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To cite this article: Sheryl L. Chang, Mahendra Piraveenan, Philippa Pattison & Mikhail Prokopenko (2020) Game theoretic modelling of infectious disease dynamics and intervention methods: a review, *Journal of Biological Dynamics*, 14:1, 57-89, DOI: [10.1080/17513758.2020.1720322](https://doi.org/10.1080/17513758.2020.1720322)

To link to this article: <https://doi.org/10.1080/17513758.2020.1720322>



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Published online: 29 Jan 2020.



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## Game theoretic modelling of infectious disease dynamics and intervention methods: a review

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### ABSTRACT

We review research studies which use game theory to model the decision-making of individuals during an epidemic, attempting to classify the literature and identify the emerging trends in this field. The literature is classified based on (i) type of population modelling (classical or network-based), (ii) frequency of the game (non-repeated or repeated), and (iii) type of strategy adoption (self-learning or imitation). The choice of model is shown to depend on many factors such as the immunity to the disease, the strength of immunity conferred by the vaccine, the size of population and the level of mixing therein. We highlight that while early studies used classical compartmental modelling with self-learning games, in recent years, there is a substantial growth of network-based modelling with imitation games. The review indicates that game theory continues to be an effective tool to model decision-making by individuals with respect to intervention (vaccination or social distancing).

### ARTICLE HISTORY

Received 3 December 2018

Accepted 15 January 2020

### KEYWORDS

Game theory; epidemic modelling; networks

### 2010 MATHEMATICS SUBJECT

### CLASSIFICATIONS

91A40; 91A80; 92D30; 92D25

## 1. Introduction

Computational epidemiology offers a diverse set of tools for modelling the spread of diseases and the effectiveness of various public health interventions, such as vaccination and social distancing. In general, individuals in the population groups affected by epidemics decide independently whether or not to follow an intervention policy, and in order to estimate the effects of these individual decisions on the overall epidemic spread, this decision-making is often represented as a separate component of a model. In large populations of interacting individuals, the interaction time, number of contacts, nature of interactions, etc. vary significantly, and this diversity is typically modelled with complex networks, aimed to accurately capture the nuances of the interaction patterns. For large-scale epidemics, however, the number of individuals in the modelled population can

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easily reach millions, demanding high computational efforts and lengthy simulation time [17, 25, 33, 45, 75].

The scale and diversity of interaction patterns call for innovative modelling methodologies that can successfully and coherently accommodate three key elements: infectious disease dynamics, interaction patterns, and the decision-making of individuals. Game theory emerged as a leading methodology to model the decision-making of individuals who face a number of intervention options, such as vaccination and social distancing. However, there is a lack of comprehensive reviews summarizing the state of the art in game-theoretic modelling of epidemic dynamics and interventions. This motivates our attempt to review, classify, and identify the current trends in this research field.

## 2. Methods

A three step process was used for selecting papers of interest, confirming to the ‘Preferred Reporting Items for Systematic Reviews and Meta-Analyses’ (PRISMA) [42] checklist. At the first step, keywords were used in Scopus to conduct the preliminary search. We focused on contemporary publications after 2000s. The keywords or keyword groupings used are:

- (epidemi\* OR disease\* OR infect\* OR outbreak OR endemic) AND (model\* OR simu\* OR dynamics)
- (game OR behavio\* OR strateg\* OR deci\*) AND (vaccin\* OR social OR preven\*)
- (networks OR node OR contact OR spatial)

The second step, the screening process, used the following criteria to narrow down the volume of papers by scanning through titles and abstracts, leaving only those of high relevance for closer inspection.

- *Model*: records should contain a mathematical model that captures the epidemic dynamics, and the behaviour change induced after some decision-making. For simplicity, agent-based models (e.g. [1, 63]) in computer science literature are not included.
- *Infectious disease*: the modelled disease is treatable and able to spread in the population from person to person through direct contact in any form. Diseases that are non-treatable (e.g. AIDS [16]) are not included.
- *Preventive measure*: the change in human behaviour is restricted to taking up a preventive measure that may influence the aggregate epidemic dynamics, including vaccination, social distancing, and/or others. However, the decision is purely voluntary and individuals have the freedom to choose something else (i.e. not taking up any preventive measure).
- *Human behaviour*: only individual human behaviour is of interest, and therefore studies of behaviours by institutions (e.g. government) and/or other life forms (e.g. animals, plants) were removed.
- *Mechanism of evaluating utilities*: the decision-making process is modelled under a game-theoretical framework by evaluating utilities of different strategies while assuming that the vast majority of the population consists of rational decision-makers.

- *Static network*: for simplicity, only static networks are considered with the focus on single-layer networks. Adaptive and time varying networks, as seen in [31], are not included.
- *English language*: only records written in English were reviewed.

The third step involved reviewing full texts of the filtered articles to confirm their eligibility for inclusion in this review, and categorizing them.

A flow chart (Figure A1) in Appendix 1 shows the process in more detail.

For categorization, we mainly considered two perspectives: categorization in terms of modelling structure, and categorization in terms of types of health strategies considered on intervention decision-making. The first perspective, *modelling structure*, can be elaborated as follows:

- *Type of models*: literature is categorized as classical models or network models. Classic models here are defined as compartmental models that consider the evolution of total population where average traits of various well-mixed population are considered (Section 3.1.1). Network models model each individual separately and the topology of their interactions is explicitly considered (Section 3.1.2).
- *Development of models*: literature is further categorized as deterministic or stochastic. Deterministic models are often governed by a set of differential equations (Sections 3.1.1.1 and 3.1.2.1), whereas stochastic models break the health status to finer discrete state spaces computed in discrete or continuous time (Sections 3.1.1.2 and 3.1.2.2).

Similarly, the second perspective, *types of health strategies considered on intervention decision-making*, is a multi-dimensional category that encompasses frequency of the game, mechanism of evaluating utilities, and strategy adoption:

- *Frequency of the game*: whether the game is non-repeated (i.e. played for once only) or repeated within a given epidemic season (Section 3.2).
- *Mechanism of evaluating utilities*: the coupling mechanism between the epidemic model and the game theoretic model may involve self-learning for each individual player, based on induction by knowledge and past experience (Section 3.2.1), or imitating other (relatively successful) players (Section 3.2.2).
- *Strategy adoption*: imitation-based coupling can be based on sampling and imitating the population (Section 3.2.2.1), or sampling individual neighbours (Section 3.2.2.2).

