


Using simulation modelling and systems science to help contain COVID-19: A systematic review

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Abstract

This study systematically reviews applications of three simulation approaches, that is, system dynamics model (SDM), agent-based model (ABM) and discrete event simulation (DES), and their hybrids in COVID-19 research and identifies theoretical and application innovations in public health. Among the 372 eligible papers, 72 focused on COVID-19 transmission dynamics, 204 evaluated both pharmaceutical and non-pharmaceutical interventions, 29 focused on the prediction of the pandemic and 67 investigated the impacts of COVID-19. ABM was used in 275 papers, followed by 54 SDM papers, 32 DES papers and 11 hybrid model papers. Evaluation and design of intervention scenarios are the most widely addressed area accounting for 55% of the four main categories, that is, the transmission of COVID-19, prediction of the pandemic, evaluation and design of intervention scenarios and societal impact assessment. The complexities in impact evaluation and intervention design demand hybrid simulation models that can simultaneously capture micro and macro aspects of the socio-economic systems involved.

KEYWORDS

agent-based model, COVID-19 pandemic, discrete event simulation, system dynamics model, systematic review

1 | INTRODUCTION

At the end of 2019, a series of pneumonia cases caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, later formally named COVID-19 by the World Health Organization (WHO).

Considering its rapid spread and highly infectious characteristics, WHO declared on 30 January 2020 that the outbreak constituted a Public Health Emergency of International Concern (PHEIC) (WHO, 2020a). Following over a year's strenuous containment efforts, COVID-19 remains poorly controlled in some countries while

others witnessed effective results. As of 14 April 2022, 500 186 525 confirmed cases have been reported globally, including 6 190 349 deaths (WHO, 2020b). As a public health crisis, the outbreak of COVID-19 not only led to high morbidity and mortality but also impacted every sector of society and exacerbated the global economic recession. Although vaccinations have been created, the pandemic may yet resist rapid resolution due to limited supply and debatable efficacy, particularly against rapidly emerging variants. Therefore, it is crucial for policymakers, healthcare planners, manufacturers of medical devices and healthcare providers to use available data and appropriate tools to better understand transmission dynamics, assess the uncertainty caused by mutations and evaluate impacts of intervention measures. Situational analysis should be conducted, and optimal interventions strategy and resource portfolio employed accordingly. More importantly, relevant research and policy implementation practices can provide critical insights for future emerging infectious diseases.

Simulation models, including compartmental model, system dynamics model (SDM), discrete event simulation (DES), agent-based model (ABM), data-driven modelling approach and machine-learning techniques, have been widely used during outbreaks to characterize spreading, capture relevant driving factors, make accurate predictions on risks and turning points, help optimally allocate resources and design and evaluate public health policies. The aforementioned models have been employed to model infectious diseases including smallpox (Epstein et al., 2002), avian influenza (Casagrandi et al., 2006), Ebola (Weitz & Dushoff, 2015), Zika (Morrison & Cunha, 2020), SARS (severe acute respiratory syndrome) (Anderson et al., 2004), MERS (Middle East respiratory syndrome) (Lee et al., 2016) and COVID-19 (Jones et al., 2020; Lai et al., 2020). Compartmental models, for example, the Susceptible-Infected-Recovered (SIR) model and its extensions, represent simplified mathematical constructs, most often using ordinary differential equations (deterministic ODEs), for modelling and simulating infectious diseases (Keeling & Danon, 2009). One of the advantages of compartmental models is its simplicity and ease of implementation, allowing for quicker implementation during an outbreak. Scholars have built a variety of compartmental models to conduct transmission analysis of COVID-19 (Mohamadou et al., 2020; Rahimi et al., 2021).

Employing an identical mathematical structure to compartmental models, SDM is broadly used to capture the non-linear dynamics of complex systems over time. It helps understand counterintuitive behaviours and policy resistance in complicated socio-economic systems. It uses coupled feedback loops that capture real-

world systems using stocks (e.g., material, people and money), flows (rate of change) and time delays (response of the system). SDM has many applications in routine and unexpected situations and acts as a decision support tool for policymakers (Allen, Mills, et al., 2020). SDM is a great simulation paradigm for integrating conventional compartmental models of infectious diseases into a more comprehensive structure used for strategical assessment of potential policy interventions (Bagni et al., 2002).

DES models are commonly used to simulate operation of systems as discrete sequence of events over time within particular contexts, such as hospitals (Eldabi et al., 2007; Jacobson et al., 2006; Jun et al., 1999). As a typical operations research technique, DES excels at characterizing resource-limited workflows and has been widely used to improve production processes, healthcare capacity planning, programme evaluations, evaluation of investment decisions and so forth (Liu et al., 2020).

ABMs, as a widely used computational modelling approach, are stochastic, often spatially or network explicit, discrete-time simulation models where the agents represent interacting actors or items of interest. One key feature is its usage of a synthetic social contact network to represent each individual in the population and heterogeneity that yields a realistic model of their sociodemographic attributes and social interactions (Lenormand et al., 2015; Liu et al., 2018). ABMs enable decision makers to recreate, visualize and predict the emergence of complex phenomena from heterogeneous interacting individuals with distinct characteristics and behaviours (Sun et al., 2020). Given its advantages of simulating heterogeneous agents in complex systems, ABM has found intensive use in capturing the spread dynamics of infectious diseases and evaluating the efficacy of relevant interventions (Davey & Glass, 2008; Epstein, 2009; Eubank et al., 2004; Kumar et al., 2013; Mabry et al., 2010; Temime et al., 2009).

Data-driven modelling approaches and machine-learning techniques are another class of models that have been widely used to provide new insights. Representative approaches, including Bayesian inference, gradient-boosting machine models, logistic regression, decision tree, support vector machine, artificial neural network and Markov chain Monte Carlo (MCMC), have been used for parameter estimation and prediction of COVID-19 outbreaks (Mbuva & Marwala, 2020; Zoabi et al., 2021). However, the literature size in this field is enormous, and they should be categorized and reviewed separately. The current review only focuses on applying three major dynamic simulation modelling traditions, that is, SDM, DES and ABM, and their hybrid models thereof in the study of COVID-19.

This systematic review aims at achieving three objectives: (1) summarizing how three simulation models and their hybrids were used in capturing and dealing with issues with different characteristics (e.g., heterogeneous agents, aggregate behaviour of homogeneous agents and process dynamics) that arose during the outbreak of COVID-19; (2) gaining a better understanding as to how different simulation approaches can help conduct a holistic situational analysis, make accurate outbreak predictions, optimize medical resource planning, evaluate alternative interventions and develop high-leverage containment policies; and (3) demonstrating how new application trends, theoretical innovations or methodological integrations (e.g., the hybrid model of ABM and SDM) were used in those simulation approaches.

The rest of the paper is organized as follows: Section 2 provides the search strategy and selection criteria and the method of search strategy, inclusion and exclusion criteria, the selection process and an overview of the data. Section 3 details the results of the systematic review. In Section 4, discussion regarding results and limitations, and public health implications are presented. Section 5 concludes this study with an executive summary and outlook on using systems simulation models in investigating emerging infectious diseases.

2 | METHODS

The review conducted is partially consistent with guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The quality of search, selection and analysis are guaranteed by using AMSTAR (Assessing the Methodological Quality of Systematic Reviews) (refer to Appendix A) (McCartney et al., 2019; Shea et al., 2017).

