

Review



Systems-Oriented Modelling Methods in Preventing and Controlling Emerging Infectious Diseases in the Context of Healthcare Policy: A Scoping Review

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Abstract: Background: Emerging infectious diseases (EIDs) arise and affect society in complex ways. We conducted a scoping review to explore how systems-oriented methods have been used to prevent and control EIDs. Methods: We used the Joanna Briggs Institute framework for scoping reviews in this study. We included peer-reviewed articles about health care systems preparedness and response, published from 1 January 2000. We considered the World Health Organisation's (WHO) list of prioritised diseases for research and development when choosing the pathogens and only included studies that considered the dynamics between the system's elements. Results: Our initial search yielded 9985 studies. After screening, 177 studies were considered for inclusion in this review. After assessment by two independent reviewers, seven studies were included. The studies were published between 2009 and 2021. Most focused on sarbecoviruses and targeted healthcare policymakers and governments. System dynamics approaches were the most used methods. Most of the studies incorporated the classical epidemiological models alongside systems-oriented methods. The studies were conducted in context of diseases dynamics and its burden on human health, the economy and healthcare systems. The most reported challenge was epidemiological and geographical data timeliness and quality. Conclusions: Systems dynamics approaches can help policy makers understand the elements of a complex system and thus offer potential solutions for preventing and controlling EIDs.

Keywords: emerging infectious diseases; systems thinking; systems approach; systems dynamics; COVID-19; SARS-CoV1; MERS-CoV; healthcare policy; pandemic; outbreak

1. Introduction

Emerging infectious diseases (EIDs) are a group of diseases affecting humans for the first time, or pre-existing diseases that are rapidly spreading in terms of the number of new cases or in new geographical areas [1,2]. The majority of EIDs are zoonotic and at least initially are transmitted from animal sources to humans through spillover [3]. Examples include COVID-19, Ebola virus, Lassa fever, Middle East Respiratory Syndrome coronavirus (MERS-CoV) and monkeypox.

EIDs are complex and not caused merely by the infectious agents themselves. Multiple factors contribute to their emergence, including increased human population size and movement within recent years, increased travel and trade, urbanisation, wars, human behaviour, and climate change [2]. In addition, there is a lack of prior knowledge and limited, if any, immunity to the emerging pathogen, which contributes to additional burden to humans' health and lives.

Preventing and controlling EIDs are important elements of our duties and responsibilities for overall public health preparedness and response. Such responsibilities play out in a complex system with multiple interacting elements and stakeholders [4]. EID preparedness



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Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). and response must ensure the readiness of the healthcare systems to anticipate and face the threats of a novel pathogen on human health and lives [5]. Readiness also includes healthcare systems resilience and ability to adequately sustain healthcare for patients in need, avoiding delays in diagnosis or treatment during EID emergencies [5].

Systems science can help conceptualize a problem as a perturbation within complex adaptive system [6]. It does so by identifying the components that make up the system and how they are linked, shaping the system's overall form and behaviour [6]. Systems scientists aim to identify leverage points within the system to provide holistic solutions instead of a response to a single aspect of a particular problem [7]. Although a systems science lens and methods have been used in infectious disease research and practice for decades, there is a gap in knowledge of how systems-oriented modelling methods in particular have been and can be used to strengthen healthcare systems' capacity in preventing and controlling EIDs. This scoping review aims to explore how systems-oriented modelling methods have been used to inform healthcare policymakers about healthcare system's preparedness and response to EIDs.

Research Question

The review's main question was: how have systems-oriented modelling methods been used to prevent and control EIDs? We were interested specifically in the preparedness and response of healthcare systems. Further sub-questions were:

- What was the context in which the systems-oriented study was conducted?
- Who were the target population?
- What was the systems-oriented aim?
- What were the main complex-systems features considered?
- What were the system's main elements?
- What were the systems-oriented methods used?
- What challenges related to systems modelling did the authors face?
- Who were the main stakeholder and how were they involved?
- What were the key lessons learned from using the complex systems approach?

Because we were interested in exploring the evidence and lessons to identify the key concepts in this topic, we chose to conduct a scoping review [8].

2. Materials and Methods

A protocol for this review was published in 2021 [9]. Below we outline the relevant steps, updated with any changes that occurred as we developed a deeper understanding of the topic.

2.1. Preparation

We started the scoping review by establishing the research team, which consisted of experts in public health, communicable diseases and systems science. Due to the illdefined characterisation of EIDs, we decided to use the list developed by the World Health Organisation (WHO) for prioritised EIDs for research and development, which they update according to global circumstances [10].

Before going forward, we searched to find whether any systematic or scoping reviews were published about the same topic. We conducted a comprehensive search in Scopus, Joanna Briggs Institute database, Cochrane database, PubMed and Epistemonikos. To our knowledge, up to the time of starting this review, there were no systematic or scoping reviews that answered our research questions. Therefore, the team agreed on the broad research question and study protocol, including the keyword and databases in this scoping review.

For this scoping review, we followed the Joanna Briggs Institute framework, which is based on previous work from Lavec and colleagues and Arskey and O'Malley's recommendations [8]. Our scoping review consists of six steps: (1) Identify the research questions, (2) Identify keywords and medical subject headings (MeSH) terms, (3) Identify relevant studies, (4) Study selection, (5) Data charting, and (6) Summarise and disseminate the results.