Further contexts for classification are possible: for example, based on a distinction between the intervention methods employed by players (either voluntary vaccination or social distancing). However, in the majority of reviewed studies, vaccination was used as the intervention mechanism, and so we did not use this context for categorization (refer to Appendix 2 for more details). Similarly, it is also possible to classify papers based on the pay-off construction methods (i.e. how the pay-off is defined: in terms of monetary value, risk assessment, years to live etc.). Adding this classification, however, would have made the categorization too convoluted (refer to Section A.2 in Appendix 2 for more details).



Strategy Adoption	Self-learning	Bauch, C.T., et al, 2003 [9]	Reluga, T.C. and Li, J., 2013 [62] Reluga, T.C., 2010 [60] Reluga, T.C., 2009 [59]
		Bauch, C.T. and Earn, D. J. D., 2004[8]	
Imitation	Non-repeated	Galvani, A.P. and et al., 2007 [32]	
		Bhattacharyya, S. and et al.,2019 [12]	
		Perisic, A. and Bauch, C.T., 2009 [52]	
		Perisic, A. and Bauch, C.T., 2009 [53]	
		Breban, R., 2011 [14]	
		Vardavas, R. and et al., 2007 [69]	
		Breban, R. and et al., 2006 [15]	
		Zhang, H. and et al.,2010 [77]	
		Eksin, C. and et al., [23]	
		Reluga, T.C. and Galvani, A. P., 2011 [61]	
		Liu, J. and et al., 2012 [43]	
		d'Onofrio, A. and et al., 2007[21]	
Network	Repeated	Feng, X. and et al., 2018 [26]	Reluga, T. et al.,2006 [58] Poletti, P. and et al., 2012 [56] Poletti, P. and et al., 2009 [57] Bauch, C. T. and Bhattacharyya, S., 2012 [7] Poletti, P. and et al., 2011 [55]
		Bauch, C. T., 2005 [6]	
		d'Onofrio, A. and et al., 2011 [20]	
		Bhattacharyya, S. and Bauch, C. T., 2011 [11]	
		Bhattacharyya, S. and Bauch, C. T., 2010[10]	
		Fu, F. and et al., 2010 [29]	
		Zhang, H. and et al., 2012 [76]	Sample Population Sample Neighbours
		Liu, X. and et al., 2012 [44]	
		Zhang, Y., 2013[78]	
		Fukuda, E., 2015 [30]	
		Cornforth, D. M. and et al., 2011 [19]	
		Li, Q. and et al.,2017 [41]	
Classical	Deterministic	Ndeffo Mbah, M.L. and et al., 2012 [47]	Bauch, C.T. and Earn, D. J. D., 2004 [8] Vardavas, R. and et al., 2007 [69] Bauch, C. T., 2005 [6] Poletti, P. and et al., 2011[55] Bhattacharyya, S. and Bauch, C. T., 2010[10] Liu, J. and et al., 2012 [43]
		Wells, C. R. and et al.,2011 [73]	
		Reluga, T.C., 2010[60]	
		Reluga, T.C. and Li, J., 2013[62]	
		Feng, X. and et al., 2018 [26]	
		Reluga, T. et al.,2006 [58]	
		Galvani, A.P. and et al., 2007[32]	Bauch, C.T. and Bhattacharyya, S., 2012 [7] d'Onofrio, A. and et al., 2007[21] Reluga, T.C., 2009 [59] Reluga, T.C. and Galvani, A. P., 2011 [61]
		Reluga, T.C., 2010[60]	
		Reluga, T.C. and Li, J., 2013[62]	
		Li, Q. and et al.,2017 [41]	
		Cornforth, D. M. and et al., 2011 [19]	
		Wells, C. R. and et al.,2011 [73]	
Stochastic	Stochastic	Perisic, A. and Bauch, C.T., 2009 [52]	Fukuda, E., 2015[30] Zhang, H. and et al.,2010 [77] Ndeffo Mbah, M.L. and et al., 2012 [47] Liu, X. and et al., 2012 [44] Zhang, Y., 2013[78] Perisic, A. and Bauch, C.T., 2009 [53]
		Zhang, H. and et al., 2012 [76]	
		Fu, F. and et al., 2010 [29]	
		Eksin, C. and et al., [23]	
		Bhattacharyya, S. and et al.,2019 [12]	

(a) Classification of literature based on game modelling

(b) Classification of literature based on population modelling

**Figure 1.** Taxonomy of present literature in epidemic modelling with game theoretic decision-making.

## 2.1. Taxonomy

The synthesis of game theory and epidemic modelling has evolved over the past decade. Starting from classical, deterministic models combined with non-repeated, population games where the players assess their pay-off using self-learning only, some recent studies have shifted to individual-based, repeated games carried out by players distributed on a heterogeneous topology and assessing their pay-off using imitation. The emergence of network models reflects a desire to mimic more realistic human behaviour, moving from the assumption of well-mixed population to populations modelled as networks with heterogeneous topology. The game theoretic modelling of decision-making focuses primarily on prevention measures, notably vaccination and behavioural changes. We argue that three criteria can be used to succinctly classify the existing literature:

- Modelling structure
- Frequency of the game
- Type of strategy adoption

Figure 1(a,b) shows that the investigations of vaccination decisions using different epidemic models and game settings have attracted considerable research interest. While earlier studies with classical models and self-learning games retained their prominence, some recent studies have focused on imitation games, especially when incorporated with individual-based models which typically allow modelling with heterogeneous topology (contact network-based modelling).

‘Modelling structure’ contrasts the classical, population based (typically compartmental) [6–9, 11, 14, 20, 43, 66] and the individual network-based [23, 29, 44, 47, 76, 77] modelling approaches. To re-iterate, classical, population-based modelling refers to the modelling method where the population is well-mixed. Thus, classical, compartmental models such as SIS and SIR are sufficient for this modelling approach although finer compartments can be used to capture properties of individuals such as their age [43]. On the other hand, in network-based models, the population can be heterogeneous in terms of their attributes, and such attributes are explicitly used in modelling the contact between individuals and the spread of disease [19, 23, 29, 30, 44, 47, 52, 53, 76, 77].

