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ORIGINAL ARTICLE

Complex Systems Approaches to Understand Drivers of Mental Health and Inform Mental Health Policy: A Systematic Review

Brent A. Langellier[1,5] · Yong Yang[2] · Jonathan Purtle[1] · Katherine L. Nelson[1,3] · Ivana Stankov[3] · Ana V. Diez Roux[3,4]

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Abstract
We conducted a systematic review of studies employing complex systems approaches (i.e., agent based and system dynamics models) to understand drivers of mental health and inform mental health policy. We extracted key data (e.g., purpose, design, data) for each study and provide a narrative synthesis of insights generated across studies. The studies investigated drivers and policy intervention strategies across a diversity of mental health outcomes. Based on these studies and the extant literature, we propose a typology of mental health research and policy areas that may benefit from complex systems approaches.

Keywords Mental health · Public policy · Complex systems · Systems science · Systematic review

Introduction

Preventing mental illness is an imperative public health challenge (Cohen and Galea 2011; Cottler 2011; NRC 2009). Globally, 11% of disability adjusted life-years lost are attributable to mental illness (Murray et al. 2013). In the U.S., estimates of the past-year prevalence of any mental illness among adults range from 18 to 26%. Data from the National Survey on Drug Use and Health suggests that the prevalence stayed fairly consistent near 18% from 2008 to 2016 (Ahrnsbrak et al. 2017). Data from the 2008–2012 Mental Health Surveillance Study suggest a past-year prevalence of any mental illness of 22.5% (Karg et al. 2014), while the 2001–2003 National Comorbidity Survey Replication suggest a higher prevalence of 26% (Reeves et al. 2011).

There is increasing recognition among mental health researchers, clinicians, and policymakers that mental health outcomes are shaped by a complex interplay between neurobiological and psychosocial systems, risk and protective factors, and mental health systems and service utilization (Cicchetti 2010; Shern et al. 2016; World Health Organization 2014). Among the risk and protective factors are physical and social environments (Fowler et al. 2009; Lee and Maheswaran 2011; Lorenc et al. 2012), interpersonal interactions (Kawachi and Berkman 2001), and socioeconomic characteristics (Cohen and Galea 2011; Eaton 2012; Lambert et al. 2015).

The drivers of mental health comprise a 'complex system' of interdependent factors at multiple levels of influence (Mabry and Kaplan 2013). Complex systems approaches like agent-based modeling (ABM) and system dynamics modeling (SDM) may be helpful in generating insights into the structure and function of the complex systems that shape mental health. Despite their increasing use in other public health areas (Carey et al. 2015; Levy et al. 2010, 2011; Nianogo and Arah 2015), there appear to be few applications of complex systems approaches in mental health research. This knowledge gap warrants attention because complex systems approaches have the potential to generate improved insights into drivers of mental health outcomes and thus better inform the design and selection of intervention strategies that span multiple contexts (e.g., neighborhoods, schools,

✉ Brent A. Langellier
bal95@drexel.edu

1 Department of Health Management and Policy, Dornsife School of Public Health, Drexel University, Philadelphia, PA, USA

2 Division of Social and Behavioral Science, School of Public Health, The University of Memphis, Memphis, TN, USA

3 Urban Health Collaborative, Dornsife School of Public Health, Drexel University, Philadelphia, PA, USA

4 Department of Epidemiology and Biostatistics, Dornsife School of Public Health, Drexel University, Philadelphia, PA, USA

5 3215 Market St, 3rd Floor, Office 356, Philadelphia, PA 19104, USA

workplaces) and scales of influence (e.g., neurobiological, interpersonal) (Cohen and Galea 2011; NRC 2009; WHO 2014). This includes policies that emphasize not only treatment of existing mental illness, but also the underlying social conditions and contexts that lead to future mental illness (Cohen and Galea 2011; Cottler 2011).

We conducted a systematic review to determine the extent to which studies have used complex systems approaches to understand drivers of mental health and to inform mental health policy. We extracted data regarding the purpose, design, and use of data for each study. We also provide a narrative synthesis of the types of insights generated by these studies. Based on our findings, complex systems literature within the broader field of public health, and major points of emphasis in mental health prevention and services research, we present a typology of questions for which complex systems approaches may be particularly insightful. We conclude by highlighting potential challenges and opportunities in using complex systems approaches in mental health research and policy.

Methods

Literature Search Strategy and Inclusion Criteria

We conducted a search of the peer-reviewed literature in April 2017 to identify studies that used ABM, SDM, or a related methodology to explore issues of mental health. Our intent was to identify computer simulation studies that used these modeling approaches, as well as conceptual studies that used empirical or participatory processes to explicate the variables and relationships in a system, but that do not necessarily include any mathematical modeling or computer simulation (Hovmand 2014). We searched three databases: PubMed, Web of Science, and Science Direct. We queried the following terms, using all combinations of one mental health term ("mental health," "depression," "post-traumatic stress disorder," "schizophrenia," and "anxiety disorder") and one modeling term ("agent based," "system dynamics," and "discrete event simulation"). We selected specific mental health conditions to include based on the top contributors to the global burden of mental illness, as identified by Vigo et al. (2016). We did not include substance abuse terms based on what we view as key differences in behavioral, biological, and social mechanisms. We focused specifically on ABM and SDM because they are recognized as key complex systems approaches pertinent to health and health policy (Hassmiller Lich et al. 2013). We included discrete event simulation because of its widespread use in health and health care policy decision support (Günal and Pidd 2010; Jacobson et al. 2006). We limited the search to results including both a mental health term and a modeling term in any field in PubMed or in the title, abstract, or keywords fields in Web of Science and Science Direct. We also reviewed the bibliographies of eligible studies to identify additional studies. To ensure methodological rigor, we adhered to the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) guidelines for conducting and reporting the review process (Moher et al. 2009).

For all studies, first we screened the title and abstract for eligibility. Where eligibility remained unclear, we read the full-text version of studies to determine eligibility. We included studies in the review if they: (1) developed and/or implemented an ABM, SDM, or DES; (2) included a behavior (e.g., utilization of mental health care services) or outcome (e.g., depression) directly related to one of the mental health conditions listed above, and (3) were published in full-text format in a peer-reviewed journal or book indexed by the PubMed, Web of Science, and Science Direct databases. We excluded conference abstracts and proceedings.

Because of our interest in studies that explore drivers of mental health or that can inform policy interventions across contexts and scales of influence, we excluded studies that: (1) were based exclusively within the context of a specific clinical or health care system (for an example, please see Zimmerman et al. 2016), (2) included exclusively biological, psychological, or other intrapersonal factors and processes (for an example, please see Tanaka 2010); (3) exclusively evaluated the clinical or cost effectiveness of a specific drug, medical technology, clinical treatment, or health system process (for an example, see Wolstenholme et al. 2010). We did not exclude based on publication date.

Data Extraction

For each publication, we extracted the following information: lead author name and date of publication, model type (i.e., ABM, SDM, DES), primary outcome, the explicit purpose of the model, reality level, key design concepts, use of data for calibration and validation, and main findings. We characterized the reality level of models using a three category system: (1) low, if the environment, agents, and parameters were stylized (i.e., implausibly simplistic) rather than linked to empirical data, (2) medium, if some but not all factors of the environment, agents, or parameters were linked to empirical data, (3) high, if the environment, agents, and parameters were all linked to empirical data (please see 'Discussion' section for further justification of assessing a model's reality level).