2.2. Identifying Keywords and MeSH Terms

After consulting the subject librarian at the School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, the initial search started on 23 March 2021 in Scopus and Google Scholar to identify keywords, MeSH terms and index terms relevant to the review. The research team agreed on the searched terms (Table 1), which were used across all databases. We searched two databases, PubMed, Web of Science, and Scopus (Appendix A). These databases were selected to allow a broad search for materials in the topic. Additionally, the research team agreed to screen the first ten pages in Google Scholar to identify any relevant studies in grey literature.

Table 1. Keywords used in the searches.

Concept	Search Terms
Systems modelling methods	Complex* systems OR system dynamic* OR agent?based OR stochastic OR network* OR compartmental model* OR multi?agent OR multi-compartment model*
Emerging infectious diseases	Emerging infectious diseases OR coronavirus OR MERS-CoV, COVID-19 OR severe acute respiratory syndrome OR SARS-CoV-2 OR SARS OR Ebola OR zika OR dengue OR Nipah OR pandemic * OR influenza OR outbreak* OR Crimean-Congo haemorrhagic fever OR rift valley fever or "diseases X"* OR Lassa fever

Coronavirus 2; SARS: Severe Acute Respiratory Syndrome Coronavirus; SARS-CoV-2: Severe Acute Respiratory Syndrom

All citations were imported into the Endnote X9 citation manager, where they were deduplicated. Next, we imported the selected citations into the web-based systematic review management software, Covidence, for the title and abstract relevance screening and full article selection. During the importation process, Covidence found and removed further duplicated citations.

2.3. Identifying Relevant Studies

Table 2 shows the inclusion and exclusion criteria. Studies were eligible if they investigated an EID in the WHO priority list [10]. After the initial search, we decided to narrow the scope of the review because the number of potential studies was too large. We made the following changes to the protocol in order to achieve this reduced scope. We decided to focus on studies conducted in the context of healthcare policy, those that considered the dynamic relationships between elements of the system (e.g., feedback loops and network effects), and we only included peer-reviewed publications (excluding grey, pre-print and unpublished reports) containing simulation models published on or after 1 January 2000. There were no limits regarding article language, geographic location or country income group of the location of study.

2.4. Study Selection

Title and abstracts were screened to exclude studies that clearly met one or more of exclusion criteria or which did not meet any of the inclusion criteria. In the next stage, a full-text review was conducted on the studies that passed screening to assess them against the eligibility criteria. In both stages, each study was independently assessed by two reviewers. In the case of disagreement, reviewers met to reach consensus.

Inclusion Criteria Exclusion Criteria Peer-reviewed reports published since 1 January 2000 Abstract-only reports Studies related to health systems preparedness and response Studies that do not include healthcare system element Emerging infectious diseases included in the prioritising diseases for research and development in emergency context list Studies on non-emerging infectious diseases by The World Health Organisation [10] Studies conducted to investigate preparedness, prevention and Studies that do not include the human population response to EIDs that affect human populations Studies of mathematical models that do not account for Considered the dynamic relationships between elements of the dynamic relationships between elements of the system outside system (e.g., feedback loops, network effects) the epidemic model Seasonal influenza

Table 2. Inclusion and exclusion criteria.

2.5. Data Charting

We developed a form for data extraction and characterisation that included: authors of the article, year and location of study, context (e.g., disease dynamics, healthcare preparedness and response, resources), target population, complex systems features considered, complex systems-oriented aim, system's elements considered, modelling and analytic methods, reported challenges during modelling and potential solutions, main stakeholders and their involvement in the study, and reported key lessons from the complex systems-oriented approach. The reviewing team discussed and agreed this form. Two independent reviewers tested the form; the reviewing team met to resolve disagreements in the data extraction. The complex systems features considered were based on the list provided by James Ladyman and Karoline Wiesner as follows [11]:

- 1. Numerosity: complex systems involve many interactions among many components.
- 2. Disorder and diversity: the interactions in a complex system are not coordinated or controlled centrally, and the components may differ.
- 3. Feedback: the interactions in complex systems are iterated so that there is feedback from previous interactions on a timescale relevant to the system's emergent dynamics.
- 4. Non-equilibrium: complex systems are open to the environment and are often driven by something external.
- 5. Spontaneous order and self-organisation: complex systems exhibit structure and order that arises out of the interactions among their parts.
- 6. Nonlinearity: complex systems exhibit nonlinear dependence on parameters or external drivers.
- 7. Robustness: the structure and function of complex system is stable under relevant perturbations.
- 8. Nested structure and modularity: there may be multiple scales of structure, clustering and specialisation of function in complex systems.
- 9. History and memory: complex systems often require a very long history to exist and also store information about history.
- 10. Adaptive behaviour: complex systems are often able to modify their behaviour depending on the state of the environment and the predisposition they make about it.

2.6. Results Summary and Dissemination

The data were aggregated in a single spreadsheet using Microsoft Excel version 16.43 (Microsoft, Redmond, USA) for validation and coding. The rows represented articles, the columns represented the data items extracted to answer the research questions and the cells contained information gathered from the selected articles. We synthesized the results using text and tables and answered each research question and sub-questions set up in the protocol for this scoping review.

3. Results

3.1. Search and Selection of Citations

We initiated this scoping review in March 2021, finding 9985 citations. After deduplication, we screened 9944 titles and abstracts and reviewed 117 full texts. After data characterisation of full-text articles, seven studies [12–18] were included (Figure 1). Many articles were excluded during the title and abstract screening because the keywords used yielded many publications outside the scope of this review or had different study designs that did not address our research question. Reasons for excluding citations at the full-text stage were: studies of mathematical models that did not account for dynamic relationships between elements of the system (n = 99), studies that did not include the healthcare policy context (n = 7) and abstract only citations (n = 4).



Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flowchart.

3.2. General Characteristics of Included Citations

The general characteristics of papers included in this scoping review are presented in Table 3. All included studies were published between 2009 and 2021, with the majority (5/7) published during the COVID-19 pandemic, in 2020 and 2021.

There were five main stakeholder categories in the included citations. Healthcare policymakers were the main stakeholders, followed by government officials, healthcare demonstrators, politicians, and academics. However, none of the studies reported involvement of stakeholders in the model development or interpretation of the results.

Different systems methods were used in the studies; the most commonly used method was system dynamics. Other methods used once in the studies were dynamic causal modelling, agent-based modelling, total interpretive structural modelling and multilayer complex network.

Characteristic	Number ($n = 7$)	
Publication year		
2009	1	
2017	1	
2020	4	
2021	1	
Publication type		
Journal article	7	
Main stakeholders		
Academics Healthcare policymakers	1	
Government	3	
Healthcare administrators	2	
Healthcare policymakers	5	
Politicians	2	
Systems methods used		
Agent-based modelling	1	
Dynamic causal modelling	1	
Multilayer complex network	1	
System dynamics modelling	3	
Total interpretive structural modelling	1	
Complex systems feature used		
Adaptive behaviour	6	
Disorder	7	
Feedback	7	
History and memory	0	
Nested structure and modularity	6	
Non-equilibrium	5	
Non-linearity	6	
Numerosity	7	
Robustness	4	
Spontaneous	7	

Table 3. General characteristics of included citations.

Regarding complex systems features, most studies exhibited most of the features in their modelling. Numerosity, disorder, feedback, and spontaneous order were noted in all included studies. Non-linearity, nested structure and modularity, and adaptive behaviour were displayed in 6/7 of the citations. Non-equilibrium featured in 5/7 of the studies. System history and memory were not seen in any of the models in the included articles.

3.3. Methodological Characteristics of Included Studies

The methodological characteristics of the included studies are presented in Tables 4 and 5. The methodological characteristics that address our research question and sub-questions are as follows:

Table 4. Extracted data: Study Characteristics and Aims.

Friston [15]2020US, Brazil, UK, France, Spain, Italy, Mexico, Belgium, Germany, CanadaLocal population of each country investigatedTo estimate the duration of population immunity and the latent states and mechanisms that affect the rate of new cases and deaths under the most likely loss of immunity.	Study	Publication Year	Country	Disease	Target Population	Aims
	Friston [15]	2020	US, Brazil, UK, France, Spain, Italy, Mexico, Belgium, Germany, Canada	COVID-19	Local population of each country investigated	To estimate the duration of population immunity and the latent states and mechanisms that affect the rate of new cases and deaths under the most likely loss of immunity.

Study	Publication Year Country		Disease	Target Population	Aims
Mutanga [12]	Mutanga [12] 2021		COVID-19	National population	To assess the range of systems dynamics modelling ability in forecasting COVID-19 dynamic and investigate the adequacy of government enforced restriction measures to control the pandemic using different "what if" scenarios. To predict the next wave of COVID-19 infection.
Scabini [16]	2020	Brazil	COVID-19	National population	To analyse COVID-19 dynamics in Brazil and to investigate the implications of future actions by the government on the healthcare system
Shin [14]	Shin [14] 2017		MERS-CoV	Healthcare staff, patients and visitors in hospitals during MERS-CoV outbreak	To investigate the effect of healthcare policy to control MERS-CoV in South Korea on terms of patient care and diseases spread in hospitals.
Silva [18]	8] 2020 Brazil		COVID-19	National population data	To simulate COVID-19 dynamics and the economic impact during different restriction scenarios.
Suresh [13]	2020	India	COVID-19	Healthcare workers (physicians, nurses, health inspectors, paramedics, hospital operation and administrative staff)	To analyse the key factors contributing to the agility of the healthcare system in controlling COVID-19 in the context of available resources during the disease dynamics.
Weixing [17]	2009	China	SARS	Population of Hubei Province	To simulate SARS-CoV-1 spread and evaluate control measures to mitigate further spread of the pathogen.

Table 4. Cont.

 Table 5. Extracted data: System Features, Methods, Stakeholders and Lessons.

Study	Main Stakeholders	Methods	System's Elements	Challenges and Potential Solutions	Key Lessons
Friston [15]	Policymakers and academics	Dynamic causal modelling	The local population is assigned a state in four distinct attributes (location, infection state, symptoms, and testing). 24 parameters specify aspects associated with state transition probabilities (e.g., the effective number of contacts, transmission strength, the efficacy of tracking and tracing).	Modelling process did not account for geospatial aspects, waves of infection or any interactions with seasonal influenza (no potential solution discussed). Inaccuracy of population demography data. Solution: building a model that accounts to population heterogeneity at a coarse-grained level by using a series of bipartitions of the latent states.	"The rate at which immunity is lost is important because it constrains the onset of any putative second wave." " the UK might expect a second wave in around January 2021. This is important because there is a window of opportunity in the next few months during which nonpharmacological interventions—especially tracking and tracing—will, in principle, be in a position to defer or delay the second wave indefinitely."

Table 5. Cont.