Studies which employ classical models can be further classified into those which use deterministic modelling [6–9, 11, 14, 20, 43, 55–57, 66] and those that use stochastic modelling [2, 13, 59–62].

‘Frequency of the game’ distinguishes between non-repeated or repeated games. When the decision-making is done only once during the epidemic spreading [6, 10, 11, 20] or seasonally within a particular ‘window of opportunity’, non-repeated games are used [26, 29, 69, 76, 77]. On the other hand, when the decision-making is a continuous process, and strategies can be dynamically changed during the spread of the epidemic, repeated games are used [7, 55–57].

‘Type of strategy adoption’ separates models by considering whether individual players use social learning to update their strategies. As noted earlier, self-learning is used when a player makes decision based on one or multiple of the following criteria: has perfect information of epidemic prevalence and other individual’s behaviour [8, 9], considers their past strategies and pay-offs in deciding the future strategies [14, 15, 69], or evaluates

their pay-off based on the current prevalence [12, 23, 52, 53]. Imitation is employed when a player adopts the strategies of other successful players. Imitation can occur either at a global level, where a player considers all other members of the population and imitates the strategies of the players with better pay-off [6, 7, 10, 20, 26, 55–58], or at a local level where a player imitates one of their (successful) neighbours [29, 30, 44, 47, 76, 77].

In the lower left quadrant of Figure 1(a), along with the upper half of Figure 1(b), a large set of studies use imitation, repeated and non-repeated population games, employing the deterministic classical modelling. The inclusion of imitation dynamics introduces social influences on individuals, in contrast to self-centred, non-communicating individuals. The implementation of imitation dynamics also allows for an adjusted time scale for information spread, so that the imitation process can take place at a faster or slower rate than the epidemic spread [55–57].

In network-based studies, clustered in the lower half of Figure 1(b), the incorporation of contact networks is a more realistic representation of the social influences exerted on individuals, particularly with respect to behavioural change. This is because social actions take place within social locales defined by geographical, social, cultural and psychological factors, which can be represented by possible network links [50]. The implementation of network-based imitation is typically applied in voluntary vaccination for recurring epidemics (e.g. influenza). Many models in this area use Gillespie algorithm [34] to compute epidemic spread, and use varying contact networks to study the interrelations between the epidemic quantifiers (vaccination coverage, infection prevalence, etc.) and the vaccination cost [29, 30, 44, 76].

Further refinements are added in later models to investigate the interplay between social influence (i.e. imitation) and self-learning with respect to vaccination costs. At the population level, this involves committed vaccinators in the population [44], and, at the individual level, the memory-fading mechanism and risk evaluation [76]. In addition, a fitness factor may be considered to govern the likelihood of imitation, on top of the imitating behaviour in the network. The attempt to increase the vaccination coverage is made by modelling or simulating committed vaccinators, who would choose to vaccinate regardless of pay-offs, and would act as ‘role models’ for their neighbours. If one is surrounded by vaccinators in the network, s/he is more likely to mimic the vaccination behaviour, contributing to vaccination coverage. The existence of committed vaccinators reduces the clustering of susceptible persons, ultimately extending the vaccination coverage. This observation is significant in a well-mixed contact network (well-mixed in terms of topology, not in terms of behaviour), where behavioural clusters are common: the committed vaccinators act as a strategy source and affect decision-making of their neighbours [44].

Another branch of research combines imitation dynamic with individual experience, considering together the social influence from imitation and the self-centred evaluations resulting from memory fading and risk perception. For example, [78] shows that imitation encourages vaccination behaviour at a low vaccination cost, while the self-centred individuals are more likely to opt for vaccination if the vaccination cost is high. This conclusion is demonstrated to hold for random and scale-free networks. The incorporation of a memory-based mechanism indicated that the memory is very sensitive to vaccination cost. With low vaccination costs, the increase in memory promotes vaccination coverage; whereas when the vaccination cost is high, the increase in memory hinders vaccination coverage.



Another point to note is that among the studies which directly use contact networks, one category of studies adopts different networks to model (i) epidemic spread and (ii) individual contacts [19], while others use the same network to model both epidemic transmission and contact patterns [12, 23, 52, 53, 77]. For example, [19] simulates epidemic spread on infinitely large random graphs where a connected pair of nodes bears a probability of transmission if one is infected. The dynamics of the vaccination game, in comparison, are built on individual's contact patterns across different networks: empirical networks in urban settings or homogeneous networks and scale-free networks as model networks. Here, an individual's decision is finalized prior to the epidemic season (i.e. non-repeated) and remains a self-centred evaluation with some input from the topology of the network as the pay-off assessment is dependent on the individual's degree  $k$ .

Among the works which use the same network to model epidemic transmissions and contact patterns, the studies [12, 47, 52, 53, 77] employ a network to describe both the vaccination decision dynamics and the transmissibility (i.e. probability of infection) through a node. For a node, the magnitude of transmissibility is proportional to the number of infectious neighbours and is updated daily. The transmissibility is then used to compute the pay-offs for vaccination and non-vaccination. Thus, an individual assesses his/her pay-off by referring to the number of infected neighbours (i.e. this depends on the topology of network), but the decision-making solely relies on his/her own evaluation and is not directly affected by the neighbour's decision. Each individual's decision on vaccination contributes to the transmissibility function, as a vaccinated individual is removed from the susceptible class and will not be infected. This iterative feature bears a significant resemblance to what has been seen in the synthesis between imitation dynamics and deterministic models [6], with different levels of social influence involved between self-learning and imitation.

## **2.2. Game theory**

Game theory is used to model scenarios where there are a number of intelligent entities, called 'players', which try to make decisions in the face of uncertainty. The players could represent individuals, groups of people, organizations, or computer programs. Each 'player' typically tries to optimize their own profit or benefit, called 'pay-off' or 'utility' of a player. To do so, each player will take a course of action among available actions, termed 'strategies'. Typically, the selection of the best course of action for one player will depend on what the other player or players will decide to do [67, 72].