2.1 | Search strategy and selection criteria

The following academic web portals and databases were searched within the designated time range: PubMed, MEDLINE, EMBASE, Web of Science, Scopus, ScienceDirect, EBSCO, Wiley and the WHO COVID-19 Database. The search strategy combined terms related to ‘discrete event simulation’, ‘discrete event system simulation’, ‘agent-based models’, ‘agent-based modelling’, ‘individual-based model’, ‘multi-agent system’, ‘system dynamics’, ‘compartmental model’, ‘hybrid simulation’, ‘coronavirus disease 2019’, ‘COVID-19’, ‘COVID-2019’, ‘severe acute respiratory syndrome coronavirus 2’, ‘SARS-CoV2’ and ‘SARS-CoV-2’. An illustration

depicting the search strategy through PubMed is provided in Appendix B.

Two independent reviewers (H.Z. and W.Z.) performed record selection by reading through papers to determine their suitability for the systematic review. Disagreements were resolved by discussion with a third person (S.L. or P.J.). Eligible papers had to meet the following inclusion criteria: (1) used any of the three simulation models (SDM, ABM and DES), their hybrid models (such as ABM + SDM and DES + SDM) or a compartmental simulation model (SIR, SEIR, modified SIR or modified SEIR, all characterized as falling into the SDM category) in investigating COVID-19; (2) included multiple naming schemes such as COVID-19, severe acute respiratory syndrome coronavirus 2 and SARS-CoV-2 (detailed in Table C1 in Appendix C); (3) acceptable COVID-19 topics were considered to include not only transmission dynamics, prediction, prevention and control strategies but also economical cost estimation, resource management and other related issues; (4) was an original study and not any form of review; (5) was written in English; and (6) was published in a journal and conference proceedings, or advance online publication, or appeared in preprint channels (e.g., <https://www.medrxiv.org/>) between 1 December 2019 and 31 December 2021.

2.2 | Data extraction and analysis

The initial search identified 4554 records; 1741 were eligible for the title and abstract screening after duplicate removal. By applying predefined criteria, 868 articles were removed by scrutinizing title, abstract or both. The remaining 873 articles were read, and 501 were excluded, which included 298 papers using compartmental models that were outside the sphere of systems simulation. As a result, 372 papers were included in the systematic review (Figure 1).

3 | RESULTS

The 372 papers cover three primary systems simulation approaches of SDM, DES, ABM and hybrids (e.g., ABM + SDM, ABM + DES and SDM + DES). Consistent with the objectives of this study, two significant categories of contribution— theoretic innovation and applications—were identified. Issues investigated by these models can be further divided into four areas: transmission dynamics of COVID-19 (72 articles), predicting trends (29 articles), intervention measures (204 articles) and impacts of COVID-19 on society

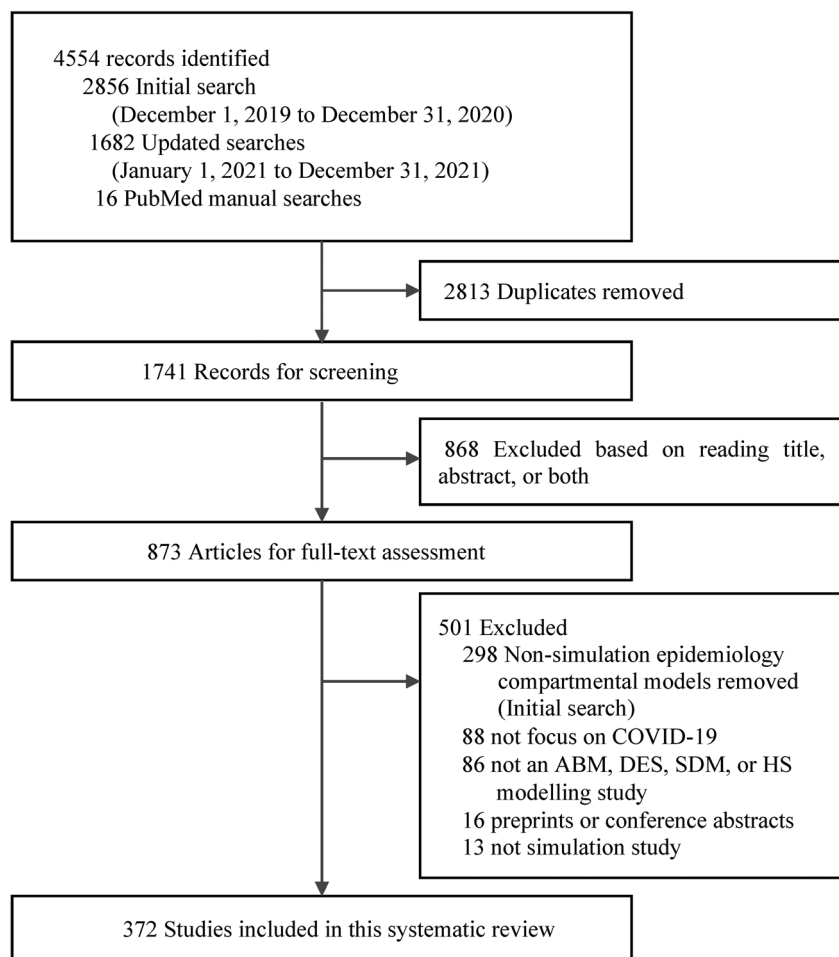


FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart for systematic review of using simulation models to help contain COVID-19. ABM, agent-based model; DES, discrete event simulation; HS, hybrid simulation; SDM, system dynamics model

(67 articles). It is worth noting that this categorization reflects the authors' judgments rather than an objective taxonomy. Figure 2 summarizes the type of simulation models, key research areas and system scale to which they were applied.

3.1 | Overview of the applications of different simulation models

Among the 372 papers, 275 (74%) used ABM. To observe emerging behaviours, the papers characterized each person or a group of persons as a heterogeneous agent interacting within a (censored) population in a synthetic social network, placing their hypothetical relationships within a region or nation (Agrawal et al., 2020; Bai, 2020; Benneyan et al., 2021; Cremonini & Maghool, 2020; Delcea et al., 2020; Raviraja et al., 2021). This social network might also contain layers of households, schools, workplaces or community and disease properties (Aleta et al., 2020; Alqithami, 2021; Altun et al., 2021; Álvarez-Pomar & Rojas-Galeano, 2021; Kamerlin & Kasson, 2020; Panovska-Griffiths et al., 2020; Rockett et al., 2020; Yang

et al., 2020). To lend a more realistic context and consequently provide more interventions, six papers also incorporated GIS-enhanced geospatial data into the simulation platform (Agrawal et al., 2020; Alvarez Castro & Ford, 2021; de Vries & Rambabu, 2021; Gharakhanlou & Hooshangi, 2020; Mahmood et al., 2020; Zhang et al., 2021) and five papers integrated human mobility data (Aleta et al., 2020; Kishore et al., 2021; Sewell & Miller, 2020; Wei et al., 2021; Zhou, Zhang, et al., 2021). To demonstrate the dynamics of the spread through interactions, 158 papers simulated the disease transmission via regular or modified SIR- or SEIR-based ABMs, where the labelled states of individuals are Susceptible, Infected, Recovered, Dead (SIRD) (Alsaed et al., 2020; Mahmood et al., 2020) or Susceptible, Exposed, Infected, Recovered, Dead (SEIRD) (Benneyan et al., 2021; Gharakhanlou & Hooshangi, 2020). Some papers also introduced more COVID-19 states, such as asymptomatic (Almagor & Picascia, 2020; Head et al., 2021; Koehler et al., 2021; Moghadas et al., 2021; Talekar et al., 2020), mild and severe symptoms (Alagoz et al., 2020; Zhang, Vilches, et al., 2020) and hospitalized (Nguyen et al., 2021;