We characterized use of quantitative data in the models for calibration and output validation. We defined calibration broadly, as any iterative process of 'tuning' the values of parameters to align specified output produced by the model with output describing the 'real' system (Railsback and Grimm 2012). For example, this might include making incremental adjustments to the rate at which individuals in a model recover from episodes of depression in order to align simulated depression prevalence trends with those observed in a real-world population. Output validation refers to comparison of output generated by the model to observed real-world data. For each model, we made a dichotomous (yes/no) assessment of whether or not data were used for calibration and validation. We also assessed whether authors reported collecting data from experts to inform, refine, and validate the structure of models (i.e., input validation). This type of data can be gathered via facilitated group sessions (e.g., participatory group modeling) in which a series of scripted activities are used to make explicit participants' mental models (Hovmand 2014). The participatory group modeling process is then used to develop a model structure that is consistent with group consensus around the conceptual model as it relates to the problem under investigation. A quantitative aspect can then be added to the conceptual model based on the available literature, extant data, and expert opinion.

Key design concepts of the models included summaries of processes, parameters (e.g., depression incidence), stock (accumulation) and flow (dynamic) variables, feedback loops, effects of networks (i.e., if agents are embedded in friendship, family, or other social networks that affect outcomes) and simulation scenarios. For ABMs, we also described key rules governing agent behavior (e.g., under what conditions and how an agent's behavior is influenced by other agents in his/her social network). We present all data extracted from each publication in Table 1, as well as a narrative synthesis of the types of insights generated across studies.

Results

Literature Search Results

The database search returned 72 publications in PubMed, 90 in Web of Science, and 27 in Science Direct (n = 187). We identified two additional publications that met the inclusion criteria by reviewing the bibliographies of included manuscripts (n = 189). After removing 65 duplicates, we screened 124 records by title and abstract and removed 112 that did not meet the inclusion criteria. Frequent reasons for exclusion include that the study did not use a complex systems approach (i.e., ABM, SDM, DES) (n = 68), did not pertain to a mental health outcome (n = 16), or exclusively evaluated a single medical technology, clinical treatment, or health system process (n = 14). We then screened the full-text version of 12 studies and identified eight for inclusion in the review (Fig. 1).

Data extracted for each publication are presented in Table 1. Publications that met the inclusion criteria consisted of five distinct SDMs, three ABMs, and zero DESs. The primary outcomes were major depression or depressive symptoms for one ABM (Mooney and El-Sayed 2016) and two SDMs (Lyon et al. 2016; Wittenborn et al. 2016), post-traumatic stress disorder (PTSD) for one ABM (Cerdá et al. 2015) and two SDMs (Ghaffarzadegan et al. 2016; Wang et al. 2013a), mental health service utilization for one SDM (Trani et al. 2016), and general physical and mental health for one SDM (Kalton et al. 2016). Three of the models (Trani et al. 2016; Wang et al. 2013a; Wittenborn et al. 2016) were conceptual SDMs that used available data sources (e.g., the published literature) and participatory methods to develop visual representations of complex systems related to mental health.

Most of the empirical studies (i.e., the five studies that are not conceptual SDMs) leveraged empirical data in some way. We classified two ABMs (Cerdá et al. 2015; Kalton et al. 2016) and one SDM (Ghaffarzadegan et al. 2016) as having a high level of realism based on the characterization of agents and environments. For example, the ABM of Kalton and colleagues (2016) integrated data from patients (e.g., demographics, behaviors), the care system (e.g., number and capacity of providers), and the criminal justice system (e.g., jail sentence duration, diversion program entry). We classified one ABM (Mooney and El-Sayed 2016) as having a low degree of realism because individuals in the model had only a limited range of characteristics (e.g., body mass index, number of network connections) and because the model explored the impact of living in an obesogenic environment but did not integrate environmental or neighborhood data. We classified the SDM of Lyon et al. (2016) as having a medium level of realism, because many of the model's parameters (e.g., stock and flow variables) were anchored to empirical data, but the characteristics of the population and school environment were stylized. Output validation was limited to the SDM of Ghaffarzadegan et al. (2016) and the ABM of Mooney and El-Sayed (2016). For example, Mooney and El-Sayed compared the simulated prevalence of depression and obesity prevalence predicted by their model to observed rates in two U.S. states.

Insights Generated by the Included Studies

One insight related to the interrelationships between different drivers of mental health outcomes (Ghaffarzadegan et al. 2016; Trani et al. 2016; Wang et al. 2013a; Wittenborn et al. 2016). For example, the conceptual SDM developed by Trani et al. (2016) examined the interrelationship between mental health care service utilization, poverty, and community and family stigma among those with mental illness in Afghanistan. The study was one of several to use stakeholder

Table 1 Characteristics of studies that used complex systems methods to explore issues of mental health

Title and author	Model type	Purpose	Primary mental health outcome/s	Reality level	Design concepts	Calibration and validation	Findings
To treat or to prevent?: Reducing the population burden of violence-related post-traumatic stress disorder (Cerdá et al. 2015)	Agent-based model	To examine violence and PTSD in an urban area under four scenarios: (1) no intervention, (2) targeted policing to violence 'hot spots', (3) increased access to cognitive behavioral therapy (CBT) for those who suffer from violence-related PTSD, and (4) combination of hot-spot policing and CBT	Annual prevalence of post-traumatic stress disorder	High—agent characteristics and parameters are empirically anchored; environment is a grid and agents are assigned to cells based on neighborhood data in New York City	Agents in the model develop PTSD at rates governed by exposure to violence and participation in cognitive behavioral therapy (CBT). Exposure to violence, in turn, is the result of individual- (e.g., socioeconomic status and demographics) and neighborhood- (e.g., neighborhood income and violence) level characteristics, as well past experiences of violence. Simulation scenarios were designed to represent interventions including: (1) increased utilization of CBT for those exposed to violence, and (2) targeted policing that reduces violence in high-crime neighborhoods. Model outcomes include exposure to violence and development of PTSD	Calibration—empirical data are used to calibration parameters related to population composition, mortality rates, residential mobility, violence victimization, perpetration, and exposure, PTSD prevalence, and mental health service use	The combination of targeted policing and CBT is more effective than either strategy in isolation. Transition to targeted policing without any increase in the number of police would result in reduced exposure to violence and PTSD; achieving the same effect would require a substantial increase in investment in CBT services
A dynamic model of post-traumatic stress disorder for military personnel and veterans (Ghaffarzadegan et al. 2016)	System dynamics	To examine trends in the population of PTSD patients among military personnel and veterans in the postwar era, and to identify policies that can help mitigate PTSD	Diagnosis of new cases of post-traumatic stress disorder	High—agent characteristics and parameters are empirically anchored as available	The model includes personnel recruited into the military that may or may not be deployed to combat zones of varying intensity, experience trauma, develop PTSD, be diagnosed with PTSD, and receive effective treatment. Military personnel then separate (i.e., transition to veteran status) and undergo similar processes and outcomes. Model outcomes include diagnosed and undiagnosed PTSD, and costs of PTSD to the military and Veteran's Administration. Simulation scenarios represent varying levels of engagement in future wars (e.g., low, medium, and high deployment to combat zones) and diagnosis, treatment, and prevention interventions	Calibration—partial model calibration to estimate values of parameters for which data were not available Output validation—output validation to compare the number and rate of PTSD diagnosed cases in the military and VA during different time periods	An optimistic scenario with 'status quo' levels of engagement in combat suggests that PTSD prevalence among veterans will be at least 10% over the next decade. During wars, resiliency-related policies are most effective for decreasing PTSD. Current policy interventions will have little to no effect on mitigating PTSD at the population level

