Opioid misuse and related morbidity and mortality	Outcomes related to the impact of PDMP	PDMP	1. PDMP implementation would affect opioid prescribing behavior, diversion/doctor shopping, misuse, and morbidity/mortality. 2. Inconsistency in the PDMP implementation in different states causes mixed findings. 3. The impact of PDMP should be considered from both benefits and harms point of view. PDMP might lead patients to use illicit drugs to manage their pain as it restricts providers' opioid prescribing.
Wakeland et al[23]	System dynamics modeling	Opioid misuse and overdose fatalities	Medical and nonmedical opioid use and addiction, opioid diversion, providers' perception of opioids, traffickers, chronic pain treatment	PDMP Reducing the popularity of nonmedical usage Tamper-resistant drug formulation	1. Policies affecting prescription opioid use should consider both the negative and positive outcomes of it such as overdoses against number of treated patients. 2. Educating the population regarding the risks associated with nonmedical use (translated to a reduction of demand of opioid nonmedical use in the simulation model) will decrease opioid overdose deaths. 3. PDMP (translated to a reduction in doctor shopping or prescription forgery in the simulation model) will decrease opioid overdose deaths. 4. The tamper-resistant formulation will significantly decrease both the supply and demand of nonmedical use, but it could increase the supply of medical opioid as it decreases providers' perceived risks; leading to more medical users experiencing accidental overdoses. The increase in chronic noncancer pain has led to increased opioid prescribing.
Aronowitz et al[24]	Conceptual modeling	Number of incarcerated individuals with opioid use	The criminal justice system, incarcerated opioid users	Medication-assisted treatment (MAT) through a conceptual model of nursing and health policy	1. MAT must be provided to prisoners who were on MAT prior to imprisonment and should be continued for those who are released. 2. MAT is more influential in substance abuse treatment rather than behavioral therapy that is the current treatment policy of prisons. For those who have no danger to their community, community-based treatment should be considered instead of incarceration.
Schmidt et al[25*]	Conceptual modeling	Key data gaps regarding pharmaceutical opioids	Medical and nonmedical opioid use and its adverse outcomes, opioid diversion	Collecting opioid-related data	New data collection is needed in the following areas to inform policy interventions: incidence diagnosis rate of chronic nonmalignant pain (CNMP), rate of opioid use to treat CNMP and its abuse rate, consume rate per each abuse, the extent of availability of opioid for nonmedical use, data on drug-seeking behaviors, fraction of diverted opioid from doctor shoppers, and amount of opioid obtained from doctor shopping or forgery.

(Continued)

Table 1. (Continued)