FIGURE 2 Summary of simulation models, research areas and system scale applied. *Note:* Numbered references are listed in the supporting information. ABM, agent-based model; DES, discrete event simulation; HS, hybrid simulation; SDM, system dynamics model [Colour figure can be viewed at wileyonlinelibrary.com]

| Scale | Country | Region | Organization | Individual | Classification of Research Topics | | | | Models |
|-------|--|---|--|--|-----------------------------------|------------|---------------|---------|--------|
| | | | | | Transmission | Prediction | Interventions | Impacts | |
| | 28, 59, 97, 99, 113, 130, 177, 255, 264, 267, 270, 274, 346, 348 262, 367 268 119, 214 | 117, 132, 170, 180, 276 101, 354, 360 33, 146 | 6, 32, 35, 56, 57, 61, 67, 71, 74, 79, 86, 95, 107, 108, 111, 115, 131, 150, 155, 160, 164, 168, 178, 182, 184, 191, 204, 205, 209, 212, 213, 216, 227, 234, 236, 237, 240, 242, 260, 265, 266, 273, 292, 295, 301, 309, 312, 321, 335, 351, 361, 364 1, 22, 41, 62, 66, 161, 176, 223, 232, 305, 310, 311 165 156 | 42, 54, 55, 145, 194, 252, 261, 280, 299, 304 38, 46, 114, 120, 138, 173, 175, 201, 233, 256, 298, 372 | ABM SDM DES HS | | | | |
| | 13, 14, 16, 17, 27, 31, 49, 69, 72, 76, 78, 80, 102, 118, 142, 157, 187, 197, 200, 218, 239, 241, 249, 263, 287, 316, 327, 345 137, 344 339 302 | 4, 34, 64, 83, 91, 141, 174, 221, 246, 272, 297, 356, 357 307, 308, 329 98 347 | 2, 5, 7, 8, 9, 10, 12, 19, 20, 29, 36, 37, 39, 50, 51, 75, 103, 104, 106, 116, 121, 126, 127, 133, 140, 149, 153, 158, 159, 167, 169, 172, 181, 183, 186, 195, 196, 198, 199, 203, 207, 219, 222, 224, 225, 226, 238, 244, 250, 251, 269, 275, 282, 283, 285, 289, 290, 291, 296, 300, 306, 318, 319, 320, 322, 325, 326, 332, 334, 336, 337, 338, 340, 352, 353, 355, 359, 365, 366, 369, 370, 85, 87, 143, 152, 171, 188, 231, 253, 258, 341, 368 | 3, 52, 92, 93, 122, 144, 192, 235, 288, 343 77, 342, 350 45, 53, 70, 281, 349 | | | | | |
| | 23, 65, 84, 88, 112, 125, 128, 136, 189, 243, 257, 279, 294, 329, 359 254, 323 | 190 | 15, 18, 21, 24, 26, 30, 40, 82, 89, 105, 110, 134, 135, 139, 147, 151, 154, 162, 179, 193, 217, 220, 229, 230, 247, 271, 317, 324, 330, 333, 362, 371 44, 47, 81, 94, 109, 206, 248, 277, 278, 303 25, 60, 259 | 58, 63, 73, 96, 123, 124, 208, 210, 211, 228 100, 129, 245, 286, 293, 315 11, 43, 68, 148, 163, 166, 185, 215, 284, 331, 363 | | | | | |
| | 48, 202, 313, 314 | | 90 | | | | | | |

Palomo-Briones et al., 2021; Son & RISEWIDS Team, 2020; Tadić & Melnik, 2020; Xu et al., 2021). In addition, spread through contaminated surfaces and objects (Tadić & Melnik, 2020) and loss of immunity (Alsaeed et al., 2020) were also simulated.

There are 54 simulation papers using SDM, accounting for 14.5% of all selected research, where one paper used a simple SIR model (Pornphol & Chittayasothorn, 2020), one paper used a SIRD model (Ibarra-Vega, 2020), two papers used a classic SEIR model (Kumar, Priya, & Srivastava, 2021; Yusoff & Izhan, 2020) and seven papers constructed a SEIRD model (Abdolhamid et al., 2021; Khairulbahri, 2021; Liu et al., 2021; Mutanga et al., 2021; Struben, 2020; Sy et al., 2021; Zhao et al., 2020). In the modified papers, new states such as pre-symptomatic (Rahmandad et al., 2021), asymptomatic (Fair et al., 2021; Sy et al., 2020), symptomatic (Currie et al., 2020; Fair et al., 2021), quarantined (Currie et al., 2020; Kumar, Viswakarma, et al., 2021; Qian et al., 2021), isolated (Niwa et al., 2020), hospitalized or in treatment (Hu et al., 2021; Qian et al., 2021; Rahmandad et al., 2021) and vaccinated (Breerton & Pedercini, 2021; Suphanchaimat, Tuangratananon, et al., 2021) were introduced into the models. In addition, without providing particular application cases, three papers built conceptual macro-level SDMs to understand the emergence of COVID-19 and system resilience and vulnerability in response to public health emergencies, respectively (Kontogiannis, 2021; Wang et al., 2020; Wang & Mansouri, 2021).

There are 32 (8.5%) simulation papers using DES. The simulation models were mainly used to assess the impact of COVID-19 on an organization's workflow and emphasized its optimization (Allen, Bhanji, et al., 2020;

Das, 2020; de Brito Jr et al., 2021; Kim et al., 2021; VanDeusen et al., 2021; Zeinalnezhad et al., 2020). Meanwhile, DES was also applied to process analysis and optimization of service facilities that had effects on COVID-19 spread, including testing facility (Çaglayan et al., 2022; El Hage et al., 2021; Gowda et al., 2021; Saidani et al., 2021; Saidani & Kim, 2021), vaccination centres (Pilati et al., 2021) and COVID-19-related hospitals (Frichi et al., 2021; Melman et al., 2021). DES research was also used to investigate different interventions for minimizing transmission risk in lab facilities (Lim et al., 2020).

There are only 11 (3%) papers concerning hybrid simulation: Six papers were a combination of ABM and DES (Asgary et al., 2020; Cimini et al., 2021; Possik et al., 2021; Qiu et al., 2021; Stapelberg et al., 2021; Tofighi et al., 2021), three papers were a combination of DES and SDM (Kang et al., 2021; Lu, Guan, et al., 2021; Warde et al., 2021) and two papers were an integration of SDM and ABM (Guo, Tong, et al., 2021; Mokhtari et al., 2021).

3.2 | Theoretic innovation and detailed application areas

3.2.1 | Theoretical innovation in simulation models

Although most research focused on specific applications of the models, 11 papers, to some extent, offered certain theoretic innovation. A study employing an individual-level network-based model (ABM) used an ensemble Kalman filter to conduct parameter estimation. The study

also showed good use of non-Markovian models to better capture the spreading dynamics (Yang et al., 2020). In a school environment setting, a study proposed an artificial intelligence (AI)-powered ABM (Valtchev et al., 2021) to examine the challenges anticipated for preventative testing of COVID-19. Two studies combined machine-learning algorithms with ABM to model the COVID-19 transmission (Ozik et al., 2021) and calculated the effects of the COVID-19 pandemic on the banking system and the real economy (Polyzos et al., 2021), respectively. Six studies integrated geospatial data with ABM, which adds spatial-temporal characteristics of COVID-19 transmission to improve containment policy. In a study for improving patients' workflow in a heart clinic during COVID-19 outbreak, timed coloured Petri nets were embedded into DES to analyse and improve the healthcare organization's performance (Zeinalnezhad et al., 2020). To capture the dynamics of health resource demand and disease transmission, a study proposed the use of Bayesian-based SDMs (Yusoff & Izhan, 2020). Another study put forward a framework for treating the total population as an inhomogeneous random social network (IRSN) (Hurd, 2020) and then conducted a theoretical exploration of IRSN and IRSN-ABM and its advantages to inform public health policy and health research.