Table 1 (continued)

Title and author	Model type	Purpose	Primary mental health outcome/s	Reality level	Design concepts	Calibration and validation	Findings
Multi-Agent-based simulation of a complex ecosystem of mental health care (Kalton et al. 2016)	Agent-based model	Builds upon Johnson et al. (2014); to examine impacts of care coordination for people with serious and persistent mental illness across multiple providers/living arrangements	Patient mental health and physical health state, each assessed as healthy, mild, moderate, or severe	High- model is anchored to data regarding patients, the care system, and the criminal justice system	The model represents an ecological system of care and living arrangements for people with serious and persistent mental illness. Key processes include transitions through mental health states (e.g., healthy, mildly unhealthy), physical environments (i.e., home, hospital, jail, homeless), substance abuse, treatment, and medication adherence. The model includes a broad set of parameters in the following categories: (1) patients (e.g., population size, adherence and behaviors, crime rates), (2) treatment plans (e.g., medicine, appointments, related living arrangements), (3) care providers (e.g., capacity, costs), (4) physical environment (e.g., probability of living arrangement, length of stay), (5) law enforcement and criminal justice (sentence duration, parole and probation). Intermediate outcomes include mental and physical health states, hospitalizations, arrests, suicide attempts, employment, crisis events, inpatient and outpatient care. Simulation scenarios represented coordination policies, including: (1) improved handoffs during provider transitions, and (2) increased appointment compliance	Calibration—the values of multiple model parameters were iteratively tuned to align outcomes with historical data Input validation—expert opinion from medical, social service, and criminal justice experts used to inform structure of model	Improving the success rate with which patients are 'handed off' during provider transitions results in improved medication compliance and reduced hospitalization and incarceration. Increasing patients' appointment compliance results in a higher proportion of patients living in private residences and decreases in hospitalization and incarceration. The model is useful for identifying likely-to-be-effective policy interventions for addressing the housing and incarceration situations of those with serious and persistent mental illness

Table 1 (continued)

Title and author	Model type	Purpose	Primary mental health outcome/s	Reality level	Design concepts	Calibration and validation	Findings
Modeling the impact of school-based universal depression screening on additional service capacity needs: A system dynamics approach (Lyon et al. 2016)	System dynamics	To help inform implementation decisions in communities related to universal depression screening in high schools	Prevalence of self-reported depression symptoms among youth; mental health screening and treatment	Medium—model parameters (e.g., stock and flow variables) were identified via available data sources and the literature using a non-exhaustive search; not anchored to a specific population; school-environment and population are stylized	Key inputs include depression prevalence, mental health service utilization among depressed and non-depressed, rate of universal screening participation, sensitivity and specificity, mental health services staff capacity, likelihood of students' using mental health services, treatment duration, recovery rates in evidence-based and non-evidence-based treatment. Simulation scenarios represented interventions, including: (1) universal screening alone, and (2) universal screening in combination with 'compensatory approaches' to address increased service demand resulting from universal screening (i.e., allocation of additional staff time and improved effectiveness of mental health services)	No calibration or validation reported in the manuscript	Universal screening results without increased treatment capacity results in a 'backlog' of youth who need but are waiting for treatment. Universal screening combined with increased treatment capacity results in faster entry into mental health services and reduces or eliminates the backlog. Implementation of an evidence-based treatment protocol has marginal positive effects on treatment effectiveness

Table 1 (continued)

Title and author	Model type	Purpose	Primary mental health outcome/s	Reality level	Design concepts	Calibration and validation	Findings
Stigma and the etiology of depression among the obese: An agent-based exploration (Mooney and El-Sayed, 2016)	Agent-based model	To explore how body norms, weight-base stigma, and social isolation shape depression risk in the obese	Cumulative incidence of depression (i.e., ever-depressed)	Low—agents generally lacked characteristics other than obesity and depression; model is not spatially explicit. Some model parameters are stylized (e.g., effect of ostracization on depression, effect of environment on body weight) while others were anchored to data (e.g., obesity prevalence)	Agents are organized in a small-world social network. There are several dynamic processes: (1) Updated BMI - each agent's BMI updates dynamically based on past BMI, an environmental-level influence referred to as 'obesogeneity', and random noise. Importantly, some agents were resistant to the obesogenic influence of the environment. (2) Social isolation - agents observe the body mass index (BMI) of their peers and drop connections with people whose BMI is 'out of sync' (i.e., above a threshold distance from the agent's own BMI, the mean BMI of the peer group, and the mean BMI of the population). (3) Ostracization and depression- an agent is considered 'ostracized' when they are dropped as a connection of another agent. In every time step that an agent is dropped, their risk of becoming depressed increases by a set amount; this amount increases with greater ostracization history. The model is used to explore simulation scenarios including: (1) a high-obesity context similar to the U.S. state of Mississippi versus a low-obesity context similar to the state of Colorado, (2) varying values of environmental obesogeneity and resistance to obesogeneity, (3) sensitivity analyses to assess sensitivity to parameter values (e.g., magnitude of peer influence, effect of depression on obesity) and aspects of the model's structure (e.g., small world versus random networks	Output validation—the authors compare depression, obesity, and BMI outcomes simulated under two scenarios to historical data in Colorado and Mississippi	The proportion of obese agents who were depressed was higher in the low-obesity context versus the high-obesity context, a result driven by the greater likelihood of ostracization (i.e., being 'dropped' as a connection) among the obese in the low-obesity context. Cumulative incidence of depression was inversely proportional to prevalence of obesity, other than in scenarios with very low levels of obesity such that there were few obese agents to be ostracized and depressed. The above findings were robust to small changes to parameter values and structure of the social network. The authors conclude that a 'relatively simple weight-based stigma mechanism' is sufficient to reproduce 'empirical findings that risk of depression in the obese [is] higher in the context where obesity [is] less prevalent.'