AUTHOR (REFERENCE)	MODELING METHOD	RESEARCH AREA/ MAIN OUTCOME	KEY FACTORS INCLUDED	TESTED OR PROPOSED SCENARIO/STRATEGY	KEY FINDINGS THROUGH MODELING OR LITERATURE REVIEW
Wakeland et al[26]	System dynamics modeling	Nonmedical opioid users and accidental overdose mortality among them	Recreational users, opioid diversion, heroin users	Tamper-resistant drug formulations Strategies for reducing diversion of opioid medicines	1. Both interventions could significantly reduce nonmedical user populations and overdose deaths in the long term. 2. Leftover medicine from prescriptions leads to diversion. Educating patients about safe storage and disposal or restricting refills could reduce leftover medicine.
Wakeland et al[27]*	System dynamics modeling	Medical and nonmedical opioid overdose deaths	Medical and nonmedical pharmaceutical opioid use, trafficking	Educational interventions	1. Increasing the providers' perceived risk of prescription opioids will raise their caution in monitoring patients with signs of abuse and eventually will reduce medical and nonmedical opioid overdose deaths. 2. Educating medical users to decrease their abuse and addiction rate will decrease medical overdose deaths, however, it will cause nonmedical overdose deaths to grow. Running educational programs to decrease the popularity of nonmedical use reduces the nonmedical overdose deaths sharply.
Widener et al[28]	Agent-based modeling	Supply side of opioids	Farmers, crops, trafficking	Economic and noneconomic incentives Blockade strategies	1. Applying border interventions such as trafficking blockades in all major exit points of opioid-producing countries could reduce the attractiveness of cultivating opioids. 2. Providing the right amount of national subsidies for licit crops could decrease the opioid production. 3. Defining the reasons why farmers choose to grow opioids is necessary before initiating policies. Increases in insurgency raise opioid production.
Wakeland et al[29]*	System dynamics modeling	Abuse, addiction, and overdose death associated with the pharmaceutical opioid treatment of chronic pain	Providers' perception of opioids, chronic pain treatment, patients on short- or long-acting and with opioid addiction	Prescriber education program Tamper-resistant formulation for an opioid Reduction in abuse and addiction rates	1. Decreasing prescription rate of opioids help tamper-resistance intervention to reduce overdoses. 2. Increased rate of chronic diseases led to a high rate of prescription opioids. Increases in addiction and opioid abuse have controlled the providers' prescribing patterns.
White and Comiskey[30]	Mathematical modeling	Heroin users in and out of treatment	Heroin users, relapse, recruiting	Prevention strategies Treatment strategies	1. The rate that susceptible people become heroin users is highly affecting the recruiting rate positively. 2. The rate that users initiate treatment after starting heroin use, and the recovery and overdose rate before getting treatment are affecting the recruiting rate inversely but proportionally smaller than #1. Preventing people from becoming opioid users is more effective than focusing on treatment strategies as there is always relapsing in treatment.
Caulkins et al[31]	Mathematical modeling	Occasional and heavy heroin use	Heroin users, cannabis and cocaine users	Primary prevention Controlling the supply of hard drugs Harm reduction	1. We cannot see the effects of an intervention on health outcome momentarily as many factors cause delays in the system. Policymakers should not make their decisions based on yearly changes in the drug use trends because drug use is a time-dependent system and big-picture thinking is needed.

(Continued)

Table 1. (Continued)

AUTHOR (REFERENCE)	MODELING METHOD	RESEARCH AREA/ MAIN OUTCOME	KEY FACTORS INCLUDED	TESTED OR PROPOSED SCENARIO/STRATEGY	KEY FINDINGS THROUGH MODELING OR LITERATURE REVIEW
Klein[32]	Conceptual modeling	Future of drug policies	Drug users	Life enhancement (increasing the quality of life) Evidence-based regulations (choosing policies based on scientific assessments of benefits and harms)	1. Drug policies are moving towards the introduction of drug consumption rooms, social supply of drugs, and heroin-assisted therapy. Supply-side interventions have failed and exacerbated drug use while harm reduction strategies had shown positive results.
Agar and Reisinger[33]	Conceptual modeling	Heroin use	Heroin users	Adapting trend theory to explain heroin use trends Impact of a drug policy on epidemics	1. Heroin trend is a complex system and we need methods that address the complexity of it. 2. As the heroin epidemic is distributed in society, we must study different groups at different social locations to understand it. 3. Open marginality—the results of a historical change that cause a large difference between the expectation of a population and the reality—creates a heroin epidemic. Changes in the delivery system (production/distribution) and drug policies usually lead the new drug epidemic.

*Purdue Pharma L.D., a pharmaceutical company, funded these studies.

Some studies included the influence of recruitment of new users and trafficking in their model, while others simply considered a very simple Susceptible-Infected-Recovered model. Most of the studies on opioid use and overdoses did not model the transition of users between prescription opioid use and nonprescription opioid use. Exceptions include Wakeland et al,[26] who considered the transition from nonmedical use of prescription opioids to heroin use, and Gatley,[20] who looked at the number of heavy users of prescription opioids who switch to heroin each year.

Conceptual modeling

The main insights of studies that employed conceptual modeling were that Klein[32] considered the future of drug policy and proposed interventions such as drug consumption rooms and social supply of drugs and suggested stopping the supply-side interventions as they exacerbate the drug use. Agar and Reisinger[33] looked at trend theory—investigating the histories of a population and supply-side of a product—and drug policy related to heroin use and reached the same conclusions as Klein:[32] controlling drug delivery systems usually exacerbates the situation and leads to a new drug epidemic. In addition, Finley et al[22] showed both positive and negative influences of PDMP on opioid use.