3.2.2 | Decoding transmission dynamics of COVID-19

There are 72 papers investigating COVID-19 transmission dynamics, with 4 simulating it through biosocial stochastic dynamics (Tadić & Melnik, 2020) and microscopic dynamics (Castiglione et al., 2021; Marzban et al., 2021; Tadić & Melnik, 2021). Seventeen papers simulated spreading mechanism and transmission dynamics within a particular venue, including the cruise ship *Diamond Princess* (Hooten et al., 2020), a long-term care facility (Smith et al., 2020), a typical large dialysis unit (Tofighi et al., 2021), a hospital (Evans et al., 2022), a construction site (Araya, 2021a, 2021b), a sporting facility (Qi et al., 2021), a school (Tupper & Colijn, 2021), a college (Gressman & Peck, 2020; Possik et al., 2021), a hypothetical facility (Cuevas, 2020), a retail store (Pantano et al., 2021; Ying & O'Clery, 2021), a supermarket (Harweg et al., 2021; Hernandez-Mejia & Hernandez-Vargas, 2020; Lu, Wang, et al., 2021; Salmenjoki et al., 2021) and a church (Farthing & Lanzas, 2021a). Nineteen papers explored COVID-19 transmission at the country level, including Australia, China, Italy, Liberia, Sierra Leone, Spain, Ukraine, the United Kingdom and the United States. Other papers also investigated the effect of some factors, including social media and

individual behaviours (Du et al., 2021; Palomo-Briones et al., 2021; Zhang et al., 2022), fear-driven behaviours (Rajabi et al., 2021), human activity patterns (Wang et al., 2021), the impact of cross-reactivity induced by exposure to endemic human coronaviruses (eHCoVs) (Pinotti et al., 2021), natural disasters (de Vries & Rambabu, 2021) and misinformation diffusion (Prandi & Primiero, 2020). In addition, one article simulated transmission of the virus, and online panic and its adverse effects on the control and prevention of COVID-19 outbreak (Guo, Li, et al., 2021). Another one study explored the relationship between the spread of COVID-19 and economic activities (Kano et al., 2021).

3.2.3 | Trend prediction of COVID-19 spreading

Twenty-nine papers focused on COVID-19 epidemic prediction, of which seven tried to estimate the R_0 in different regions (Müller et al., 2021; Rypdal et al., 2021; Yang et al., 2020) and countries (Guo & Xiao, 2020; Hoertel, Blachier, Blanco, Olfson, Massetti, Rico, et al., 2020; Kolokolnikov & Iron, 2021; Krivorotko et al., 2022). Most studies made prediction regarding cumulative infections (Hunter & Kelleher, 2021; Latkowski & Dunin-Kplicz, 2021) and deaths (Ghaffarzadegan & Rahmandad, 2020), mortality (Benneyan et al., 2021; Lu, Guan, et al., 2021), daily testing capacity required (Fiore et al., 2021), hospital admissions (Warde et al., 2021) and demand for intensive care unit (ICU) beds (Bartz-Beielstein et al., 2021; Garcia-Vicuña et al., 2021; Irvine et al., 2021) and so forth as different interventions, such as physical distancing (Aghaei & Lohrasebi, 2021), various lockdown (Hoertel, Blachier, Blanco, Olfson, Massetti, Rico, et al., 2020; Uansri et al., 2021) and vaccination strategy (Suphanchaimat, Nittayasoot, et al., 2021; Suphanchaimat, Tuangratananon, et al., 2021). The rest predicted the future spread under school reopening (España et al., 2021; Rypdal et al., 2021; Son & RISEWIDS Team, 2020), city reopening (Yin et al., 2021), society activities reopening (Cremonini & Maghool, 2020) and international borders reopening (Pham et al., 2021). By considering the Alpha, Gamma and Delta variants, one study (Sah et al., 2021) evaluated the dominance of these variants in the United States.

3.2.4 | Evaluation of intervention measures for control and prevention

Among the papers, 204 mainly focused on evaluation of both pharmaceutical interventions (PIs) and non-pharmaceutical interventions (NPIs). The main objectives

of these papers were not to provide point or path prediction but rather to understand and evaluate the impacts of intervention measures on the transmission dynamics of COVID-19. Regarding PIs, 28 papers discussed vaccine strategies and their effects. Fatehi et al. (2021) evaluated the effectiveness of two forms of therapies, that is, remdesivir and convalescent plasma (CP) therapy. Forty-five papers evaluated the impacts of different NPIs on COVID-19 containment in specific organizations, including elementary or secondary schools (Asgary et al., 2021; Morrison et al., 2021; Zafarnejad & Griffin, 2021), colleges and universities (Bahl et al., 2021; Brennan et al., 2021; Goyal et al., 2021; Kharkwal et al., 2021; Lv et al., 2021), hospital (Campos et al., 2022; Huang et al., 2021; Mukherjee et al., 2021), army training post (España et al., 2021), refugee camp (Gilman et al., 2020), nursing and care home (Holmdahl et al., 2021, 2022; Kahn et al., 2022; Lasser et al., 2021; Nguyen et al., 2021; Stevenson et al., 2021), long-term care facility (Vilches et al., 2021), church (Rothrock et al., 2021), supermarket (Tong et al., 2021) and construction site (Alzu'bi et al., 2021). Three of them explored the effects of NPIs on special events, including two rituals of the Hajj (Al-Shaery et al., 2021), wedding ceremony (Alzu'bi et al., 2021) and indoor gathering (Farthing & Lanzas, 2021b).

There were 158 papers related to interventions evaluation at the national and regional levels (refer to Table 1). The six major categories of NPIs used are as follows: (1) mobility restrictions used to prevent seeding during the early outbreak period, including public transport and travel restrictions; (2) identification mechanisms, including screening, testing, diagnosing and reporting; (3) isolation and quarantine measures, including forced isolation, self-quarantine, community isolation and contact tracing of people who were suspected or confirmed to have the disease or who were exposed to the infected; (4) social distancing or contact restrictions implemented to reduce the risk of exposure at the community level, including lockdown, curfew, staying at home and workplace and school closures; (5) personal preventive measures including personal protective equipment (PPE; e.g., facemasks) and frequent handwashing; and (6) healthcare capacity or hospital capacity, including isolation or quarantine beds and ICU beds. The PI at the national and regional levels referred to vaccination strategy.

Seen from Table 1, most papers investigated the outcomes of enacting one to three types of NPIs. Isolation/quarantine and social distancing were the most widely studied NPIs. Three phases of the pandemic were often observed by these studies: (1) Lockdown was imposed to prevent rapid spread at the initial stage, necessitating

strict mobility restrictions; (2) normalized prevention and control measures such as social distancing and personal protective measures were enforced when lockdown was lifted, production was resumed and schools and other service outlets were reopened; and (3) when the vaccine was developed and produced, NPIs and vaccination were combined to fight against COVID-19. Hence, it is imperative to use simulation research to understand the impacts of different interventions during distinct stages to identify cost-effective measures.