Study	Main Stakeholders	Methods	System's Elements	Challenges and Potential Solutions	Key Lessons
Mutanga [12]	National authorities	System dynamics model	They divided the national population into stocks (susceptible, exposed, infected, recovered and deceased), with flows between them representing the time in which individuals will move from one stock to the other. The model also contained multiple connected variables (e.g., R0, restriction measures, rate of contacts within the community, diseases duration and rates of individuals moving from one stock to another).	The modellers estimated homogenous population mixing, which might not represent the actual magnitude of COVID-19 spread in South Africa. The authors also mentioned that the national data might be sub-optimal due to the novelty of the pathogen. Solution: to replicate the model using current knowledge of COVID-19 and using a different timeline where data aggregation, including reporting and testing, are more accurate.	The systems dynamics model conducted in the study was proven beneficial to inform policymakers about prediction, prevention and control of COVID-19 with a small yet acceptable error. The study supports lockdown as a measure to prevent healthcare systems from collapsing.
Scabini [16]	Healthcare policymakers and government	Multilayer complex network	The model's layers represent the social interactions/activities between the population, including home, work, transport, school, religious activities and random. The nodes represent people, and the edges are social contacts between the nodes. The epidemic dynamic was also considered. Individuals were categorised as susceptible, infected-asymptomatic, infected-mild, infected-sever, infected-critical, recovered and dead.	The main challenge the authors faced was related to Brazil's geographic and demographic nature. Other challenges included insufficient data and lack of testing. Solution: This study can be repeated in other countries to check if the results are replicated.	The isolation measures in the study are insufficient and could significantly burden the healthcare system and mortality in Brazil. Social distancing is significant to reduce the peak of the pandemic curve. Returning to "normality" would cause a new peak in the pandemic's wave and the need for ICU beds would surpass the country's capacity.
Shin [14]	Health care policymakers and administrators in government and private sectors	System dynamics model	Model A: Stocks represent the susceptible and infected population at emergency rooms and the flow represent the infectious rate. The variables in model A represent types and frequencies of contact between people in the emergency room (ER occupancy rate, number of contacts made in the ER, susceptible contacts at ER, contact between infected and uninfected people at ER, probability of contact with infected patient at ER, total population at ER, patient arrival at ER, number of visitors per patient) and infectivity of MERS. Model B: Stock represents the general ward's susceptible and infected population. The variables represent infectivity of MERS, room occupancy, fractions of rooms with different frequencies, type and probability of contact and visitors.	The author reported a cultural challenge where family members in South Korea are expected to attend to patients even when healthcare staff are available which might lead to an increase in new cases. Solution : To understand the mental model for the studied population and find leverage points for a desirable outcome.	In hospitals, the number of MERS-CoV infections showed no significant difference between single and multiple room occupancy during the low infectivity period. However, it was increased between patients during the high infectivity period. High emergency room occupancy was associated with a higher risk of infection when compared to low occupancy emergency rooms. The number of visitors was directly related to increased infections among inpatients.

Study	Main Stakeholders	Main Methods System's Elements keholders		Challenges and Potential Solutions	Key Lessons		
Silva [18]	Politicians, healthcare policymakers	Agent-based model	Agents that make up the society in the model are people and their environment. The agents were grouped into families, business and government. The model contained input parameters (e.g., epidemiology, socioeconomic and demographic) and output parameters.	The scenarios of this study were done on a simulated society; the situation might differ slightly if the author considered confounding factors from real society. Solution: to validate the results by simulating the scenarios for real-world populations.	Lockdown and partial lockdown are best-case scenarios to mitigate the risk of COVID-19 in the context of human lives and health but have a significant impact on the economy. Vertical isolation (isolating infected individuals and high-risk groups) and "Do nothing" approaches had the worst income. The best scenarios were partial isolation (restricting the movement of the agents), using facemasks and social distancing.		
Suresh [13]	Healthcare managers and government	Total interpretive structural modelling (TISM)	Factors that make up the agility system in hospitals including building a Rapid Response Team (RRT), leadership support for the RRT, readiness for change, team members' adaptability, strategy fit to match the demand and capacity, accessibility and availability of the required resources, training and development, collaboration and resilience, embracing technology and innovations, multi-tasking and decision making, biomedical waste management, cost-effectiveness, and their interrelationships. Those factors are categorised into five groups according to their influence on the overall hospital agility.	Presenting the interaction of the factors within the model is not very clear at first sight. Solution: feedback back and forth between two factors can be presented with two arrows rather than one.	Using a framework like TISM can help increase agility in the hospitals and improve managers' decision-making when the most influencing factors and their interrelations are mapped and leverage points are explored rather than making decisions based on instinct and experience that might be suitable to the problem at hand. In this paper, the authors indicated that availability of resources, proper training and collaboration, and resilience are key factors in improving agility in hospitals.		
Weixing [17]	Healthcare policymakers and government	System dynamics model	They divided the local population into a community, quarantine areas and hospital compartments. Each compartment contains individuals divided into susceptible, latent, infected, recovered and deceased, with flows between them.	The results indicated that most SARS-CoV-1 cases were imported to Hubei from nearby regions. However, events from transportation were not considered in the model. Solution: incorporating modes of transportation in and out of Hubei into future models.	Healthcare in Hubei province is adequate and could control and mintages the risk of SARS-CoV-1. The optimal priority is to quarantine infected patients and reduce the time delay between diagnosis and hospitalisation. Most of the new cases in Hubei were imported from nearby regions		

Table 5. Cont.

3.3.1. How Are Systems-Oriented Modelling Methods Used to Investigate How to Prevent and Control Emerging Infectious Diseases (EIDs)?