### **2.2.1. Nash equilibrium**

Nash equilibrium is one of the pivotal concepts in game theory [46], describing a strategic decision-making environment, in which there exists a set of strategies from which no perfectly rational player would benefit by deviating, with rationality defined as the tendency to maximize one's own utility. Nash equilibrium is defined for both pure and mixed strategies [46]. A pure strategy is a strategy that is consistently adopted by a player during a repeated game (until a conscious decision is made by that player to switch to another pure strategy). If a mixed strategy is adopted, each pure strategy available to a player is selected according to a premeditated probability distribution which defines the mixed strategy. Therefore, pure strategies can be thought of as special cases of mixed strategies, where

each available strategy is selected with a probability of either 1 or 0 at each round of the iterated game.

### **2.2.2. Rationality**

Recent studies have adopted a more realistic scenario by including irrationality to mimic those individuals whose decisions are not made completely rationally [56, 57]. Here a lack of rationality could mean either making decisions for the ‘public good’ (or letting the ‘public good’ influence their decisions), or, while being totally selfish, arriving at decisions which are not at the best interest of the individual concerned, due to some reason. Some literature [56, 57] included the term  $\tilde{\mu}$  (at a rate  $\tilde{\mu} \ll 1$ ) as a ‘rationality parameter’ to describe players who randomly switch between strategies or who rarely change regardless of the pay-off balance. This irrationality is modelled as  $\tilde{\mu}(1 - x)$  and  $\tilde{\mu}x$  where  $x$  is the fraction of the population that adopts a certain strategy.

### **2.2.3. Bounded rationality**

It has been observed that in experimental settings, players deviate substantially from the predictions given by Nash equilibrium [37]. One key reason for this deviation is the non-perfect, or bounded rationality of the players, due to possible lack of information available about the strategies adopted by the opponents and their respective pay-offs, limitations in cognitive capacity of the players or the limitation of computational time available to make the strategic decision [37, 38]. Advanced equilibrium models, such as the ‘Quantal Response Equilibrium (QRE)’ have been proposed [35] to arrive at equilibrium solutions accounting for bounded rationality of players.

## **2.3. Epidemic-dependent pay-off calculation**

To reach a decision, individuals either try achieving utility maximization or comparing the pay-offs of two strategies. The decision-making process is modelled in two ways: (a) Self-learning, or (b) Imitation. There is a clear conceptual difference between the two mechanisms: through self-learning, individuals rely on their knowledge, memory and personal perception and awareness of the disease, while imitation dynamics puts individuals into an environment where personal decisions are influenced by the choices of the population, or their neighbours, where the neighbours are determined by the topology of the contact network. Either way, individuals assess their risk of infection before reaching to a decision; therefore, the function of pay-offs is often expressed using epidemic-dependent parameters. Information about the current disease prevalence can be relatively accurate and objective, assuming such information is timely and obtained from reliable sources, such as news published on trustworthy media channels or directly obtained from public health authorities [31]. Many different methods of pay-off construction present in current literature (see Section A.2 in Appendix 2 for more information). One of the widely used techniques is to construct pay-offs using timely epidemic prevalence information to assess infection risks. Equation (1) shows an example in a social distancing game where the two strategies from which individuals can choose are to adopt altered behaviour (i.e. taking protective measures),  $s_{alt}$ , or live normally without any change,  $s_{nor}$ . By altering behaviour, it is assumed that one would stay away from highly infectious hotspots (e.g. highly populated

areas) and consequently reduce the risk of infection [57].

$$\begin{aligned} E_{nor} &= -m_{nor}I(\tau) \\ E_{alt} &= -k - m_{alt}I(\tau) \end{aligned} \quad (1)$$

where  $m_{nor}$  and  $m_{alt}$  are parameters that show the risk of symptoms development induced by strategies  $s_{nor}$  and  $s_{alt}$ , and  $m_{nor} > m_{alt}$ .

In cases where vaccines are assumed to be perfect and risk-free, individuals turn to evaluate the benefit and past experience of vaccination, as seen in models incorporating inductive games [14, 15, 69]. In cases where vaccines are not perceived as risk-free, many recent models claim that accurate information on current disease prevalence may not be readily available and/or accessible to all individuals due to information delay or limited sources of information [10, 14]. An example would be information obtained by word of mouth within an enclosed community or neighbourhood. The resulting disease prevalence, known as the perceived disease prevalence, may not necessarily be a true reflection of actual disease prevalence and can be highly subjective [76]. Some models purposely calibrate true disease prevalence to a perceived case to mimic the inaccuracy of information encountered in reality. Equation (2) shows an example of pay-off functions considering perceived disease prevalence. Pay-offs are expressed in expected lifespan (number of years of life) after infection [52].

$$\begin{aligned} E_{inf} &= (1 - \lambda_{perc})\alpha + \lambda_{perc}[(1 - d_{inf})L] \\ E_{vac} &= (1 - d_{vac})L \\ \lambda_{perc} &\approx \lambda \end{aligned} \quad (2)$$

where  $\lambda_{perc}$  is the perceived transmissibility, obtained from the epidemic model,  $d_{inf}$  and  $d_{vac}$  are deaths from infection and vaccination, respectively,  $L$  represents 'healthy' years of life with lifelong immunity and  $\alpha$  is years to live with continued susceptibility.

### 3. Results

#### 3.1. Modelling structure

We begin with generic reflections on the existing literature, followed by a detailed analysis and classification.

##### 3.1.1. Classical models

The standard epidemic theory is developed on the concept of compartmentalization which divides the population into several compartments based on their health status [39]. Epidemic dynamics are captured by tracking how individuals move across these compartments and only the evolution of total number of individuals in each state is considered. A commonly used compartmentalization approach is known as 'S (susceptible), I (infected), R (recovered)' or SIR [13]. Initially, the individuals are marked as susceptible to infection. When a disease breaks out, the susceptible individuals encounter those who are infected and are moved to the infected compartment at some rate. The infected individuals are eventually removed when they recover (with or without immunity). Here, we refer to these

models as ‘classical models’ [48]. This basic framework of compartmentalization on population level is widely used by a large number of models with many extensions (e.g. dividing the population into finer compartments) by incorporating age [43, 65], gender [65], vaccination status [9], etc. However, classical models are based on a simplifying assumption that individuals are placed in a well-mixed population (i.e. individuals interact with each other at the same contact rate). In reality, the number of contacts each individual has varies from one to another and is likely to be considerably smaller than the size of population [39, 70].