3.2.5 | Evaluating cross-sectoral impacts of the COVID-19

Apart from research on COVID-19 spread dynamics and evaluation of implementing different interventions, 67 relevant papers investigated the impacts of the pandemic and related NPIs on various sectors. Ten papers investigated the disruptions and uncertainties to the supply chain caused by the COVID-19 pandemic (Achmad et al., 2021; Burgos & Ivanov, 2021; Choudhary et al., 2021; Duan et al., 2021; Ghadge et al., 2021; Moosavi & Hosseini, 2021; Nguyen, 2021; Sinha et al., 2020) and the post-pandemic recovery strategies (Ivanov, 2021; Rahman et al., 2021). Twenty papers explored the other sectors at the national and regional levels, including industrial network (Song et al., 2020), tourism (Gu et al., 2021; Luo et al., 2021), national security (Prikazchikov et al., 2021), food-energy-water (Calder et al., 2021), economy (Chen et al., 2021; Fosco & Zurita, 2021; Inoue et al., 2021; Inoue & Todo, 2020; Sharma et al., 2021), financial (Spelta et al., 2021), social activity (de Brito Jr et al., 2021; Schmidt & Albert, 2021; Weibrecht et al., 2021), healthcare (Schlüter et al., 2021), employment (Marreros et al., 2021) and transport and land-use (Habib & Anik, 2021). As the pandemic led to great collateral damage or process disruption to a variety of organizations, including banks (Shahabi et al., 2021), airlines (Delcea et al., 2020; Milne et al., 2020, 2021), ambulatory endoscopy centres (Das, 2020), heart clinics (Zeinalnezhad et al., 2020), laboratories (Lim et al., 2020) and outpatient dialysis services (Allen, Bhanji, et al., 2020), necessary countermeasures were adopted to lower the risk of transmission and to improve effectiveness of these measures. Simulation models can help organizations across diverse sectors develop and evaluate scenarios, ask counterfactual 'what-if' questions and identify and implement cost-effective organization-level infection prevention and control mechanisms. In addition, one paper simulated the consequences of medical costs of keeping the US economy running as normal under different counterfactual paths (Chen et al., 2020). Another

TABLE 1 Evaluating pharmaceutical interventions (PIs) and non-pharmaceutical interventions (NPIs) at the national, regional and organizational levels

| Study | Mobility restrictions | Identification | Isolation and quarantine | Social distancing | Self-prevention | Vaccination | Hospital capacity |
|--|-----------------------|----------------|--------------------------|-------------------|-----------------|-------------|-------------------|
| 188 | √ | × | × | × | × | × | × |
| 85, 121, 266, 337 | × | √ | × | × | × | × | × |
| 35, 56, 167, 196, 216, 231, 236, 258, 273, 311 | × | × | √ | × | × | × | × |
| 8, 10, 22, 39, 41, 67, 74, 79, 106, 107, 111, 126, 143, 149, 156, 160, 168, 176, 195, 199, 203, 209, 219, 224, 226, 227, 232, 237, 253, 282, 291, 300, 312, 332, 352, 359, 364 | × | × | × | √ | × | × | × |
| 19 | × | × | × | × | √ | × | × |
| 6, 9, 50, 150, 198, 212, 213, 269, 275, 289, 306, 334, 336, 370 | × | × | × | × | × | √ | × |
| 20, 29 | √ | × | √ | √ | × | × | × |
| 338 | √ | × | √ | √ | √ | × | × |
| 172 | √ | × | √ | × | × | √ | × |
| 57 | √ | × | × | √ | × | × | × |
| 244 | √ | × | × | √ | √ | √ | × |
| 186 | √ | × | × | × | √ | × | × |
| 301 | √ | × | × | × | × | × | √ |
| 103, 116, 133, 158, 164, 178, 184, 207, 250, 260, 369 | × | √ | √ | × | × | × | × |
| 66, 140, 159, 169, 205, 234, 242, 251, 305 | × | √ | √ | √ | × | × | × |
| 5, 181, 318, 365 | × | √ | √ | √ | √ | × | × |
| 182 | × | √ | √ | √ | √ | √ | × |
| 36, 131, 321 | × | √ | √ | √ | × | √ | × |
| 366 | × | √ | √ | × | √ | √ | × |
| 1, 2, 12, 37, 153, 155, 238, 265, 283, 296, 310, 340, 351, 353, 355, 368 | × | × | √ | √ | × | × | × |
| 183, 225, 285, 292, 319 | × | × | √ | √ | √ | × | × |
| 61, 320 | × | × | √ | √ | √ | √ | × |
| 32 | × | × | √ | √ | × | √ | × |
| 290 | × | × | √ | × | × | × | √ |
| 51, 75, 223, 325 | × | × | × | √ | √ | × | × |
| 240 | × | × | × | √ | √ | √ | × |
| 95, 104, 361 | × | × | × | √ | × | √ | × |
| 108 | × | × | × | √ | × | × | √ |

Note: The numbered reference table is attached in the supporting information.

paper simulated the impacts of labour migration policies under different hypothetical scenarios on the economic growth of a host country during the pandemic (Kozlovskiy et al., 2020).

4 | DISCUSSION

Most papers emphasized that their research objectives were to simulate the transmission dynamics of COVID-19 under multiple interventions and inform public health decisions. About half focused on NPIs and vaccination strategies. Because interventions practised at organizations and individual levels exhibited much greater heterogeneity, only cases of NPIs and vaccination strategies implemented at the national or regional level were sorted and summarized.

4.1 | Insights of policy design on NPIs

NPIs played a critical role in slowing the spread in the absence of vaccination. Based on simulated results in Canada, without appropriate NPIs, a majority of the country's population might contract the disease, which would collapse the health system and consequently lead to even higher mortality (Ogden et al., 2020). Simulation studies in other countries suggested possible epidemic rebounds or a new wave spike if quarantine (Hoertel, Blachier, Blanco, Olfson, Massetti, Limosin, & Leleu, 2020) or social distancing (Brereton & Pedercini, 2021; Rice et al., 2020) were lifted prematurely. However, the pandemic will continue to batter the economy if stringent NPIs are not lifted (Ghaffarzadegan & Rahmandad, 2020). Therefore, it is important for a dynamically informed trade-off between designing and implementing NPIs and minimizing their adverse effects on society. Systems simulation models have contributed significantly to informing public health decisions by testing necessary assumptions from policymakers and identifying solutions by considering the timing, stringency and combination of NPIs.

4.1.1 | Timing of NPIs

A simulation paper concluded that the timing of NPI implementations, adherence to the measures and timing of lifting relevant measures have significant impacts on the development of the epidemic (Alagoz et al., 2021). A simulation paper in Shenzhen (Zhang, Cheng, et al., 2020) revealed that the proper timing of NPIs not only generated the most effective outcomes but also achieved

the minimum negative social costs. Specifically, their results showed that local infection numbers could have been reduced by 35% if migrant workers or travellers coming from Hubei province followed the '14-day compulsory quarantine' 1 week ahead of schedule. By contrast, the local infection number could rise by 4% if delayed by a week, demonstrating the advantage of using simulation to identify an ideal intervention window. The simulation results also revealed that the number of local infections could have been 50% lower if patients were hospitalized immediately after symptom onset.