Among the systems-oriented studies included in this review, six simulated the dynamics of an EID [12,14–18]. The modellers in these studies incorporated the classic susceptible, exposed, infected, recovered (SEIR) epidemiological model alongside systems-oriented modelling which considered the investigated population's environment. Another study, by Suresh et al., did not simulate disease dynamics. Instead the authors used systems methods to examine what factors contributed to the agility of hospitals to face challenges caused by COVID-19 [13]. They derived a five-level system demonstrating factors that supported the agility of hospitals to prepare and respond to EIDs. These factors included a trained rapid response team, effective leadership, strategies for managing resources and cost-effectiveness, readiness to change, adaptability, collaboration and resilience. They also demonstrated in their model how those factors make up the different levels and how the levels are connected.

Three studies used systems methods to predict an upcoming period of growth during an ongoing pandemic or epidemic [12,15,16]. They examined COVID-19 dynamics, population demography and types of public health policies to control the pandemic. Finally, five studies used systems methods to simulate the consequences of non-pharmaceutical public health strategies for controlling EIDs. Shin et al. used retrospective data to simulate how hospital policies affected the dynamics of MERS-CoV in South Korea in emergency rooms and inpatient wards. They took into account the infective status of patients, types of contacts, number of visitors and room occupancy [14]. Silva et al. simulated the effect of policy measures on COVID-19 burden on human health, life and the economy [18]. Magna et al. simulated multiple "what if" scenarios to investigate the "best approach" to control and mitigate the risk of COVID-19. They argued that the best approach for public health policy would be to find measures that would decrease the number of new cases and would be acceptable by the public [12]. Weixing et al., and Scabini et al., used systems methods to evaluate the types and effectiveness of local public health policy to control SARS-CoV-1 and SARS-CoV-2, respectively [16,17].

3.3.2. In What Contexts Were the Systems-Oriented Studies Conducted?

In the included studies, systems-oriented modelling methods were used to investigate how to prevent and control EIDs in the context of diseases dynamics, the burden on human health and life, economic burden and readiness of healthcare systems. All seven studies were conducted in the context of novel coronaviruses preparedness and control. Five studies were on SARS-CoV-2 [12,13,15,16,18], one study on SARS-CoV1 [17] and one study on MERS-CoV [19]. Friston et al., Mutanga et al., and Scabini et al. used the methods to assess the impact of COVID-19 dynamics on the numbers of new cases and deaths [12,15,16]. They did so by simulating scenarios for different local public health interventions. In addition to the epidemiology of the pandemic, Silva et al. included socioeconomic variables to assess the impact of COVID-19 on the economy [18]. Suresh et al. focused on the healthcare setting rather than the national population. Their study focused on the context of the healthcare system to assess its resilience and agility to face challenges related to COVID-19 by identifying and strengthening leverage points. Weixing et al. used compartmental models to assess local SARS-CoV-1 prevention and control measures within a single province [17]. Finally, Shin and colleagues conducted their study in the context of healthcare system policy in preventing and controlling MERS-CoV. They incorporated cultural expectations for patient care into their model and how they affected the spread of MERS-CoV in hospitals [14].

3.3.3. Who Was the Target Population?

All the articles included in this review studied the local population in countries where the studies were conducted. The population scale, however, differed between the studies. Friston et al., and Mutanga et al., used national populations [12,15]. However, while Mutanga and colleagues focused on the population of South Africa [12], Friston and colleagues' study was multinational. involving the US, Brazil, UK, France, Spain, Italy, Mexico, Germany and Canada [15]. Weixing and colleagues conducted their study on the local population of Hubei province in China. They did so to assess the effectiveness of local public health measures and to investigate if new cases were primarily local or imported from other areas in China [17]. Due to the large size, the complex demography of Brazil and challenges with data collection, Scabini and colleagues used the demography of the national population to parameterize a simulated population in their agent-based model, where they

built a multi-layered model representing the interactions between individuals and the disease dynamics [16]. The agents represented people in their environment, with input parameters including epidemiology, socioeconomic status, demography and produced epidemiology and economical response variables [18]. Suresh and colleagues used the healthcare population in their study. They included physicians, nurses, health inspectors, paramedics, hospital operation and administrative staff [13]. Shin and colleagues also focused on the healthcare workforce in addition to patients and visitors in South Korean hospitals during the MERS-CoV outbreak.

3.3.4. What Were the Main Complex-Systems Features?

Given the novelty of an EID, all included articles did not exhibit the "history and memory" feature of complex systems. The inclusion of the remaining complex system features is presented in Table 6.

	Systems Feature									
First Author	Numerosity	Disorder and Diversity	Feedback	Non- Equilibrium	Spontaneous Order and Self- Organisation	Non- Linearity	Robustness	Nested Structure and Mod- ularity	History and Memory	Adaptive Be- haviour
Friston [15]	Х	Х	Х		Х	Х				Х
Mutanga [12]	Х	Х	Х	Х	Х	Х	Х	Х		Х
Scabini [16]	Х	Х	Х	Х	Х	Х	Х	Х		Х
Shin [14]	Х	Х	Х		Х	Х		Х		Х
Silva [18]	Х	Х	Х	Х	Х	Х		Х		Х
Suresh [13]	Х	Х	Х	Х	Х		Х	Х		Х
Weixing [17]	Х	Х	Х	Х	Х	Х	Х	Х		Х

Table 6. Systems feature used in the citations.