There are two common modelling approaches in classical models: deterministic modelling and stochastic modelling.

**3.1.1.1. Deterministic modelling.** In deterministic models, the epidemic spread is governed by a set of differential equations. For example, a deterministic SIR model variant [3, 13, 39] is shown as:

$$\begin{aligned}\frac{dS}{dt} &= -\beta SI \\ \frac{dI}{dt} &= \beta SI - \gamma I \\ \frac{dR}{dt} &= \gamma I\end{aligned}\tag{3}$$

where  $S$ ,  $I$ ,  $R$  are number of susceptible, infected and recovered population,  $\beta$  is the transmission rate of the disease,  $\gamma$  is the recovery rate.

**3.1.1.2. Stochastic modelling.** While deterministic classical models formulate population transfer between health status using rates, stochastic classical models use transitional probabilities to model epidemic process. The use of probabilities incorporated randomness in modelling; and so deterministic models can be seen as an approximation of stochastic models [2]. An example of the stochastic modelling processes is a continuous time Markov chain (CTMC) [2] used in [59, 60, 62], for which the changes in an individual’s health state are described by a continuous-time Markov process:

$$\frac{dp}{dt} = Qp\tag{4}$$

where  $p(t)$  is the transitional probability that an individual occupies any state at time  $t$ , and  $Q$  is the transition-rate matrix. The definition of  $Q$  depends on the formulated epidemic models (e.g. SIR and SIS). For an SIR model shown in Equation (3),  $Q$  can be expressed as:

$$Q = \begin{bmatrix} -\beta I & 0 & 0 \\ \beta I & -\gamma & 0 \\ 0 & \gamma & 0 \end{bmatrix}\tag{5}$$

where  $I(t)$  represents the number of infected individuals at  $t$ . The transition-rate matrix  $Q$  is also used to construct utility and/or pay-off in repeated games. Refer to Section 3.2.1.2 to see how it is incorporated in repeated, social distancing games.

### 3.1.2. Network-based models

Classical models (both deterministic and stochastic models) assume well-mixed population, thus, the number of contacts is assumed to be equal for all individuals at a given disease stage. In reality, however, the number of contacts per individual varies across the population. One common approach to mimicking the varying number of contacts in the real world is to model the population as a network with either homogeneous topology, e.g. Erdős-Rényi random networks [22], heterogeneous topology, e.g. scale-free networks [4], small-world networks [71], or other empirically derived topologies [18, 49], reflecting inherent differences in social systems [39, 51]. During an epidemic, the relative importance of a network node may vary over time as well, and several centrality measures have been developed to capture these dynamics [49, 54].

In a contact network, a node can represent an individual [23, 29, 30, 44, 52, 53, 76–78] or a larger subpopulation seen in deterministic models [41]. The contacts with other nodes are represented by edges. It is generally assumed that the probability of transmissibility through a node is dependant on the number of edges (i.e. the node's degree).

Networks can remain *static* during an epidemic, implying that the network degree distribution is unchanging during the contagion. This is only possible when the epidemic spread is much faster compared to the evolution of contacts among the affected individuals. On the other hand, networks can continue growing at a rate which is comparable with the rate of epidemic spread – that is, they can be dynamic (i.e. time varying) [70]. Although time varying networks have attracted considerable research interest [31], for simplicity, this review focuses on static, undirected, and unweighted networks only.

**3.1.2.1. Deterministic modelling.** Deterministic network models can be seen as multi-group meta-population models in which population is grouped by network-dependent criteria, such as the number of edges [19, 41]. Often, there is a multitude of subcompartments per health compartment, each governed by a differential equation and population within the same sub-compartment is assumed to be well-mixed, similar to deterministic classical models seen in Section 3.1.1.1. Such models have also been used to model meta-population dynamics with population mobility. In this case, each node represents a city and the edge represents possible travels [48].

**3.1.2.2. Stochastic modelling.** Many stochastic models [29, 30, 44, 76] use Gillespie algorithm [34] to simulate epidemiological process. As a variant of a dynamic Monte Carlo method, Gillespie algorithm is an efficient algorithm that accounts for non-Markovian properties (See [29] for detailed procedures). An alternative in stochastic network models is to use a continuous-time networked Markov process, as seen in [23]. See [48] for detailed description of networked Markov processes.

## 3.2. Types of health strategies considered in intervention decision-making

In this review, only two-player games are included but a ‘player’ can be interpreted as an individual or as a fraction of the population. The game can be non-repeated or repeated game based on the game frequency. This section describes how non-repeated and repeated games are constructed in relation to different types of epidemic models.

To investigate the coupling between the epidemic model and the game, it is essential to ascertain when and how the game is played in the model:

- Non-repeated games: these are stand-alone games that are only played once, possibly during a fixed window of time [6, 8–11, 15, 20, 29, 44, 52, 69, 76–78]
- Repeated games: games that are played repeatedly within the simulation of the epidemic model [7, 55–57, 59, 60, 62]

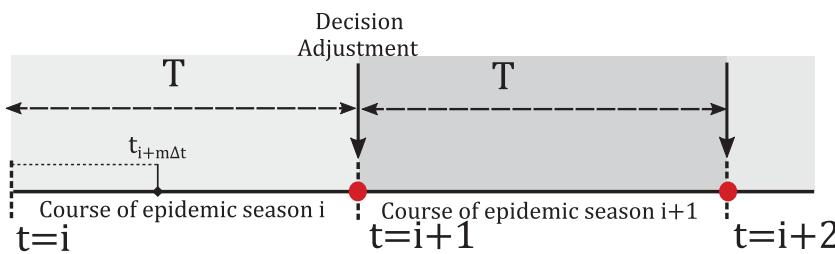
Non-repeated games are used when the game is played once only (e.g. vaccination game with lifelong immunity), or when there is a short, fixed window of opportunity to play the game. For example, vaccination is only available at a specific time per infection season (such as influenza vaccination). In these cases, vaccination games are played once per epidemic season either prior to a forthcoming breakout [15, 29, 44, 69, 76, 78], or during the epidemic [6, 8–11, 20, 52, 77]. In the first case, the games are independent of the epidemic transmission during epidemic propagation and individuals rely on information from last epidemic season and past vaccination experience to form decisions. In the second case, although vaccination games are only played once per person, there is a flexible window of opportunity for individuals to choose when to vaccinate as the epidemic progresses, not necessarily restraining the game at a particular time as seen in the first case. In both cases, however, games are treated as non-repeated although they could be played more than once within a person's lifespan (i.e. once every epidemic season).