4.1.2 | Duration of NPIs

One paper (Ibarra-Vega, 2020) simulated the infection trends under three different lockdown arrangements: one extended 60-day lockdown, a 30-day lockdown followed by a 30-day smart lockdown and an initial 40-day lockdown followed by a 30-day smart lockdown. The results suggested that an extended initial lockdown and then gradually returning to normal activities is highly effective, demonstrating the need for policymakers/implementers to choose the lockdown duration carefully. Niwa et al.'s (2021) study showed that mild and continuous lockdown could have better containment outcomes than strong and intermittent ones. Although extended lockdown did have remarkable impacts on reductions in infections and deaths (Kersting et al., 2021), a country or region should make trade-offs between the control results of COVID-19 spread and the economic development and social well-being.

4.1.3 | Stringency of NPIs

Using the reduction in contact rate to stand for the stringency of lockdown, an ABM was used to simulate the number of infected people and death under 100%, 50%, 25% and 10% of the typical contact rate (Alsaeed et al., 2020). The results revealed that minimized contact rate—i.e., adopting stringent interventions—lowered infection and mortality compared with mild interventions. Another paper (Pornphol & Chittayasothorn, 2020) used SDM to derive similar conclusions by simulating the outbreak in Phuket, Thailand, using a contact rate of 33%, 23%, 11% and 5% of the normal. A paper (Makarov et al., 2020) developed ABM to predict the epidemiological dynamics in Moscow under three scenarios. The simulation results showed that the deployment of restrictive measures could reduce cumulative mortality counts. Another ABM simulation paper evaluated the effects of different stringency levels in social distancing (Silva

et al., 2020). The results concluded that lockdown and conditional lockdown had the highest negative impacts on the economy but were also best in lowering infections and mortality. Wearing facemasks and 50% social isolation adherence was identified as the best scenario to achieve the balance between preserving lives and minimizing negative economic impact. Kersting et al.'s (2021) study proved that strict measures were an effective way of buying time to expand healthcare system capacities and improve prevention measures.

4.1.4 | The combination strategy of NPIs

Relying on a single NPI cannot effectively contain COVID-19 and mitigate side effects (e.g., supply chain disruption caused by lockdown) caused by NPI monotonicity. Upon the reopening of society coexisting with endemic SARS-CoV-2, only combining multiple NPIs can prevent subsequent waves of COVID-19 (Gharakhanlou & Hooshangi, 2020).

The variances in demographic characteristics, culture, socio-economic structures, transportation systems, healthcare systems and public health governance between regions induce differences in the transmission dynamics of COVID-19. Consequently, region-specific NPIs portfolios are demanded. A systems simulation model is optimal to help find the most feasible combination of NPIs by testing various assumptions and implementation paths. More importantly, by considering different timing and stringency of NPIs, simulation outputs can improve the public health policy and system towards the evolving pandemic. Moreover, evaluating those adopted implementation paths undoubtedly increases the system preparedness and supports appropriate countermeasures.

4.2 | Insights on vaccination

In our review, the vaccination-related literature mainly investigated delayed second-dose vaccination, vaccine compliance, vaccination effectiveness, daily vaccination rate, daily vaccine administering capacity, vaccination coverage and vaccination prioritizing strategies. Regarding prioritizing vaccination, strategies had considered age-stratified strategy, risk and vulnerable groups prioritizing strategy (Aguas et al., 2021; Moghadas et al., 2021) and spatial distribution strategy (Tatapudi et al., 2021; Zhou, Zhou, et al., 2021). However, given that many countries, especially those third-world countries, are not capable of producing vaccines, more simulation research

should be carried out to understand the dynamic interplay between the vaccine supply–demand and the choice of different NPIs, which therefore can inform the public health policy. Simulation models intending to understand the interactions among the immune protection period from vaccination, vaccine effectiveness against different virus variants, vaccine administration capacity, vaccination coverage, vaccine supply capacity and hospital capacity could also be explored.

4.3 | Outlook for applying systems simulation models

4.3.1 | Demanding more application areas

This review identified under-served research areas. Only one paper simulated the transmission of COVID-19 via suburban railways (Talekar et al., 2020). With the availability of big data from air transportation, highway/railway network and public transit, spatial ABMs can be built based on mobility patterns of travellers or urban populations to simulate the transmission of COVID-19 (or other emerging infectious diseases) via intra- or inter-city transport network. It is worth noting that, considering the complexity and resources needed for modelling, the purpose of modelling is to simply reality correctly by capturing critical characteristics of the target system, not entirely. Simulation models, for example, using DES, can also help public design facilities to consolidate the implementation of NPIs.

Categorized literature shows that the scales of previous research range from individual, organizational, regional to national levels. Some simulation papers evaluate the impacts of COVID-19 and NPIs on the broader socio-economic system, such as collateral damage to healthcare system, national or regional economy. A key opportunity exists to construct a macro-level SDM to better understand the cascading impacts on the interconnected global economy and, subsequently, global governance of public health. Microscopic level simulations were also not employed within the papers. Simulation models such as SDM or ABM could be used to simulate the airborne dynamics and transmission of SARS-CoV-2, which can bolster NPIs, such as face shields, more rigorous definitions of safe distance and spraying disinfectant. Within-host microscopic level simulation can illustrate the competition between the virus, immune system and associated inflammatory responses such as cytokine storm syndrome (COVID-19-CSS), evolutionary dynamics (e.g., new variants) and virus–host cell interaction dynamics.

4.4 | Demanding more theoretical innovation and ensuing applications

4.4.1 | Hybrid systems simulation models

The ability of hybrid systems simulation models to concurrently capture heterogeneities of individuals and homogeneities of the population demonstrates good use in public health, which requires public policy design from both micro and macro angles (Brailsford et al., 2019). For instance, in the research on COVID-19, hybrid models such as ABM&DES, ABM&SDM or SDM&DES can simultaneously simulate the spread within a community or city and evaluate the impact of treatment capacity improvement in hospitals and their dynamic mutual interactions. Taking another example, a hybrid DES&ABM model used for studying a hospital providing COVID-19 treatment is capable of simulating the following events and actions: (1) DES can simulate the capacity change caused by staff scheduling, process rearrangement and set-up of the quarantine area, which creates a process that might lead to the infection of staffs; (2) ABM supports simulation of the infection of staff under the settings, which informs the removal of infected staffs; (3) removal of infected staff necessitates the rescheduling of staff in (1), which increases the workload on incumbent staff; and (4) overwhelmed staffs have higher risk to be infected, which further changes the status of (2).

As the world heads into something closer to an endemic regime and active surveillance systems are being scaled back, there is great promise for the deployment of techniques that can aid in the early and effective detection of localized outbreaks and provide decision support needed for effective enactment of localized public health measures and (critically) triggering of surge capacity when health system utilization is likely to exceed certain thresholds. Of particular demonstrated ability and effectiveness are routinized use on daily basis of techniques such as particle MCMC (PMCMC) and particle filtering coupled with COVID-19 dynamic models to provide 'online' processing of regularly or episodically sampled passive and (where available) active localized surveillance data. Such systems inform day-to-day updated probabilistic estimation and reporting of latent epidemiological and health system quantities of interest. In addition to supporting estimation, such models can have a demonstrated effectiveness for use in probabilistically projecting forward estimated evolution of estimated epidemiology and acute-care demand in a way that can serve as the basis for triggering surge capacity, for example, in emergency care. They can also be used to examine 'what-if' counterfactuals involving public health measures. A key need is to inform such systems with

sufficiently rich and current data to inform such projections. In addition to whatever public health and health system indicators are available (including data from syndromic surveillance systems in emergency departments and hospital admissions tests), such systems have a demonstrated capacity to further employ wastewater indicators, time series generated from symptom-like references on social media and online searches that may be indicative of symptoms of SARS-CoV-2 infection.