3.3.5. What Was the Systems-Oriented Aim?

Overall, a systems-oriented approach was used to investigate how to prevent and control EIDs by presenting estimates of projected consequences of different public health policy choices. Friston and colleagues aimed to estimate the duration of effective immunity, to predict the second wave of SARS-CoV-2 and inform policymakers about precautionary and preventive measures [15]. Shin et al., Weixing et al. and Suresh et al., aims were to assess the ability of healthcare systems to respond and control threats related to EIDs [13,14,17]. While Weixing et al., and Shin et al., examined the readiness of the current healthcare system to respond to the threats of an EID, Suresh and colleagues were more focused on what factors make up the network to strengthen the response system to the threats. Finally, for Silva et al., Muntanga et al., and Sacabini et al., the aim was on the readiness of the whole country to face the challenges and burdens caused by SARS-CoV-2 [12,16,18]. The three articles examined the effect of public health measures on the duration of the pandemic wave and provided recommendations for future policies.

3.3.6. What Were the Main Systems Elements?

Overall, the systems elements used in seven articles were attributes of the local population, patients and visitors to hospitals during an EID outbreak and pre-identified key factors that influence healthcare settings' readiness and resilience when faced with an EID.

Five of the included articles used the national population and their environments as systems' elements and employed a version of the classic susceptible, exposed, infected, recovered (SEIR) epidemiological model [12,15–18]. Weixing and colleagues assigned individuals to different compartments (community, quarantine area, and hospitals). Each compartment represented subgroups of susceptible, exposed, infected, recovered and deceased individuals [17]. Mutanga et al. used a stock and flow diagram for their model. They divided the national population into five stocks, namely susceptible, exposed, infected, recovered and deceased (SEIRD), with other model parameters including the reproductive number, rate or contacts within the community, disease duration and the rate at which individuals move from one stock to the other [12]. Similarly, Sabini et al. used a variation

of the classical SEIR model. They assigned a stock for the exposed population because they assumed that all exposed individuals were infected. They also divided the infected population into four groups (asymptomatic, mild, severe and critical) in addition to susceptible, recovered and deceased individuals. Friston and colleagues assigned four attributes to the local population (location, infection status, symptoms and testing). They then divided each attribute into smaller compartments representing the state of individuals. They also considered the heterogeneity of exposure, susceptibility and transmission of the local population [15]. In addition to the SEIR model, Silva and colleagues used a compartmental model to represent the elements (agents) activity cycle and a system map to illustrate the economic relations between systems elements [18]. The other two included articles used the local population to focus on healthcare setting as systems elements. Shin et al. used patients, caregivers and visitors during the MERS-CoV outbreak in South Korea as systems elements [14]. They also used stock and flow diagrams to assess the spread of infection in the emergency room and hospital wards [14]. Suresh and colleagues took a different approach. After identifying the key leadership and managerial factors that support the agility of hospitals to combat COVID-19, they used these factors as the elements [13].

3.3.7. What Were Systems-Oriented Methods Used?

The most commonly used systems simulation method among the included articles was systems dynamics. Other methods included causal dynamic modelling, agent-based modelling, Total Interpretive Structural Modelling and multilayer complex network methods. In addition, all articles included a variation of a classical, SEIR epidemic model. Three used systems dynamics methods. Weixing et al., and Shi et al., started with a simple conceptual model for SASR-CoV1 and MERS-CoV. Later, they created systems dynamic models accounted for disease dynamics in the context of their study populations [14,17]. In contrast, Mutanga and colleagues did not present a conceptual model. However, their systems dynamics model is similar to that of Weixing and Shi. It included the SEIR model and different variables representing the COVID-19 situation in South Africa [12]. Friston and colleagues used dynamic causal modelling. Their approach focuses on probability densities rather than disease dynamics. For example, rather than assuming an individual is either infected or recovered, an individual can be infected and asymptomatic [15]. Silva and colleagues employed an agent-based model, focusing on individuals (agents) in a closed simulated society, with a variety of socioeconomic and epidemiological parameters, in order to run different "what if" scenarios simulating different health policies [18]. Finally, Suresh and colleagues used the Total Interpretive Structural Modelling approach. After performing a literature review to identify factors that influence hospital agility to face COVID-19, they collected and analysed responses from healthcare workers, created a matrix from these responses and finally created a graph presenting the disclosed factors and how are they are connected [13]. Sabino and colleagues used the multilayer complex network method, extending the SEIR model to include multilayers representing social interactions in Brazil [16].

3.3.8. What Challenges Related to Systems-Modelling Did the Authors Face?

In four articles, the authors mentioned challenges, related to data collection and data accuracy in building the models. Friston et al.'s and Mutanga et al.'s main challenge was data collection and accuracy during an ongoing pandemic [12,15]. Friston and colleagues also mentioned that cross-infection with other diseases like influenza contributes an extra challenge in the modelling process [15]. In addition to inaccuracy in disease dynamic data, Scabini and colleagues faced other challenges because of Brazil's geography and demography, which can compound data inaccuracies [16]. Weixing and colleagues reported challenges related mainly to the data collection environment. They used retrospective hospital data relating to patients and visitors during the SARS-CoV1 outbreak in Hebei province in China and mentioned errors in time recording of visits [17]. Shin et al., Silva et al., and Suresh et al. did not report any challenges.