Table 1 (continued)

Title and author	Model type	Purpose	Primary mental health outcome/s	Reality level	Design concepts	Calibration and validation	Findings
Community based system dynamic as an approach for understanding and acting on messy problems: a case study for global mental health intervention in Afghanistan (Trani et al. 2016)	System dynamics (conceptual), not quantified	To use community based system dynamics and group model building sessions to examine interactions between multiple factors and actors to examine low service utilization in Afghanistan for those with mental illness	Mental health care service utilization among those with mental illness	No formal model was implemented	Participants identified three major balancing feedback loops and four major reinforcing feedback loops that constitute a hypothesis of how system components interact to produce consistently low service utilization among those with mental illness. Balancing feedback loops include: (1) increased treatment leads to reduced symptoms and more medical compliance, (2) utilization of care costs money, which magnifies poverty and reduces ability of poor people to pay for future utilization of services, (3) treatment needs associated with mental illness and poverty is linked to stressors caused by risk of falling deeper into poverty via additional utilization. Reinforcing feedback loops include: (1) as understanding of mental illness increases, families' stigma lessens, (2) social isolation of people with mental illness leads to increased community stigma related to mental illness, which increases the likelihood that people with mental illness will be mistreated, experience fear, and be socially isolated, (3) stigmatizing norms and values among families lead to increased community stigma and vice-versa, (4) stigma that leads to mistreatment of people with mental illness leads to adverse symptomatology, which can have a positive relationship with family and community stigma	Input validation—the authors used community based system dynamics to develop and inform model structure	Introduction of mental health care services alone will not be sufficient to meaningfully improve the condition of individuals with mental illness if community stigma and poverty are not addressed

Table 1 (continued)

Title and author	Model type	Purpose	Primary mental health outcome/s	Reality level	Design concepts	Calibration and validation	Findings
A conceptual model of the psychological health system for U.S. active duty service members: an approach to inform leadership and policy decision making (Wang et al. 2013b)	System dynamics (conceptual)	The authors used published data regarding service member deployment, PTSD symptoms and accession data, a review of relevant literature regarding the military service-cycle, and key informant interviews to build a conceptual system dynamics model of the U.S. military psychological health system "service-cycle" from accession (i.e., recruitment and enlistment) and deployment to future psychological health screening and treatment	Incidence, diagnosis, and treatment of post-traumatic stress disorder	The authors identified empirical data as appropriate for many stocks and flows; however, no formal model was implemented	The authors developed a conceptual SD model illustrating stocks and flows from accession through treatment, which depicts entry into the military, deployment, return, diagnosis, treatment and discharge. The model characterizes several individual-, unit- and enterprise- (e.g., funding) level factors in the service-cycle. Furthermore, the authors explicate multiple balancing feedback loops: (1) service members experience stress as the result of past mental health history, trauma, and other factors; pre-traumatic factors like education, mental health history, and social support (e.g., from unit and family) can cause post-traumatic growth and then resilience, which decreases experiences of stress, and (2) a preventive screening feedback, whereby increases in preventative screening can lead to more and quicker diagnosis of PTSD, heightened awareness of PTSD, increased resources, better services, and thus a lower rate of PTSD	Input validation—the authors interviewed key informants to help inform and refine model structure	The model helped to make explicit military leaders' mental models regarding the military service cycle. The model helped senior leadership to identify levers for action to improve PTSD outcomes among service members. Multiple stock and flow variables can be manipulated via leadership decisions (e.g., the accession rate is controlled by the Accession Policy). The model is also useful for generating insights into the effect of inherent time delays on PTSD (e.g., delay from onset rate and diagnosis rate to PTSD awareness and government pressure to increase preventive and treatment resources)

Table 1 (continued)

Title and author	Model type	Purpose	Primary mental health outcome/s	Reality level	Design concepts	Calibration and validation	Findings
Depression as a systemic syndrome: mapping the feedback loops of major depressive disorder (Wittenborn et al. 2016)	System dynamics (conceptual)	To conduct a review of the depression literature to inform development of a conceptual model of major depressive disorder	Major depressive disorder	No formal model was implemented	The model focuses on mechanisms of MDD pathogenesis, feedback loops, and inertial factors. The causal loop diagram includes drivers of MDD, as well as the interactions among drivers. The diagram further defines key reinforcing feedback loops and exogenous drivers of MDD (e.g., gender, socioeconomic status). Broadly, the feedback loops can be classified within the following dimensions: cognitive, social and environmental, and biological. For example, the 'social and environmental' dimension includes a 'social isolation' loop through which dysfunctional behavior leads to weakened social ties and poor interpersonal relationships. This social isolation, in turn, increases exposure to stress, leads to negative affect and processing and dysfunctional behavior	Input validation—model structure was derived from the literature and face validated with experts	The authors draw high-level insights implied by the structure of the model: (1) most research views MDD as an outcome of exogenous factors, but feedback loops within the system suggest that MDD is at least partially endogenous, (2) the importance of each feedback loop for MDD pathogenesis depends on the values of stock and flow variables, (3) the set of feedback loops that 'trap' individuals within a reinforcing MDD cycle may vary between individuals (because there are many such reinforcing feedbacks). These insights suggest further research to understand conditions under which different elements of the system become more or less important

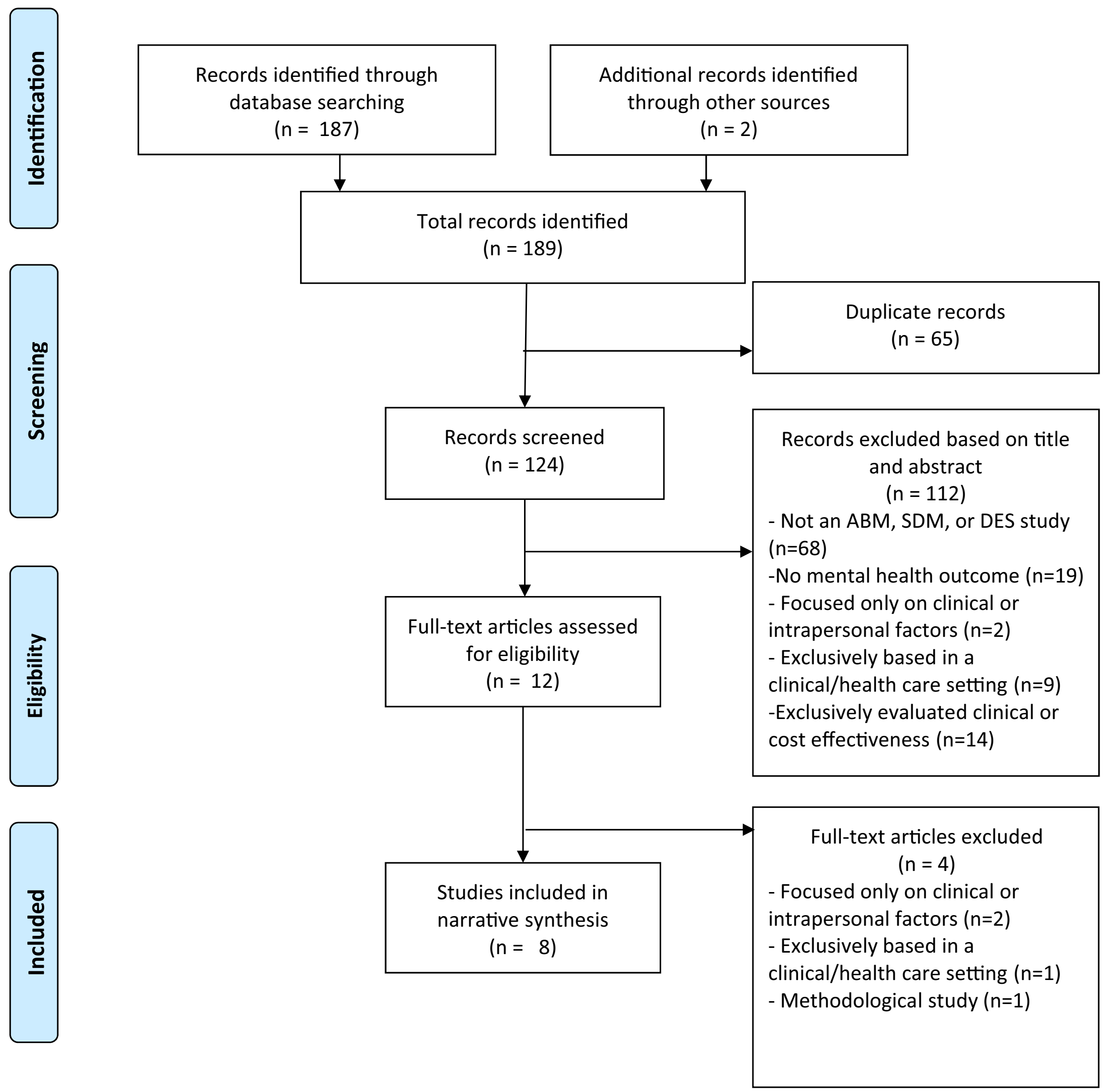

Fig. 1 PRISMA flow diagram of study identification, screening, eligibility, and inclusion