Repeated games, on the other hand, are played repeatedly during the epidemic simulation. Individuals are given the option to play the game at any time during the course of an epidemic season and their strategies vary over time as the epidemic progresses. This is normally the scenarios where the decision to be made is whether to take prophylactic measures or not. Such a decision, clearly, is reversible as one can easily change from adopting self-protection to living in a normal lifestyle, or vice versa. Therefore, the strategy can change for every iteration and results in a more intricate linkage between the games and the epidemic model since the input (i.e. risk pay-offs) to initiate the games relies on the output from the epidemic model, while the input to the epidemic model itself depends on the decisions players make [7, 55–57, 59, 60, 62].

Earlier studies [8, 9] used non-repeated games with a deterministic SIR epidemic model to derive analytical solutions in population. In more recent studies, non-repeated games have been extended to simulation-driven and network-based applications through the use of stochastic network models [29, 44, 76, 78]. In the case of seasonal epidemics, there is an imaginary window of time between epidemic season  $i$  and  $i + 1$  during which individuals can change their strategy, which is known as 'decision adjustment'.

Figure 2 highlights the difference between non-repeated and repeated games used in intervention modelling. In a particular epidemic season  $i$ , which has a length of  $T$ , the spread of infection starts from time  $t = i$  and simulated with time-steps with size  $\Delta t$  until it reaches  $t = i + 1$ . Repeated games are typically played at each of the  $m$  time steps, where  $m = T/\Delta t$  over the course of epidemic season  $i$ . Non-repeated vaccination games can be played in two ways:

- (1) during the window of time between epidemic season  $i$  and  $i + 1$  (which, in reality, may be several months) during which individuals can change their strategy (the vaccine



**Figure 2.** Non-repeated and repeated games in intervention modelling. Non-repeated games are played either prior to the commencement of an epidemic season or between different epidemic seasons. Repeated games are played several times during a single epidemic season and played with a certain time interval  $\Delta t$  over the length of a particular season  $i$ , and end when that epidemic season  $i$  comes to an end. Therefore, the term 'repeated' is used in the context of a particular season, rather than the whole lifetime of an individual.

concerned should be administered within a certain ‘window of opportunity’, either once in a lifetime or between seasons, and not during the epidemic propagation);

- (2) at each of the  $m$  time steps although the player may not be able to switch strategy at every iteration, because vaccines typically provide protection over a certain period of time, and the length of protection relies solely on the strength of the vaccine, and may be greater than  $\Delta t$ .

For re-occurring diseases such as influenza, vaccines normally last until the end of the epidemic season  $i$  and wear off before the next wave of epidemic at season  $i+1$ . Therefore, a player who plays the vaccination game within the season means s/he is able to vaccinate any time within the season, but cannot undo the decision to vaccinate within that particular season. Hence, in certain vaccination games [6, 10, 11, 20], one strategy (not to vaccinate) is reversible, whereas the other strategy (to vaccinate) is not reversible. Individuals then face the same decision – whether to vaccinate or not – in epidemic season  $i+1$ . Some vaccines, however – typically those for childhood disease – provide lifelong protection so there is no need for re-vaccination for vaccinated individuals. In such cases, there will be no ‘season’ involved, and one strategy (to vaccinate) is irreversible lifelong although unvaccinated individuals can choose to vaccinate any time within the season. If no restraint is imposed on the timing of vaccination, individuals refer to the current disease prevalence to decide whether they need to vaccinate.

### 3.2.1. Self-learning

The early epidemic models that incorporated games [8, 9, 69] considered human responses through individual awareness and knowledge without social learning, whereby non-communicating and self-centred individuals make decisions purely by themselves after evaluating pay-offs from the two strategies. Players are often assumed to have the perfect information about the current disease prevalence and other player’s actions [8, 9] or to make decision based on their memories of previous events [15, 69]. Self-learning was used extensively in earlier studies [8, 9, 69] because of its simplicity but did not capture the influence of human interaction and imitation behaviours. Nevertheless, these induction-based

self-learning games provides a foundation for game-theoretic frameworks used in more recent studies.

**3.2.1.1. Non-repeated games.** Early studies [8, 9] incorporated game theory into epidemic modelling through non-repeated games at the population level in which each individual in the population weighs the costs and benefits of two strategies, aiming to maximize individual gain. Voluntary vaccination is the most widely studied concept [8, 9, 32, 61], where the dilemma faced by a player focuses on risks and benefits associated with a defined vaccine. Commonly coupled with a classical deterministic model, such games take some parameters of pay-off functions from the epidemic model, for example, the infected fraction of the population. After evaluating the risks of different strategies, individuals make decisions on voluntary vaccination, which can be fed back to the epidemic model as an input updating the vaccination coverage (i.e. the fraction of the vaccinated population). This method has been applied to studies investigating the optimal level of voluntary vaccination coverage for childhood diseases and vaccine scare [8], vaccination policy for smallpox in preparation for a possible outbreak [9], H1N1 vaccination strategies [64], influenza vaccination [32].