3.3.9. Who Were the Main Stakeholders? Moreover, How Were They Involved?

The main stakeholders were healthcare policymakers, governments and politicians. All the studies were conducted to provide evidence-based recommendations to these stakeholders to inform national public health policies aimed at reducing the burden of EIDs by preventing, controlling, and mitigating their risk to the local population. However, none of the stakeholders had any role in developing the models included in the articles or the interpretation of the results.

3.3.10. What Were the Key Lessons Learned from Using the Complex Systems Approach?

Three of the included articles mentioned lessons learned during the systems model development process. Overall, the main lesson was that there was always room for model improvement when appropriate data are available. Additionally, there was a desire to account for parameters that go beyond disease dynamics, like social, demographic, or economic aspects, which would provide a more holistic perspective on what is going on during an EID. For example, Friston et al., and Scabini et al. stated that their models could be improved by including and/or stratifying the demographic groups by age and ethnicity. The latter also suggested incorporating the clinical presentation of the diseases within the model [15,16]. Silva and colleagues stressed the importance of considering the population's social interactions and economic status to provide a better representation of the pandemic effects on the investigated population [18]. Weixing et al., Shin et al., Mutanga et al., and Suresh et al. did not report or indicate any lessons learned while building their models.

4. Discussion

Our review indicates that systems-oriented modelling methods used in the context of preparedness and response in the face of EIDs can be valuable in identifying healthcare policy approaches and actions for preventing and controlling EIDs. Most of the included studies focused on disease dynamics within the context of the multiple linked elements of the complex systems generating EID threats in a particular population, providing the basis for running simulations of different "prevention" scenarios. Other studies' contexts included healthcare resilience, resource allocation and the economic impact of EIDs.

A variation of the classical SEIR epidemiological model was used in most of the studies, showing that systems methods are not meant to replace classical epidemiological methods. Instead, they can complement evidence provided by other methodological approaches, providing opportunities for original research and potential collaborations between epidemiologists and systems scientists. Systems-oriented modelling differs from classical mathematical modelling in its focus and approach to problem-solving. Instead of analysing a particular problem, systems modellers mainly focus on systems' elements and their connections. By simulating real-world problems, systems modellers can make clear to policy makers the feedback loops affecting outcomes in the system and thus make tangible recommendations about where solutions might lie [19,20]. Another difference is that not all systems-oriented methods involve mathematical modelling, but rather may point qualitatively, in diagrammatic form initially, to causal loops affecting the outcomes [21–23]. In addition, systems modellers can incorporate multiple sub-systems, which build bridges between different stakeholders, including healthcare policymakers, governments, the private sector, healthcare workers and society. This can be useful in examining and improving healthcare system resilience during a public health crisis posed by EIDs threats [22]. Hence, systems methods can offer a birds-eye view of healthcare systems and their links to connected systems within a society, eschewing a reductionist approach policy and its implementation [24].

The main challenges reported by the authors while using a systems approach to prevent and control EIDs were related to the availability and accuracy of epidemiological data. Data availability and accuracy are constrained by EIDs' novel nature, by environmental factors, and by the geography or demography of the studies' locations and populations. These factors lead to imprecision in observed data which might hinder model calibration. However, Cassidy and colleagues argued that systems methods are less affected by this issue than classical mathematical methods [25]. Moreover, methods to assess the impacts of these uncertainties in the models' results can explore the sensitivity to these effects and help prioritize which aspects of the models or their inputs would benefit the most from more accurate and timely data.

All included studies focused on sarbecoviruses, with the first study published in 2009. However, in addition to sarbecoviruses, the WHO also prioritizes other EIDs for research and development [10]. Our review sheds light on how systems approaches can be used for future research and practice on these diseases. Moreover, the global community has learned from the current COVID-19 experience that the consequences of an uncontrolled EID are more extensive than previously imagined and can lead to a significant burden not only on human health but also on the economy and how society functions. Thus, it is necessary to use a holistic approach for problem-solving when it comes to EIDs, to which systems science can contribute.

The main lesson learned from our review is that systems methods are adaptable and informative. Besides the possibility of systems modellers to further develop existing models when clinicians have deeper understanding of an EID and/or more data are available, there is an added value in considering the dynamic relationship between systems elements and/or other features of complex systems. Moreover, incorporating socioeconomic and demographic data to diseases dynamics in systems models can provide a more holistic presentation of the magnitude and burden of an EID, which in turn helps in producing more specific recommendation to a particular situation or a population.

Our review noted some limitations of systems-oriented methods. The model development process and validation were not transparent in all the included studies, making it challenging for researchers to reproduce the results [25,26]. In addition, the models varied in depth and detail and the reporting style was inconsistent across studies. These limitations are expected because systems methods have only been used recently in EID prevention and control research. With more adaptation of systems methods in EIDs and healthcare policy research, there is a need for clear guidelines in terms of visualisation, transparency and reporting style to enhance reproducibility [25]. Other limitations of systems methods in healthcare policy are their inability to represent all the spill-over phenomena in a healthcare system and the (deliberate and necessary) oversimplification that is inherent to the modelling process [26].

Limitations and Strengths

The main limitation of our review is that due to the volume of COVID-19 research reported during the current pandemic, relevant literature may have been published since our original search. Due to the lead time between searches and reporting a review, there is a need in a rapidly changing situation such as the COVID-19 pandemic to strike a balance between keeping the searches up-to-date and sharing the findings at a point at which they are useful. It is possible that some reports used systems-oriented modelling methods but did not allude to it in their title, abstract or keywords/descriptors.