A further need involves hybrid models that tie in the representation of acute COVID-19 with Long COVID outcomes and with the patient flow for care-seeking. Understanding and effectively resourcing such patient flow is essential given the large volumes likely to be driven not only by Long COVID sequelae but also by the care needs of deferred (and often worsened) conditions, consequences of disruptions of preventive and screening processes during the pandemic and rehabilitation needs and to address mental health service delivery for needs emerging from or worsened by the pandemic.

Whereas some hybrid methods do impose added computational burden, others allow hybrid methods to significantly reduce the computational burden that would extend from a traditional DES model or (especially) ABM. A notable example is hybrid methods that use an aggregate characterization for part of a model (e.g., low-risk populations or people at earlier stages of a risk continuum) and that reserve individual-level representation for the subpopulations of focal interest (e.g., those who have been exposed to or infected by SARS-CoV-2). This approach has been used successfully in some extant but unpublished COVID-19 models and to a high degree of success for other conditions, such as dementia (Evenden et al., 2020), diabetes in pregnancy (Freebairn et al., 2020) and chronic kidney disease (Gao et al., 2017). Future research on ABM could reduce the computational burden by constructing smaller scale models (with fewer agents) to anticipate what the results would be produced by a much larger model (Osgood, 2009).

4.4.2 | Other innovations

This systematic review examined applications of GIS-enhanced geospatial data to ABM, which also offers a promising direction for tempo-spatial analysis of simulation models. Parameter estimation approaches are necessary for robust systems simulation models and their hybrids. So far, among the least square, maximum likelihood estimation (MLE), Monte Carlo (MC) and MCMC, least square is the most commonly used method (Guan et al., 2020). The PMCMC (Andrieu et al., 2010) and deep learning (Muhammad et al., 2021), as two promising

parameter estimation approaches, are attracting growing attention of many scholars in systems simulation. PMCMC is a powerful method to explore high-dimensional parameter space using time-series data. Combining emerging technologies, such as AI, machine learning, big data analytics and blockchain (Muhammad et al., 2021), with traditional models is indispensable when developing high-leverage policies and interventions to mitigate the impacts of COVID-19. This is especially useful for governments, institutions and organizations to accelerate knowledge accumulation and governance learning towards future emerging diseases and their impacts on the complicated socio-economic system.

4.5 | Limitations

Although conventional epidemiology compartmental models are the basis for building SDM and ABM, they are limited in capturing the non-linear causalities between driving factors and system behaviours in the socio-economic system in which the COVID-19 epidemic is embedded and, consequently, are too narrowly scoped to evaluate the broader impacts of multiple interventions. Nevertheless, the applications of such traditional research were reviewed (Appendix D).

5 | CONCLUSIONS

This systematic review found that systems simulation models exemplified by SDM, ABM and DES have been widely used to model the COVID-19 transmission dynamics, trend prediction of the pandemic and societal impact assessment and in evaluating and designing intervention scenarios from the scales of an individual, organization, region and state. Majority of the papers focused on simulating the outcomes and impacts of alternative intervention measures, which are very suitable to inform public health policy and implementation science. ABM was the mostly common-used modelling approach and covered more research areas. Future research areas could be extended to studies on transmission dynamics of COVID along with transportation networks, evaluation of the collateral damages to the healthcare system and economy, assessment of the post-pandemic policies and microscopic level simulation for understanding the competition between virus, immune system and associated inflammatory responses. As for the innovations in simulation methods, the complexities in impact evaluation and intervention design for containing COVID-19 or future emerging infectious diseases necessitate the use of hybrid simulation models that can simultaneously

capture the micro and macro aspects (e.g., understanding individual behaviours and decision-making, within-host viral dynamics and population-based interventions and resource allocation) of the socio-economic system involved.

STATEMENT ON THE CONTRIBUTION

By systematically reviewing three major system simulation approaches, that is, system dynamics model (SDM), agent-based model (ABM) and discrete event simulation (DES), and their hybrids in COVID-19-related research, our manuscript offers four major contributions. First, we attempt to summarize how three different simulation models and their hybrids were used in capturing and dealing with different issues that arose during outbreak of COVID-19. Secondly, this study is to gain better understanding as to how different simulation approaches can help conduct holistic situational analysis and counterfactual analysis, make accurate outbreak predictions, optimize medical resource planning, evaluate alternative interventions and develop high-leverage containment policies. The third contribution is to demonstrate how new application trends, theoretic innovation or methodological integration (e.g., hybrid model of ABM and SDM) were used in those simulation approaches. And the last but not the least contribution of this study is to indicate some future innovative research on the three system simulation approaches, which include (1) hybrid models simultaneously capturing micro and macro aspects of the socio-economic systems involved; (2) within-host microscopic level simulation understanding competition between the virus, immune system and associated inflammatory responses; (3) more parameter estimation methods for SDM, ABM, DES and their hybrids; and (4) models for capturing the interactions between pandemic progression and hospital service capacity planning, and so forth.

DATA AVAILABILITY STATEMENT

All relevant data have been included in the supporting information.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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APPENDIX A: CRITICAL APPRAISAL PREVENTING BIASED ASSESSMENT

Critical appraisal preventing biased assessment using AMSTAR:

The quality of the reviews will be evaluated using modified AMSTAR criteria:

- Was an 'a priori' design for the review provided?
- Was a comprehensive search undertaken (including relevant search terms and at least two databases)?
- Were the studies selected for inclusion by at least two independent researchers?
- Were there clear inclusion and exclusion criteria?
- Was the status of publication ignored in the inclusion/exclusion criteria?
- Were the data extracted independently by at least two researchers?
- Was the scientific quality of the included studies assessed and documented?
- Was the scientific quality of the included studies used appropriately in formulating conclusions?
- Were the methods used to combine the findings of studies appropriate?
- Was the likelihood of publication bias assessed (if possible)?
- Were there important conflicts of interest that may have impacted on the conclusions?

APPENDIX B: EXAMPLE OF IMPLEMENTING SEARCH STRATEGY FOR LITERATURE THROUGH PubMed

1. #1 Search (((coronaviridae[Mesh:noexp] OR coronavirus[Mesh] OR 'coronavirus Infections'[Mesh] OR corona[tw] OR corona'[tw] OR 'coronavirus'[tw] OR coronavir*[tw] OR Betacoronavirus[Mesh] OR Betacoronavirus[tw])))
2. #2 Search (((pneumonia[Mesh:noexp] OR pneumonia, viral[Mesh:noexp] OR Viruses[Mesh]) and ('Disease Outbreaks'[Mesh] OR Epidemiology [Mesh])))
3. #3 Search (((#1 OR #2) AND 2019/11:2020/2 [crdt]))
4. #4 Search (((2019-novel-corona*[tw] OR 2019-new-corona*[tw] OR '2019-nCOV'[tw] OR 'coronavirus disease 2019'[tw] OR 'Corona Virus Disease 2019'[tw] OR '2019 coronavirus disease'[tw] OR COVID-19[tw] OR COVID-2019[tw] OR 'severe acute respiratory syndrome coronavirus 2'[Supplementary Concept] OR 'severe acute respiratory syndrome

coronavirus 2'[tw] OR SARS2[tw] OR SARS-CoV2 [tw] OR SARS-CoV-2[tw]))

5. #5 Search ((#4 OR #3))
6. #6 Search (((('discrete event simulation'[tw] OR 'Discrete event system simulation' [tw] OR DES[tw] OR 'agent-based model*[tw] OR ABM[tw] OR 'Individual based model*[tw] OR 'multi-agent system'[tw] OR 'system dynamics'[tw] OR SD[tw] OR 'hybrid simulation'[tw] OR 'compartmental model*[tw]))))
7. #7 Search ((#5 AND #6))