Investigated interventions

We categorized all the tested interventions in these studies into preventive or therapeutic interventions based on the guidelines reported by Smith et al[34] and identified their ultimate targets in Table 2. The most common interventions applied in these studies to eradicate the epidemic were educational programs (4 studies), PDMP (3 studies), tamper-resistant drug formulation (3 studies), treatment strategies and medication-assisted treatment (MAT) (3 studies), and supply-side interventions (3 studies).

Discussion

Our analyses revealed that most studies have focused on prescription opioids or heroin individually. They have not modeled the transition of patients from prescription opioids to heroin and synthetic opioids like fentanyl. This transition is important because the supply of prescription opioids has decreased due to the awareness campaigns targeting providers prescription behavior, or PDMP.[35] However, the use of heroin and synthetic opioids outside of the medical system continues to grow[8] due to their lower costs and higher availability.[20,36] Therefore, a reliable model for policy analysis must consider heroin and synthetic opioids, which are more potent than prescription opioids[7,37] and are the leading drivers of opioid overdoses in the recent years, in addition to prescription opioids. The most significant waves of the rise in opioid overdoses death have been in 2000 due to prescription opioids, 2010 due

Table 2. Interventions used in the studies of modeling impact in development of policies to control the opioid epidemic.

INTERVENTIONS	TARGET	PREVENTIVE/THERAPEUTIC
PDMP[20,22,23]	Providers	Therapeutic
Provider education programs[21,27,29]	Providers	Both
Patient education programs[23,27]	Patients	Both
Tamper-resistant prescription forms, diversion control[23,26,29]	Drug diversion	Both
Supply-side interventions[28,31,32]	Illegal producers	Preventive
Prevention strategies[30,31]	Patients	Preventive
MAT strategies[21,24,30]	Patients	Therapeutic

to heroin, and 2013 due to synthetic opioids like fentanyl outside of medical settings.[38] One reason that we do not see this transition phase in the selected articles might be the timeframe of their study and the data available to them.

Furthermore, most studies have focused on the treatment of chronic pain and none considered the rate of prescribing opioids for acute pain, which may be an individual's first introduction to opioid use.[23] In addition, no study investigated the role of age or geographic locations on health outcomes. The reasons could be due to the lack of historical data, as was mentioned by researchers, or just for simplification purposes in their research.

In the following sections, we explore some of the features of the selected articles including modeling approaches, funding, and limitations that can assist modelers and researchers in their modeling work. Then we provide our suggestions for future modeling practices.

Modeling approaches

One finding of this scoping review is that system dynamics simulation modeling seems more practical than other techniques such as agent-based modeling or mathematical modeling to study a complex problem like an opioid epidemic for policy analysis purposes. One reason might be limited historical data available to researchers since system dynamics modeling facilitates the use of aggregated data and does not require comprehensive datasets. Another reason may be that system dynamics is a reliable tool for policy analysis as it studies the underlying structure of the system and reveals the relationship among variables in the system.[39] Moreover, it assists modelers in communicating the results to other stakeholders such as policymakers.

Limitations of the selected articles

Besides their significant results, these 14 selected articles have four main limitations: the lack of historical and empirical data, validation of models, over simplifications in their models for a complex issue like an opioid epidemic, and the short time horizon of the policy period. Modeling is the art of simplification but it is necessary to provide a valid and reliable model for policy analysis purposes. One way to check the robustness and validity of models is to use the historical data and replicate its behavior but sometimes we do not have access to enough data. We agree with Schmidt et al[25] that more data are needed for opioid studies, as lack of data leads to the weak estimation of variables through the model, as evidenced in most of the selected articles. Regarding the policy period and according to Caulkins et al,[31] the progression of users through states of drug use takes a long time and drug use is a time-dependent system; to see the effect of this dynamic on final outcomes we need to consider a longer policy period.