(e.g., community members, academics, content experts) engagement methods to elucidate key variables, relationships, and feedback loops in the multiple systems driving mental health outcomes. The study found that "vicious cycles" linking stigma to social isolation and poverty to utilization of costly mental health services are key drivers of low service utilization. Another example is the ABM developed by Mooney and El-Sayed (2016), which found that weight-based norms can lead to social ostracization of obese people and, ultimately, to depression. These interrelationships are thus a plausible mechanism for observed comorbidities in obesity and depression.

Another type of insight related to the structure and functioning of complex systems which may provide opportunities for the prevention, screening, and treatment of mental health conditions (Cerdá et al. 2015; Ghaffarzadegan et al. 2016; Kalton et al. 2016; Lyon et al. 2016; Wang et al. 2013a). For example, Wang and colleagues (2013a) developed a conceptual SDM of PTSD development, screening, and treatment among service members within the context of the U.S. military service cycle. The model elucidated time delays in the psychological health system, including those between the onset and diagnosis of PTSD among service members. Awareness of PTSD was also identified as an important issue among the public and politicians, an issue with the potential to delay decisions among politicians and administrators to increase government funding for PTSD prevention and treatment. These time delays can lead to discordance between the need for services and the timing of funding decisions. One of the implications of the study was that better communication between military leaders and lawmakers can help counteract the potentially-negative effects of these time delays.

Studies also provided insight into strategies that combined multiple interventions to improve mental health service delivery. Cerdá et al. (2015) developed an ABM suggesting that the combination of targeted policing and cognitive behavioral therapy may be more effective at addressing violence-related PTSD than either policy in isolation. Similarly, Lyon et al. (2016) developed an SDM to examine the likely effectiveness of depression screening and treatment programs in high schools, including “business-as-usual,” universal screening, and universal screening and enhanced treatment capacity. A main finding was that implementation of universal screening alone may result in a bottleneck of youth in need of mental health services that were waiting for treatment.

Discussion

Public health researchers and funding agencies that have called for complex systems approaches to understand how interdependent variables at multiple scales of influence impact health and produce population-level patterns like racial/ethnic and income disparities (Diez Roux 2011; Fink et al. 2016; Lambert et al. 2015; Mabry and Kaplan 2013). In this paper, we sought to determine the extent to which complex systems approaches have been used in mental health research, and to advance the use of these approaches in mental health by extracting key data and insights from the literature. Relative to the use of complex systems approaches in the broader field of public health focused on physical health issues (Carey et al. 2015), particularly chronic disease (Nianogo and Arah 2015), obesity (Levy et al. 2011), and smoking (Levy et al. 2010), we found few such studies focused on mental health outcomes.

The studies we reviewed generated important insights into drivers of mental health and potential policy interventions to improve mental health. We extracted several key pieces of data regarding each model, including the reality level and use of data. We assess reality level because models that are heavily anchored to empirical data regarding specific contexts (e.g., a city), populations (e.g., low-income population in that city), and processes (e.g., parameter values derived from a longitudinal study of that population) are often developed for different purposes and generate different types of insights than models that are more stylized. Models with a high degree of realism, for example, may be developed to predict the effects of a policy implemented in a specific context. A tradeoff is that the implications of these models may be less informative and generalizable across contexts, populations, and outcomes than models less strictly tied to empirical data that explore more general and broadly-applicable processes and mechanisms. In general, we identified studies with both a high (Kalton et al. 2016) and low (Mooney and El-Sayed 2016) degree of realism.

We found that the studies included in the review all generally made at least some use of empirical evidence to inform the values of key parameters, calibrate the values of parameters for which data were not available, and validate outcomes produced by models. As described further below, a challenge in using complex systems approaches is ensuring that insights generated by models are real and don’t simply ‘reflect back’ decisions made in the model design process. Continued comparisons with empirical evidence can help build credibility in the causal structures that underpin complex systems models. For example, the mechanisms posited by Mooney and El-Sayed (2016) to explain the observed association between obesity and depression can be further validated using longitudinal studies that collect data regarding obesity, depression, and social stigma at various points throughout the life course.

Typology of Complex Systems Approaches to Mental Health

Complex systems approaches are particularly useful for addressing the following types of questions related to mental health: (1) questions that involve the influence of factors defined at multiple levels that can interact with each other, (2) questions that involve strong feedbacks (e.g., feedbacks between physical and mental health), (3) questions related to the effects of policies and interventions that are distal in nature, because they either operate over a long time horizon (e.g., early childhood interventions), at a level above individuals (e.g., changes to the environment), or ‘upstream’ in a causal chain (e.g., poverty reduction on mental health outcomes), and (4) questions pertaining to the conditions necessary for a policy or intervention to be successful.

Complex systems approaches allow the inclusion of factors defined at different levels. They also allow investigation of how the effect of a given factor varies depending on the state of other factors in the system. For example, the conceptual SDM developed by Wittenborn et al. (2016) includes cognitive, biological, social, and environmental drivers of depression. This is an excellent example of how complex systems approaches can leverage research across disciplines (e.g., neurobiology, psychology, social epidemiology) regarding the structure and function of drivers of mental health conditions. Complex systems modelers can then conduct in silica studies to build preliminary evidence regarding how these drivers interact, as well as in support of policy interventions that involve factors across multiple scales of influence.

Feedback loops play a particularly prominent role in the pathogenesis of mental health conditions because of bi-directional relationships involving neurobiological and psychosocial systems, mental health, physical health, and social and environmental risk and protective factors (Renn et al. 2011). Systems approaches can help the role of these feedbacks in shaping individual- and population-level mental health outcomes, as well as implications for policies and interventions. For example, the ABM of Cerdá et al. (2015) demonstrated that a transition to hot-spot policing (i.e., increasing police presence in violent neighborhoods) without any increase in the size of the police force could have an effect on violence-related PTSD comparable to the effect of a much larger investment in providing treatment to past victims or perpetrators of violence. This is likely due to an important but unanticipated 'amplifying effect' that results from reinforcing feedback loops, since preventing an individual act of violence reduces exposure to violence among community members, and exposure to violence is a risk factor for future perpetration of violence.

Systems models can serve an important role in assessing policies and interventions that are temporally or conceptually distal, either because their effects will play out over a long time horizon or because they target variables that are far upstream in the causal chain of the outcome of interest. For example, Ghaffarzadegan et al. (2016) assess the long-term effects of policies to help mitigate PTSD among U.S. service members. One of the key findings of their study is that it can take several decades (i.e., around 40 years) to mitigate the psychiatric consequences of war. This study illustrates the utility of systems models for exploring temporally-distant outcomes of policies and interventions that are not amenable to experimental evaluation.