As for the strengths of this review, we performed a comprehensive search using agreedupon keywords (with the support of a subject librarian) linked to the WHO list of EID for research and development and followed the Joanna Briggs Institute guidelines for scoping reviews [8,10], guided by a protocol that was reviewed by the research team and peer reviewed [9]. Additionally, we maintained transparency on the need to narrow the scope of the review due to time limitations arising from university regulations governing doctoral studies. Additionally, the reviewing process was done by two independent reviewers.

5. Conclusions

Systems methods can be used to prevent and control EIDs in many ways. The value of systems methods in preparedness and response of healthcare systems to EIDs have been increasingly appreciated because they account for the complexity of this group of diseases.

A range of methods was identified, they were used either alone or in combination with other epidemiological methods. Finally, we conclude that systems methods may help in designing policies to improve healthcare system resilience in response to EIDs.

Recommendations for Future Research

Since systems science is multidisciplinary, we encourage collaboration between researchers from different disciplines to prevent and control EIDs. Teams comprising systems scientists, epidemiologists, systems engineers and social scientists can build systems models to provide a deeper understanding of the EID threat to societies. COVID-19 was prominent in the studies that were included in this review. Systems-oriented methods take account of context, and models and interventions designed in one context might not be helpful in the contexts of different diseases, places or times, for example. As of now there is relatively limited evidence available from the practical application of systems-oriented methods in EID control, and we therefore encourage systems researchers and policymakers to evaluate and report their past and future experiences of implementing systems-oriented methods in EIDs prevention and control.

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Conflicts of Interest: The authors declare no conflict of interest.

Appendix A. Keywords Search across Databases

Appendix A.1. PubMed 23/3/21, 1905 Results

(Emerging-infectious-disease*[Title/Abstract] OR coronavirus[Title/Abstract] OR MERS-CoV[Title/Abstract] OR COVID-19[Title/Abstract] OR severe-acute-respiratory syndrome[Title/Abstract] OR SARS-CoV-2[Title/Abstract] OR SARS[Title/Abstract] OR Ebola[Title/Abstract] OR avian-influenza[Title/Abstract] OR zika*[Title/Abstract] OR dengue[Title/Abstract] OR nipah[Title/Abstract] OR pandemic*[Title/Abstract] OR outbreak* OR Crimean-Congo-haemorrhagic-fever[Title/Abstract] OR rift-valley-fever [Title/Abstract] OR lassa-fever[Title/Abstract])

AND

(complex* near/2 system*[Title/Abstract] OR system-dynamic*[Title/Abstract] OR agent-based[Title/Abstract] OR stochastic[Title/Abstract] OR compartmental-model*[Title/Abstract] OR multi-agent[Title/Abstract] OR multi-compartment-model*[Title/Abstract] OR network near/2 analys*[Title/Abstract])

Appendix A.2. Web of Science 23/3/21, 1880 Results

(

TI=("Emerging infectious disease*" OR coronavirus OR MERS-CoV OR COVID-19 OR "severe acute respiratory syndrome" OR SARS-CoV-2 OR SARS OR Ebola OR "avian influenza" OR zika* OR dengue OR nipah OR pandemic* OR outbreak* OR "Crimean Congo haemorrhagic fever" OR "rift valley fever" OR "disease X" OR "lassa fever") OR AB=("Emerging infectious disease*" OR coronavirus OR MERS-CoV OR COVID-19 OR "severe acute respiratory syndrome" OR SARS-CoV-2 OR SARS OR Ebola OR "avian influenza" OR zika* OR dengue OR nipah OR pandemic* OR outbreak* OR "Crimean Congo haemorrhagic fever" OR "rift valley fever" OR "disease X" OR "lassa fever")

) AND

(

TI=(complex* W/2 system* OR "system dynamic*" OR "agent based" OR agent-based OR stochastic OR "compartmental model*" OR "multi agent" OR multi-agent OR "multi compartment model*" OR "multicompartment model*" OR "multi-compartment model*" OR network W/2 analys*)

OR

AB=(complex* W/2 system* OR "system dynamic*" OR "agent based" OR agentbased OR stochastic OR "compartmental model*" OR "multi agent" OR multi-agent OR "multi compartment model*" OR "multicompartment model*" OR "multi-compartment model*" OR network W/2 analys*)

)

Appendix A.3. Scopus 23/3/21, 9230 Results

TITLE-ABS(Emerging infectious disease*) OR TITLE-ABS(coronavirus) OR TITLE-ABS(MERS-CoV) OR TITLE-ABS(COVID-19) OR TITLE-ABS(severe acute respiratory syndrome) OR TITLE-ABS(SARS-CoV-2) OR TITLE-ABS(SARS) OR TITLE-ABS(Ebola) OR TITLE-ABS(avian influenza) OR TITLE-ABS(zika*) OR TITLE-ABS(dengue) OR TITLE-ABS(nipah) OR TITLE-ABS(pandemic*) OR TITLE-ABS(outbreak*) OR TITLE-ABS(Crimean Congo haemorrhagic fever) OR TITLE-ABS(rift valley fever) OR TITLE-ABS(disease X) OR TITLE-ABS(lassa fever)

)

AND

(TITLE-ABS(complex* W/2 system*) OR TITLE-ABS(system dynamic*) OR TITLE-ABS(agent?based) OR TITLE-ABS(stochastic) OR TITLE-ABS(compartmental model*) OR TITLE-ABS(multi?agent) OR TITLE-ABS(multi?compartment model*) OR TITLE-ABS (network W/2 analys*)

)

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