Quality and quantity of the selected articles

In this study, we did not evaluate the study quality of articles since the purpose of scoping reviews is to include articles based on their relevance and not their quality. However, we examined the journal impact factor of the included studies to evaluate their impact; as the impact factor can have an important role especially in the quality assessment of recently published articles.[40,41]

Fourteen modeling studies were published on the opioid epidemic (using our inclusion criteria). Among them, only one was published in a journal that had a CiteScore less than 1 (0.68).[32] Three articles were published in journals with an impact factor higher than 2.[26,27,29] One of the included studies was a published thesis[20] and another study was a preprint published in arXiv.[21] The rest of the articles were published in journals with an impact factor less than 2. Based on the impact factor, we can say that the overall quality of these studies is moderate.

In addition to the impact factor, we also considered the funding resources of these articles. Only eight received funding.[22,25-27,29-31,33] Our study, similar to the literature, shows a low amount of financial support for modeling studies on the opioid crisis from various public health organizations.[42] Increasing public funding for modeling research will be helpful in combating the opioid epidemic. Table 3 shows the funding resources for the selected articles.

Table 3. Funding resources for the selected articles.

AUTHOR (REFERENCE)	FUNDING RESOURCE
Gatley[20]	None
Battista et al[21]	None
Finley et al[22]	Substance Abuse Working Group of the Joint Program Committee 5/Military Operational Medicine Research Program, US Army Medical Research and Materiel Command
Wakeland et al[23]	None
Aronowitz et al[24]	None
Schmidt et al[25]	Purdue Pharma L.P.
Wakeland et al[26]	National Institute of Health/National Institute on Drug Abuse (NIDA) grant
Wakeland et al[27]	Research grant to Portland State University funded by Purdue Pharma L.P.
Widener et al[28]	None
Wakeland et al[29]	Purdue Pharma L.P.
White and Comiskey[30]	The Health Research Board of Ireland with the support of the National University of Ireland
Caulkins et al[31]	This work was funded in part by the Robert Wood Johnson Foundation, the Qatar Foundation, the Victorian Health Promotion Foundation, and the Colonial Foundation Trust and forms part of the Drug Policy Modeling Program
Klein[32]	None
Agar and Reisinger[33]	NIDA

From a quantity perspective, only 14 studies were selected. Several reasons can be attributed to these limited numbers. One is the lack of comprehensive data on various aspects of the opioid epidemic such as in the supplier, provider, and consumer levels[25] as data are fundamental for modelers to provide a valid model. Another reason could be the unfamiliarity of the policymakers and public health specialists with the application of modeling procedures for solving public health problems.[42,43] In addition, lack of funding, as was mentioned, is another barrier for modelers.

Our suggestions

Overall, we propose modelers to consider the following recommendations to develop a better decision support tool that could inform policymaking.

Supply side. We recommend including the treatment of acute pain, in addition to chronic opioid use, in future modeling practices. Trafficking, doctor shopping, and forgery are the other aspects of opioid supply into the communities that should be included. From a broader perspective, more research is needed to study the reasons farmers choose to cultivate illicit crops rather than licit ones and how we can provide more incentives to alternate this dynamic. The only study in our selected articles that investigated the supply side of opioids was done by Widener et al,[28] in which the authors suggest border interventions such as trafficking blockades in all major exit points to prevent the exportation of opioids from other countries such as Afghanistan.

Perceptions. Among the articles we reviewed, only two of them looked at providers' perceptions and how they affect the system.[23,29] Both considered the role of providers' perceptions of risk and its influence on providers prescribing behavior. To model perceptions, we can follow the Health Belief Model outlined by Becker;[44] it is being used to predict decisions about health care and its constructs such as perceived susceptibility, barrier, and benefits can be used to model the patients and providers perceptions toward opioids and addiction treatment. Our review highlights the shortage of perception modeling in this epidemic although perceptions are playing critical roles in patients and providers decisions toward opioid use and prescription.

Unstudied factors. Although studies mentioned in Table 1 looked at a variety of factors, none addressed the influence of geographic factors on opioid overdoses, and none investigated the different dynamics of the opioid epidemic in different age groups. These two aspects may play an important role in the current epidemic; to develop a reliable policy analysis tool, we should include these factors in our modeling practices.