An example of the non-repeated population game in relation to voluntary vaccination [8] involves a scenario in which each individual in the population of size  $N$  decides on the vaccination strategy  $S$ , represented by the probability of vaccination. The proportion of the vaccinated population is represented by  $p$ . The pay-off evaluation is denoted by morbidity risk  $r$ ; a relative parameter defined as the ratio between the morbidity risks from vaccination and infection as  $r = r_v/r_i$ . The risk of infection at a defined vaccination coverage with vaccination fraction  $\theta$ , is denoted as  $\pi_\theta$ . The expected pay-off of an individual playing strategy  $S$  is then given as follows:

$$E(p, \theta) = -rS - \pi_\theta(1 - S) \quad (6)$$

The aim is to obtain the optimal vaccination strategy  $S^*$ , known as the *Nash equilibrium*, so that no player can improve his or her pay-off by changing to a different strategy. Since the population is homogeneous in terms of contact patterns in population games, the optimal vaccination coverage for the population is equal to the probability of vaccination for each individual,  $\theta^* = P^*$ . The risk of infection  $\pi$  is derived from the epidemic model and the value reduces with greater  $\theta$ . One important parameter that affects  $\theta$  is the basic reproduction number,  $R_0$ , i.e. the number of secondary infections produced on average by an infected index case within a susceptible population. Notably,  $R_0$  can also set an epidemic threshold, or interval in finite-size networks [24, 36], above which an epidemic will spread (i.e.  $R_0 > 1$ , also see discussion in Section 3.3). If  $\theta$  exceeds the threshold for herd immunity  $\theta' = 1/R_0$ ,  $\pi_{\theta \geq \theta'} = 0$ , the risk of infection becomes zero and the disease is naturally eradicated. To obtain the Nash equilibrium,  $S^*$ , the pay-off gain to an individual playing  $S$  in the population is expressed as [8]:

$$\Delta E = (\pi_{(N-1)S^*+S} - r)(S - S^*) \quad (7)$$

A unique strategy  $S = S^*$  exists for any given relative risk,  $r$ , and  $\Delta E$  is strictly positive. There are two pure Nash equilibria  $S^* = 0$  or  $1$ , and a mixed equilibrium  $0 < S^* < 1$  [8]. The condition to achieve these equilibria is affected by  $r$  and  $\pi$ . When the vaccine is perceived as more risky than infection  $r \geq \pi_0$ , the Nash equilibrium strategy is never

to vaccinate. If  $r < \pi_0$ , the Nash equilibrium is to vaccinate with non-zero strategy  $S^*$  at vaccination coverage  $\theta^* \in (0, \theta')$  such that  $\pi_{\theta^*} = r$ . Therefore, the mixed Nash equilibrium  $S^*$  yields a suboptimal vaccination coverage  $\theta^* > \theta'$  [8]. The analytical method is an implicit application of Markov decision process theory in closed form.

Non-communicating individuals often act in their own self-interest and do not share their decision with others [15, 69]. The independent decisions may be made between epidemic seasons (i.e. remain static during a season), as shown in Figure 2. The decision-making process relies on one's experience from the last epidemic season, with an assigned value  $V_n^i$  and two independent parameters, memory  $s$  and adaptability  $\varepsilon$ . Taking vaccination games as an example [69], the probability  $\omega_{n+1}^i$  that an individual  $i$  chooses to vaccinate is given in Equation (8):

$$\omega_{n+1}^i = (1 - \varepsilon)\omega_n^i + \frac{\varepsilon V_{n+1}^i}{(s^{n+1} - 1)/(s - 1)} \quad (8)$$

with  $0 < \varepsilon < 1$  and  $V_{n+1}^i = sV_n^i$ . The induction in relation to the possibility of vaccination is coupled to the epidemic model through  $V_n^i$  which is dependent on the vaccination coverage  $p$  and the probability of infection at current vaccination coverage  $q(p)$ . Some studies [9, 64, 66] use an added compartment in the deterministic SIR model representing the 'vaccinated' fraction  $V(t)$  to explicitly track the vaccinated population.

Non-communicating non-repeated games can also be implemented on networks. An individual can play the game at each time step when coupled with a network model in which each individual is seen as a node with contacts as links. In this case, although the health compartmentalization of the population is still used to identify an individual's health status, the population fraction of each health compartment is no longer calculated mathematically. Instead, the epidemic propagation is modelled through a single parameter, the total probability  $\lambda$  that a node becomes infected each day with  $n_{inf}$  infectious neighbours.  $\lambda$ , as the output from the epidemic model, is used to construct pay-offs; consequently, the decision on vaccination affects the number of infected neighbours for a node and the probability of infection. The process is dynamic because it is iterated at each time step (i.e. each day in this case), forming a loop-like feeding pattern [52, 77]. An example is given in Equation (9), taken from [52].

$$\begin{aligned} \lambda_{perc} &= 1 - (1 - \beta_{perc})^{n_{inf}} \\ E_{inf} &= (1 - \lambda_{perc})\alpha + \lambda_{perc}[(1 - d_{inf})L] \\ E_{vac} &= (1 - d_{vac})L \end{aligned} \quad (9)$$

where  $\beta_{perc}$  is the perceived probability of node-to-node transmission,  $E_{inf}$  is the pay-off for non-vaccinators and  $E_{vac}$  is the pay-off for vaccinators;  $\alpha$  is the pay-off for individuals with continued susceptibility,  $L$  is the pay-off for individuals with lifelong immunity,  $d_{inf}$  the probability of death due to infection, and  $d_{vac}$  is the probability of death due to vaccine-related complications.

**3.2.1.2. Repeated games.** Non-communicating individuals can practice social distancing at each point in the epidemic using stochastic model, as seen in [59, 60, 62]. People can

choose to pay a cost related to social distancing to reduce their risk of infection. The payoff from practising social distancing is represented by the expected present value of each state ( $\mathbf{V}$ ), which is defined using transition-rate matrix (also see Section 3.1.1.2) as [60]:

$$-\dot{\mathbf{V}} = (\mathbf{Q}^T - h\mathbb{I})\mathbf{V} + \mathbf{v} \quad (10)$$

where  $\mathbf{Q}^T$  is the transpose of  $\mathbf{Q}$ ,  $\mathbb{I}$  is an identify matrix, and  $h$  is the discount rate.