A further example is the potential use of complex systems approaches to elucidate the causal pathways through which features of neighborhoods and communities can lead to mental illness. For example, Wilkinson and Pickett (2017) recently commented on decades of research suggesting that mental illness is the "most recent addition" to the list of negative health outcomes that seem to increase in countries with high levels of income inequality. They argued that the causal pathways through which income inequality impacts health are mediated by social capital and trust, and that this mediating effect is likely related to neurological systems like the human brain's behavioral dominance system. Complex systems approaches could help to conceptualize and test whether hypothesized causal mechanisms that link individual-level income, community-level income inequality, social interactions, and neurological processes can explain observed patterns in mental illness both within and between countries.

Complex systems models can identify the conditions necessary for a policy or intervention to be successful. For example, Trani et al. (2016) developed a conceptual SDM to explore mental health care service utilization among Afghanis with mental illness. The model suggests that increasing availability of mental health care services is unlikely to produce a meaningful improvement in mental health outcomes because service utilization is highly dependent on community stigma and poverty. It makes intuitive sense that improving access to mental health services would improve utilization and, ultimately, mental health outcomes; however, this simplistic view overlooks the interrelated nature of multiple factors within the same complex system. In this case, people's decision to use mental health care services is influenced by the level of stigma within the community, as well as their own poverty status.

Complex systems models can help anticipate and address unforeseen and unintended consequences of policies and interventions. As described by Lipsitz (2012), the policy levers and regulations used to improve population health outcomes can lead to unintended consequences that are difficult to predict due to the very complexity of systems that impact health, as well as unforeseen responses from important actors in the system (Lipsitz 2012). These unintended consequences can have a critical impact on the success of policies and interventions.

An example can be drawn from the Community Mental Health Centers Act in 1963 that intended to transition from a paradigm of care for those with severe mental illness centered around large, custodial facilities (i.e., mental hospitals), to a more decentralized system in which patients receive treatment and rehabilitation in facilities in their own communities. The impact of the policy was constrained by a range of implementation challenges, including lack of an adequate system to offer comprehensive and coordinated services in communities, as well as public discontent from having people with severe mental illness living in their communities (Bassuk and Gerson 1978; Stevens et al. 2006). Complex systems approaches can help to elucidate these types of implementation challenges *a* priori: (1) stakeholder engagement methods like community-based system dynamics modeling can help elucidate key variables and relationships in the system in which a policy is being implemented (e.g., Trani et al. 2016), (2) formal SDMs can help identify bottlenecks in service capacity (e.g., Lyon et al. 2016), and (3) ABM can help to understand how diverse actors will respond to a change in the system.

Challenges and Opportunities

Both challenges and opportunities remain for application of complex systems methods in mental health research. Implementing systems models requires that explicit decisions be made about the boundaries of the model, or which types of variables will be included and which will be considered exogenous. As a general rule, models should be as parsimonious as possible while still maintaining the detail necessary to yield new insights (Railsback and Grimm 2012). Parsimony is particularly important in simulation studies, because as the number of "moving pieces" in a model increases it becomes increasingly difficult to interpret the results and understand how and why emergent properties of the system (i.e., results driven by the function of the system as a whole but that cannot be traced specifically to any of the system's component parts) are generated. Decisions about the scope and boundaries of models should be closely related to the specific questions that the model is trying to answer (Hammond 2015).

For example, the conceptual SDM developed by Wittenborn et al. (2016) found that the literature on major depressive disorder supported 13 reinforcing feedback loops involving nearly four dozen relationships between two dozen variables. The study was highly informative as a conceptual tool for understanding the important role of feedback loops in development of major depressive disorder, but if the entire system were implemented via a computer simulation it would be difficult to identify the mechanisms driving any unanticipated results. Simulation studies based on this work would benefit from an iterative approach, with initial efforts focused on exploring the relationships and feedback loops that comprise each of the sub-systems (e.g., cognitive, social) delineated by Wittenborn. Once the structure and function of variables and relationships in each of the dimensions are better understood, larger efforts that integrate multiple sub-systems would be more likely to generate comprehensible insights.

Many complex systems studies use computer simulations to explore counterfactual scenarios. These counterfactuals can be used to estimate the effects of a hypothetical policy or intervention (for example, the SDM of Lyon et al. 2016) or to explore causal mechanisms posited to drive mental health (for example, the ABM of Mooney and El-Sayed 2016). Because modelers construct the virtual worlds in which the simulations run, an important challenge when interpreting results, particularly those that are unanticipated or counterintuitive, is understanding whether the model is providing actual insights, or simply 'reflecting back' decisions made in the model design process. Models are necessarily a simplification of the more complicated environments and systems that drive mental health in the real world; the goal in model design is to represent important aspects of the system being investigated in a way that is consistent with the underlying causal pathway and neither overly simplistic (i.e., leaves out important causal structures) nor overly complicated (i.e., includes structures that are unnecessary and make model outputs less comprehensible). Getting this process right is always a challenge, and even more so if the causal structures being explored are not well understood.

As described by Wittenborn et al. (2016), accurately representing the underlying causal mechanisms will be a challenge in complex systems approaches to mental health because of information deficits regarding many mechanisms that drive mental health and how these mechanisms intersect. Particularly in areas where causal mechanisms are poorly understood, the modeling process should be viewed as an iterative exercise: by working in tandem with epidemiologic and policy intervention research, models can help to inform the questions we ask, refine our understanding of the mechanisms driving mental health, and help to generate new insights into how these mechanisms intersect and can be leveraged by policy interventions to improve mental health. Generally speaking, there is a real opportunity to continue to use empirical evidence and data to inform, validate, and lend credibility to models. Comparison to empirical evidence can help to assess whether unanticipated or counterintuitive results are plausible and insightful, or simply reflect misspecification of the underlying mechanisms.

Given the multiple scales of factors that influence mental health, complex systems approaches should seek out multidisciplinary collaborations. An ABM that examines the cumulative effects of stress on mental health across the life course, for example, may benefit from working with cognitive scientists to understand neurobiological processes in the stress response system, and with social scientists to develop a model of exposure to neighborhood stressors. This collaborative process can be mutually beneficial: working with content experts can help modelers to produce more robust and structurally-valid models, and the results of modeling studies can help shed light on important structures and mechanisms for which data do not currently exist (Brown et al. 2012).

Participatory methods like community-based systems dynamics can facilitate involvement of key mental health stakeholders in the modeling process, by building capacity in complex systems thinking and a platform to describe the complex systems that drive mental health (Hovmand 2014). The study by Trani et al. (2016), which used community based system dynamics modeling to examine mental health and stigma in Afghanistan, provides an illustrative example of how this can lead to refinement of mental models, new understanding of systems problems, and identification of leverage points for policy interventions.

Limitations

This study has both strengths and limitations. Strengths include the structured systematic search strategy, use of multiple databases, and that it is the first literature review of which we are aware to narrowly focus on complex systems approaches to mental health. Potential limitations include that we may have missed studies that used different terminology than that for which we searched, or that were published in journals not indexed by the search engines we used. We did not extract all data from each study that may be of use to other mental health researchers seeking to employ complex systems approaches. For example, similar reviews in other topical areas (e.g., Nianogo and Arah 2015) extracted data regarding the software used and whether a conceptual framework was presented. We chose not to extract this information because our focus was on understanding the types of questions that complex systems approaches are being used for in mental health, as well as characterizing important design elements, use of external data, and key findings.