APPENDIX C: INCLUSION AND EXCLUSION CRITERIA

TABLE C1 Inclusion and exclusion criteria

| Inclusion criteria | Exclusion criteria |
|---|---|
| Research topic: Focus on COVID-19. Not only the paper focuses on the spread of COVID-19, the paper related to the COVID-19 has been taken into consideration | Research topic: Not related to COVID-19. COVID-19 is only mentioned in paper, but the actual research topic has nothing to do with COVID-19 |
| Modelling: Simulation modelling, including agent-based modelling (ABM) (or individual-based model), system dynamics (SD), discrete event simulations (DES) and hybrid simulation (combine two or more of ABM, SD and DES) | Modelling: Simulation modelling is not the main model used in paper |
| Study type: Paper was the original study not the any form of review paper | Study type: The type of the paper is preprint or conference abstracts |
| Study language: Writing in English | |

APPENDIX D: QUICK REVIEW OF TRADITIONAL COMPARTMENTAL MODELS IN COVID-19 RESEARCH

Compartmental models have played a pivotal role in understanding the outbreak dynamics of epidemic and pandemic. In our quick review, we found that 298 papers employed compartmental models to investigate the

TABLE D1 Categorization for examples from traditional compartmental model studies

| Key research areas | Publication |
|---|--|
| Prediction of the COVID-19 | |
| COVID-19 outbreak progression | Chen et al., 2020; Ianni & Rossi, 2020; Santamaria-Holek & Castano, 2020; Youssef et al., 2020 |
| Initial epidemic features | Romo & Ojeda-Galaviz, 2020; Wang, Ding, et al., 2020 |
| Basic reproduction number (R_0) estimation | Aggarwal & Rajpu, 2020; Dharmaratne et al., 2020; Eksinchol, 2020; Kumar et al., 2020; Masud et al., 2020; Serhani & Labbardi, 2020; Sundaresan et al., 2020; Wang, Tang, et al., 2020 |
| Estimation of transmission parameters | Deng, 2020; Kain et al., 2020; Mbuva & Marwala, 2020; Vattay, 2020 |
| Acute-care service demand dynamics | Dagpunar, 2020; Koeppl et al., 2020; Rivera-Rodriguez & Urdinola, 2020; Semenova et al., 2020; Singh & Bajpai, 2020 |
| Long-term trend prediction | Zhan, Tse, Lai, et al., 2020 |
| Investigation of the timing and size of second waves | Eguíluz et al., 2020; Friston et al., 2020; Glass, 2020 |
| Evaluate impacts of non-pharmaceutical intervention (NPI) measures | |
| Mobility restrictions | Liu, He, et al., 2020; Scala et al., 2020; Sun, He, et al., 2020; Wang, Zhu, et al., 2020 |
| Lockdown | Alrashed et al., 2020; Buonomo & Marca, 2020; Lyra et al., 2020; Morozova et al., 2021 |
| Quarantine | Barbarossa et al., 2020; Batista et al., 2020; Khyar & Allali, 2020; Sun, Duan, et al., 2020; Zu et al., 2020 |
| Contact restrictions | Liu, He, et al., 2020; Rădulescu et al., 2020; Yousif & Ali, 2020 |
| Social distancing | Childs et al., 2021; Das & Samanta, 2020; Wickramaarachchi et al., 2020; Zhao & Feng, 2020 |
| Facemask use or face cloth covering | Gondim, 2020; Khan et al., 2020 |
| School closure | Gathungu et al., 2020; Röst et al., 2020 |
| Exit strategies | Ghamizi et al., 2020 |
| Other areas | |
| Vaccination strategies | Buckner et al., 2020; Libotte et al., 2020; Etxeberria-Etxaniz et al., 2020 |
| Healthcare burden | Miller et al., 2020 |
| Cost estimation of school and workplace closure | Suwantika et al., 2020 |
| Impact of relaxing existing control measures | Currie et al., 2020 |
| Risk of return to workplaces | Zhang, Ge, Liu, et al., 2021 |
| Indirect transmission mechanisms (e.g., surface-based infection within public spaces) | Meiksin, 2020 |
| Model specifics | |
| Classic model | |
| SIR (Susceptible, Infected, Recovered) | Libotte et al., 2020; Molnár et al., 2020 |
| SEIR (Susceptible, Exposed, Infected, Recovered) | Aggarwal & Rajput, 2020; Ahmad et al., 2020; Etxeberria-Etxaniz et al., 2020; Morrison & Cunha, 2020; Wang, Fang, et al., 2020 |
| SEIRD (Susceptible, Exposed, Infected, Recovered, Death) | Edeki et al., 2020; Kumar et al., 2020; Rivera-Rodriguez & Urdinola, 2020 |
| Extended or modified models added some new states | |
| Asymptomatic | Arándiga et al., 2020; Batista et al., 2020; Das & Samanta, 2020; Di Giamberardino et al., 2021; Rajagopal et al., 2020; Wang, Wang, et al., 2020; Zhao et al., 2020 |

TABLE D1 (Continued)

| Model specifics | Publication |
|---|---|
| Quarantined | Buonomo & Marca, 2020; Kumari et al., 2020; Liu, Zheng, et al., 2020; Masud et al., 2020; Serhani & Labbardi, 2020; Vyasarayani & Chatterjee, 2020; Zhao & Feng, 2020 |
| Hospitalized | Garba et al., 2020; Ghamizi et al., 2020; Wang, Ding, et al., 2020 |
| Insusceptible (e.g., protected by the vaccine) | Buckner et al., 2020; Kumari et al., 2020; Xu et al., 2020 |
| Added other new insights or methods | |
| Age-stratified compartmental models | Rădulescu et al., 2020; Röst et al., 2020; Castilho et al., 2020; Balabdaoui & Mohr, 2020 |
| Network-based compartmental models utilized the human migration data collected from the Baidu Migration Porta | Kumari et al., 2020; Liu, He, et al., 2020; Zhan, Tse, Fu, et al., 2020 |
| Cellular Automata (CA) | Molnár et al., 2020; Zhan, Tse, Fu, et al., 2020 |
| Long Short-Term Memory (LSTM) recurrent neural network | Chen et al., 2020; Yang et al., 2020; Zheng et al., 2020 |
| Machine learning | Kiruthika et al., 2020; Muhammad et al., 2021 |

outbreak of the COVID-19 in different regions and countries across the world, namely, Asia (e.g., China, India, Pakistan, Kazakhstan, Japan, South Korea, Bangladesh and Saudi Arabia), America (e.g., the United States, Brazil, Argentina and Mexico), Europe (e.g., Italy, the United Kingdom, Germany and Spain), Oceania (e.g., Australia and New Zealand) and Africa (e.g., South Africa and Kenya), and some papers covered more than one country or region. We simply, from key research areas and models, summarize parts of studies, and the details are shown in Table D1 in Appendix D.

Although compartmental models are simple and easy to implement and have been widely used to capture transmission dynamics of infectious diseases at the population level, they strictly rely on the assumption of homogeneous mixing, or mass action, which fails to consider individual heterogeneity within the compartmental groups and simplifies the complexities of interactions occurred in the social networks. ABM and DES can capture the heterogeneity of individuals in a system and events in a process, respectively. Therefore, SDM (compartmental model-based systems simulation), ABM and DES can work in parallel or work in a hybrid mode to simultaneously capture heterogeneity and homogeneity in a system if necessary.

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