In addition, the importance of socioeconomic conditions and demographic factors in this epidemic has been investigated earlier.[4,45,46] Including these factors in simulation models requires strict assumptions and herculean efforts. However, to facilitate the inclusion of them into our analysis, expanding modeling techniques (through combining different techniques together such as simulation modeling with GIS techniques[47]) and improving opioid-related databases can be helpful.

Table 4. Preventive and therapeutic interventions that either were not included in our selected articles or were not explored enough.

INTERVENTIONS	TARGET	PREVENTIVE/THERAPEUTIC
Increasing awareness of the risks associated with opioid (RX Awareness)	Public awareness	Preventive
Safe disposal	Drug diversion	Both
Controlled substance tracking and monitoring	Illegal buyers	Both
Needle exchange, case management, drug consumption room, social supply of drugs, heroin-assisted therapy	Opioid users	Therapeutic
Immunity from prosecution, naloxone over-the-counter or by prescription	Overdoses	Therapeutic

Each intervention is targeting a different sector of the opioid epidemic.

Health outcomes. Some of the selected articles considered the overdoses from prescription opioids and heroin, prescription opioid abuse and misuse, and nonmedical use of prescription opioids. However, opioid misuse and overdoses from synthetic opioids such as fentanyl should be considered as well in future models. In addition, considering all these trajectories together provides a comprehensive model for policy analysis purposes.

Interventions. Policymakers and public health officials have initiated many interventions to stem the opioid epidemic; however, these efforts have not eradicated the epidemic, nor has the effectiveness of these interventions been comprehensively evaluated. Some interventions may be effective in one setting and ineffective in others, or may even exacerbate the epidemic. One reason for this policy resistance lies in the fact that we usually operate within a narrow mental model—that is, we fail to see the problem from the right angle, and the time period over which we evaluate our interventions is too short. Therefore, over time, we will face the same problem, maybe with intensified consequences. To avoid policy resistance and the emergence of new issues, we must take a long view, developing a more "big-picture" approach.

We recommend the inclusion of interventions (mentioned in Table 4) for policy analysis in future models and exploring the influence of some others—that were previously evaluated and suggested (Table 2)—such as safe disposal in more detail. Among suggested interventions, drug consumption room, social supply of drugs (providing access to drugs where there is no profit consideration), and heroin-assisted therapy (providing the medical heroin prescription to high-risk heroin users) are very controversial; however, they have preliminarily positive results such as decreasing the number of opioid overdoses.[48–52]

Limitations

Because we focused our search strategies on simulation and conceptual modeling of opioid use and misuse affecting public policy or public health decision-making, we did not assess studies on modeling outside of policy or public health parameters. We did not include economic models since they investigate the efficiencies of interventions which was outside the scope of this review, and there is already a recent study in this area conducted by Chetty et al,[53] which assists policymakers in identifying efficient health interventions. In addition, we did not review interventions applied in different healthcare facilities, such as clinical settings or providers' offices.

Conclusions

We systematically synthesized the literature to document the research articles that strive to address the opioid epidemic through simulation and conceptual modeling. Most articles have focused on the overdoses from prescription opioids or heroin separately, and have not included the transition of patients from prescription opioids to heroin. Factors such as age and geographic locations and their association with opioid misuse and overdose have not been included in these models. This scoping review provides policymakers and public health officials with critical, useful modeling techniques in studying the complex system of the opioid epidemic. In addition, it delineates gaps or areas needing further study in conceptual modeling, and provide researchers with the variables they need to consider in developing a reliable, valid decision support tool. Implementation of these findings and suggestions can enhance policymaking tools that will improve public health and policymaking process.

Authors' contributions

NS initiated this project and RH supervised it. A specialist/librarian (MM), developed strategies for and searched eight databases based upon requests from NS.

Two reviewers (NS and SSS) screened studies for inclusion. When consensus was not reached, a third person (RH) reviewed the study and served as the tie-breaker.

NS created the first draft of the manuscript and all the other authors revised it critically. After several revisions, all authors approved the final version.

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Availability of data and material

We developed strategies for and searched eight databases. See Additional File 1 for search strategies.

Supplemental Material

Supplemental material for this article is available online.

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