Conclusion

The studies we identified have provided useful insights into the pathogenesis of mental health outcomes, as well as potential policy and intervention strategies to improve mental health. Continued integration with empirical evidence will help build credibility in the insights generated by these models. We also found that simulation-based studies ranged from those with high levels of reality that are strongly tied to data regarding specific contexts, populations, and health outcomes, to those with low levels of reality that explore more broadly-relevant mechanisms that impact mental health. Generally, opportunities remain for expanded use of complex systems research as a complement to other methodologies in mental health research. We have presented a typology of research questions that complex systems methods are well-suited to address, as well as identified some of the potential challenges to developing impactful systems models for mental health research and policy.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Research Involving Human and Animal Participants This article does not contain any studies with human participants or animals performed by any of the authors.

Appendix

See Table 2.

Table 2 Complex systems terms and definitions

Term	Definition
System	A set of elements or parts that is coherently organized and interconnected in a pattern or structure that produces a characteristic set of behaviors, often classified as its 'function' or 'purpose' (Meadows, 2008)
Model	A purposeful representation of some real system (Railsback and Grimm 2012; Starfield et al. 1990)
Mental models	A cognitive representation of a real dynamic system (Doyle and Ford 1998; Hovmand 2014)
Causal loop diagram	Causal maps that provide a broad view of the different components of a system, including major subsystems and how these are related through multiple feedback loops (Brennan et al. 2015)
Agent-based model	Models where unique or autonomous entities that usually interact with each other and their environments. Agents can be humans, businesses, or other entities that pursue specified goals (Railsback and Grimm 2012)
System dynamics modeling	An approach that involves development of causal diagrams and/or computer simulation models that portray processes of accumulation and feedback (Homer and Hirsch 2006)
Community based system dynamics	A participatory method for involving stakeholders in a modeling process (Hovmand, 2014)
Feedback loop	The mechanism (rule or information flow or signal) that allows a change in a stock to affect a flow into or out of that same stock. A closed chain of causal connections from a stock, through a set of decisions and actions dependent on the level of the stock, and back again through a flow to change the stock (Meadows 2008)
Reinforcing feedback loop	An amplifying or enhancing feedback loop, also known as a 'positive feedback loop' because it reinforces the direction of change. These are vicious cycles or virtuous cycles, depending on whether the outcome is detrimental or desirable (Meadows 2008)
Balancing feedback loop	A stabilizing, goal-seeking, regulating feedback loop, also known as a 'negative feedback loop' because it opposes, or reverses, whatever direction of change is imposed on the system (Meadows, 2008)
Stock	An accumulation of material or information that has built up in a system over time (Meadows 2008)
Flow	Material or information that enters or leaves a stock over a period of time (Meadows 2008)

References

Ahrnsbrak, R., Bose, J., Hedden, S., Lipari, R., & Park-Lee, E. (2017). Key substance use and mental health indicators in the United States: Results from the 2016 National Survey on Drug Use and Health (HHS Publication No. SMA 17-5044, NSDUH Series H-52). *Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration (SAMHSA). NSDUH Data Review*. https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR1-2016/NSDUH-FFR1-2016.htm.

Bassuk, E. L., & Gerson, S. (1978). Deinstitutionalization and mental health services. *Scientific American, 238*(2), 46–53.

Brennan, L. K., Sabounchi, N. S., Kemner, A. L., & Hovmand, P. (2015). Systems thinking in 49 communities related to healthy eating, active living, and childhood obesity. *Journal of Public Health Management and Practice, 21*, S55–S69.

Brown, C. H., Kellam, S. G., Kaupert, S., Muthén, B. O., Wang, W., Muthén, L. K., et al. (2012). Partnerships for the design, conduct, and analysis of effectiveness, and implementation research: Experiences of the prevention science and methodology group. *Administration and Policy in Mental Health and Mental Health Services Research, 39*(4), 301–316. https://doi.org/10.1007/s10488-011-0387-3.

Carey, G., Malbon, E., Carey, N., Joyce, A., Crammond, B., & Carey, A. (2015). Systems science and systems thinking for public health: A systematic review of the field. *BMJ Open, 5*(12), e009002.

Cerdá, M., Tracy, M., Keyes, K. M., & Galea, S. (2015). To treat or to prevent?: Reducing the population burden of violence-related post-traumatic stress disorder. *Epidemiology (Cambridge, Mass.), 26*(5), 681–689. https://doi.org/10.1097/EDE.0000000000000350.

Cicchetti, D. (2010). Resilience under conditions of extreme stress: A multilevel perspective. *World Psychiatry, 9*(3), 145–154. https://doi.org/10.1002/j.2051-5545.2010.tb00297.x. doi.

Cohen, N., & Galea, S. (2011). *Population mental health: Evidence, policy, and public health practice*. New York: Taylor & Francis.

Cottler, L. B. (2011). *Mental health in public health: The next 100 years*. Oxford: Oxford University Press.

Diez Roux, A. V. (2011). Complex systems thinking and current impasses in health disparities research. *American Journal of Public Health, 101*(9), 1627–1634.

Doyle, J. K., & Ford, D. N. (1998). Mental models concepts for system dynamics research. *System Dynamics Review, 14*(1), 3–29.

Eaton, W. W. (2012). *Public mental health*. Oxford: Oxford University Press.

Fink, D. S., Keyes, K. M., & Cerdá, M. (2016). Social determinants of population health: A systems sciences approach. *Current Epidemiology Reports, 3*(1), 98–105.

Fowler, P. J., Tompsett, C. J., Braciszewski, J. M., Jacques-Tiura, A. J., & Baltes, B. B. (2009). Community violence: A meta-analysis on the effect of exposure and mental health outcomes of children and adolescents. *Development and Psychopathology, 21*(1), 227–259.

Ghaffarzadegan, N., Ebrahimvandi, A., & Jalali, M. S. (2016). A dynamic model of post-traumatic stress disorder for military personnel and veterans. *PLoS ONE, 11*(10), e0161405.

Günal, M. M., & Pidd, M. (2010). Discrete event simulation for performance modelling in health care: A review of the literature. *Journal of Simulation, 4*(1), 42–51. https://doi.org/10.1057/jos.2009.25.

Hammond, R. (2015). Appendix A: Considerations and best practices in agent-based modeling to inform policy. In R. Wallace, A. Geller & V. A. Ogawa (Eds.), *Assessing the use of agent-based models for tobacco regulation*. Washington, DC: National Academies Press (US).

Hassmiller Lich, K., Ginexi, E. M., Osgood, N. D., & Mabry, P. L. (2013). A call to address complexity in prevention science research. *Prevention Science, 14*(3), 279–289. https://doi.org/10.1007/s11121-012-0285-2.

Homer, J. B., & Hirsch, G. B. (2006). System dynamics modeling for public health: Background and opportunities. *American Journal of Public Health, 96*(3), 452–458.

Hovmand, P. S. (2014). *Community based system dynamics*. New York: Springer.

Jacobson, S. H., Hall, S. N., & Swisher, J. R. (2006). Discrete-event simulation of health care systems. In R. W. Hall (Ed.), *Patient Flow: Reducing delay in healthcare delivery* (pp. 211–252). Boston: Springer.

Kalton, A., Falconer, E., Docherty, J., Alevras, D., Brann, D., & Johnson, K. (2016). Multi-agent-based simulation of a complex ecosystem of mental health care. *Journal of Medical Systems, 40*(2), 1–8.

Karg, R. S., Bose, J., Batts, K. R., Forman-Hoffman, V. L., Liao, D., Hirsch, E., et al. (2014). Past year mental disorders among adults in the United States: Results from the 2008–2012 Mental Health Surveillance Study. *CBHSQ Data Review*, 1–94.

Kawachi, I., & Berkman, L. F. (2001). Social ties and mental health. *Journal of Urban health, 78*(3), 458–467.

Lambert, K. G., Nelson, R. J., Jovanovic, T., & Cerda, M. (2015). Brains in the city: Neurobiological effects of urbanization. *Neuroscience and Biobehavioral Reviews, 58*, 107–122. https://doi.org/10.1016/j.neubiorev.2015.04.007.

Lee, A. C., & Maheswaran, R. (2011). The health benefits of urban green spaces: A review of the evidence. *Journal of Public Health, 33*(2), 212–222.

Levy, D. T., Mabry, P. L., Graham, A. L., Orleans, C. T., & Abrams, D. B. (2010). Exploring scenarios to dramatically reduce smoking prevalence: A simulation model of the three-part cessation process. *American Journal of Public Health, 100*(7), 1253–1259.

Levy, D. T., Mabry, P. L., Wang, Y. C., Gortmaker, S., Huang, T. K., Marsh, T., et al. (2011). Simulation models of obesity: A review of the literature and implications for research and policy. *Obesity Reviews, 12*(5), 378–394.

Lipsitz, L. A. (2012). Understanding health care as a complex system: The foundation for unintended consequences. *JAMA, 308*(3), 243–244. https://doi.org/10.1001/jama.2012.7551.

Lorenc, T., Clayton, S., Neary, D., Whitehead, M., Petticrew, M., Thomson, H., et al. (2012). Crime, fear of crime, environment, and mental health and wellbeing: Mapping review of theories and causal pathways. *Health & Place, 18*(4), 757–765.

Lyon, A. R., Maras, M. A., Pate, C. M., Igusa, T., & Vander Stoep, A. (2016). Modeling the impact of school-based universal depression screening on additional service capacity needs: A system dynamics approach. *Administration and Policy in Mental Health and Mental Health Services Research, 43*(2), 168–188.

Mabry, P. L., & Kaplan, R. M. (2013). Systems science: A good investment for the public's health. *Health Education & Behavior, 40*(1 suppl), 9S–12S.

Meadows, D. H. (2008). *Thinking in systems: A primer* (pp. 77–78). White River Junction, VT: Chelsea Green Publishing.

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *BMJ*. https://doi.org/10.1136/bmj.b2535.

Mooney, S. J., & El-Sayed, A. M. (2016). Stigma and the etiology of depression among the obese: An agent-based exploration. *Social Science & Media, 148*, 1–7. https://doi.org/10.1016/j.socscimed.2015.11.020.

Murray, C. J., Vos, T., Lozano, R., Naghavi, M., Flaxman, A. D., Michaud, C., et al. (2013). Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: A systematic analysis for the Global Burden of Disease Study 2010. *The Lancet, 380*(9859), 2197–2223.

National Research Council. (2009). *Preventing mental, emotional, and behavioral disorders among young people: Progress and possibilities*. Washington, DC: National Academies Press.

Nianogo, R. A., & Arah, O. A. (2015). Agent-based modeling of non-communicable diseases: A systematic review. *American Journal of Public Health, 105*(3), e20–e31.

Railsback, S. F., & Grimm, V. (2012). *Agent-based and individual-based modeling: A practical introduction*. Princeton: Princeton University Press.

Reeves, W. C., Strine, T. W., Pratt, L. A., Thompson, W., Ahluwalia, I., Dhingra, S. S., et al. (2011). Mental illness surveillance among adults in the United States. *MMWR Surveillance Summary, 60*(Suppl 3), 1–29.

Renn, B. N., Feliciano, L., & Segal, D. L. (2011). The bidirectional relationship of depression and diabetes: A systematic review. *Clinical Psychology Review, 31*(8), 1239–1246. https://doi.org/10.1016/j.cpr.2011.08.001.

Shern, D. L., Blanch, A. K., & Steverman, S. M. (2016). Toxic stress, behavioral health, and the next major era in public health. *American Journal of Orthopsychiatry, 86*(2), 109.

Starfield, A., Smith, K., & Bleloch, A. (1990). *How to model it: Problem solving for the computer age*. New York: McGraw-Hill.

Stevens, R., Rosenberg, C. E., & Burns, L. R. (2006). *History and health policy in the United States: Putting the past back*. New Brunswick: Rutgers University Press.

Tanaka, S. (2010). Model-based parametric study of frontostriatal abnormalities in schizophrenia patients. *BMC Psychiatry, 10*, 17. https://doi.org/10.1186/1471-244x-10-17.

Trani, J. F., Ballard, E., Bakhshi, P., & Hovmand, P. (2016). Community based system dynamic as an approach for understanding and acting on messy problems: A case study for global mental health intervention in Afghanistan. *Conflict and Health, 10*, 25. https://doi.org/10.1186/s13031-016-0089-2.

Vigo, D., Thornicroft, G., & Atun, R. (2016). Estimating the true global burden of mental illness. *The Lancet Psychiatry, 3*(2), 171–178. https://doi.org/10.1016/S2215-0366(15)00505-2.

Wang, J. Y., Glover, W. J., Rhodes, A. M., & Nightingale, D. (2013a). A conceptual model of the Psychological Health System for U.S. active duty service members: an approach to inform leadership and policy decision making. *Military Medicine, 178*(6), 596–606. https://doi.org/10.7205/milmed-d-12-00429.

Wang, J. Y., Glover, W. J., Rhodes, A. M., & Nightingale, D. (2013b). A conceptual model of the Psychological Health System for US active duty service members: An approach to inform leadership and policy decision making. *Military Medicine, 178*(6), 596–606. https://doi.org/10.7205/milmed-d-12-00429.

Wilkinson, R. G., & Pickett, K. E. (2017). The enemy between us: The psychological and social costs of inequality. *European Journal of Social Psychology, 47*(1), 11–24. https://doi.org/10.1002/ejsp.2275. doi.

Wittenborn, A., Rahmandad, H., Rick, J., & Hosseinichimeh, N. (2016). Depression as a systemic syndrome: mapping the feedback loops of major depressive disorder. *Psychological Medicine, 46*(3), 551.

Wolstenholme, E., Monk, D., & Todd, D. (2010). Dynamic cost benefit analysis for mental health reform. *Kybernetes, 39*(9/10), 1645–1658.

World Health Organization. (2014). *Social determinants of mental health*. Geneva: World Health Organization.

Zimmerman, L., Lounsbury, D. W., Rosen, C. S., Kimerling, R., Trafton, J. A., & Lindley, S. E. (2016). Participatory system dynamics modeling: Increasing stakeholder engagement and precision to improve implementation planning in systems. *Administration and Policy in Mental Health and Mental Health Services Research, 43*(6), 834–849. https://doi.org/10.1007/s10488-016-0754-1.