Assuming  $V_I = -1$  and  $h = 0$ , a reduced SIR model with repeated social distancing game is considered as:

$$\begin{aligned} \frac{dS}{dt} &= -\sigma(\bar{c})IS \\ \frac{dI}{dt} &= -\sigma(\bar{c})IS - I \\ -\frac{dV_S}{dt} &= -(1 + V_S)\sigma(c)I - c \end{aligned} \quad (11)$$

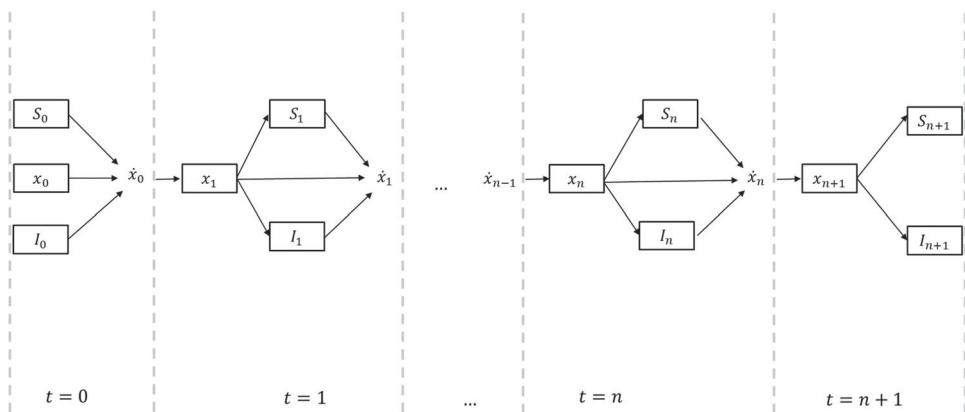
where  $S$  and  $I$  are number of susceptible and infected population in each disease generation,  $V_S$  is the expected present value in susceptible state,  $c$  represents one individual's investment strategy and  $\bar{c}$  represents an aggregated average of all individual investments in the population,  $\sigma(c)$  is a function representing the effectiveness of social distancing.

It is found that social distancing is only adopted until part-way into the epidemic, when prevalence is sufficiently high. Individuals typically would adopt social distancing at the start or end of the epidemic. Social distancing can make a difference in containing epidemic if  $\sigma(c)$  is high (i.e. effective social distancing) and  $R_0$  is above the threshold value of 1. The impact of social distancing, measured by the net saving from social distancing, also has an upper limit when  $R_0$  is around 2, at which each individual saves around 30% of the cost of epidemics.

### 3.2.2. *Imitation*

People learn to adopt new strategies by imitating others who have adopted more successful strategies. This learning process, or imitation dynamics, can take place both at the population or the individual level: an individual encounters others in the population and adopts their strategy if they have received higher pay-offs. What differentiates the two levels is the assumption of a well-mixed population: an adoption process carried out at the population level assumes that each individual has the same chance of meeting the rest of the population, whereas an adoption process at the individual level assumes that the contacts of an individual are limited to his/her neighbours in a defined network.

**3.2.2.1. *Individuals imitate population.*** In a well-mixed population, people are divided into two groups according to their strategies. An individual playing with strategy  $A$  encounters those playing with strategy  $B$  at a constant rate. If there is an expected gain in pay-off by switching from strategy  $A$  to strategy  $B$ , the individual would do so after comparing pay-offs [6, 7, 10, 20].



**Figure 3.** For a population game adopting imitation dynamics in a SIR deterministic model. Here,  $S_0$  and  $I_0$  represent the initial proportions of susceptible and infected people in the whole population respectively. Similarly,  $x_0$  represents the initial fraction of vaccinated people in the population, and  $\dot{x}_0$  represents the rate of change of this fraction at time  $t = 0$ . Similarly,  $S_n, I_n, x_n$  and  $\dot{x}_n$  represent the fraction of susceptible individuals, the fraction of infected individuals, the fraction of vaccinated individuals, and the rate of change of the fraction of vaccinated of individuals, at time  $t = n$  respectively.

Assuming the fraction of the population playing strategy A is  $x$ , the rate of change of  $x$  is defined as:

$$\frac{dx}{dt} = \sigma \Delta E x(1 - x) \quad (12)$$

where  $\Delta E = E(A) - E(B)$ , and  $E(A)$  and  $E(B)$  are the pay-offs for playing strategy A and strategy B respectively, and  $\sigma$  is the sampling rate.

By adopting imitation dynamics at the population level, the rate of change for each compartment in the SIR epidemic model depends on the fraction of the population choosing a certain strategy. The coupling runs according to the following scheme. Given the initial conditions for the number of infected  $I_0$  and the number of susceptible  $S_0$  individuals (from the SIR model), and the fraction of the population  $x$  playing strategy A in the game,  $dx/dt$  is computed, updating the fraction  $x$  after playing the game by comparing the pay-off at each time step. The updated value of  $x$  is used, in turn, to update the size of each compartment in the SIR model. If  $E(A)$  and  $E(B)$  are dependent on the disease prevalence  $\lambda$ ,  $dx/dt$  continue to depend not only to  $x$ , but also  $I_t$  and  $S_t$ . The schematic of this mechanism is shown in Figure 3. The simulation is iterated until the epidemic spread is eradicated or it reaches an endemic state [6, 55–57].

An example of how a non-repeated vaccination game with imitation dynamics sampling the population coupled with a deterministic SIR epidemic model [6] follows this scheme:

$$\begin{aligned} \frac{dS}{dt} &= \mu(1 - x) - \beta SI - \mu S \\ \frac{dI}{dt} &= \beta SI - \gamma I - \mu I \\ \frac{dR}{dt} &= \gamma I - \mu R + \mu p \end{aligned}$$

$$\frac{dx}{dt} = \sigma x(1-x)[-r_v + r_i m I] \quad (13)$$

**3.2.2.2. Individuals imitate neighbours.** In this adoption, the behaviour of imitating others is still valid, but an additional constraint is applied such that individuals can only learn from their neighbours in a defined network. Assuming  $i, j$  are connected individuals in a network, their respective pay-offs for the currently adopted strategy are given by  $E_i, E_j$ . Strategy imitation occurs between epidemic seasons (i.e. during the decision adjustment period shown in Figure 2) and each individual decides whether to change his/her strategy for the upcoming epidemic season. For an individual  $i$ , he/she selects a random neighbour  $j$  to compare pay-offs. Naturally, if  $j$  plays with a different strategy and has a higher pay-off,  $i$  is more likely to imitate  $j$ 's strategy and thereby change strategy [29, 30, 44, 76, 78]. The probability that an individual  $i$  adopts an individual  $j$ 's strategy is given by the Fermi function:

$$f(P_j - P_i) = \frac{1}{1 + \exp[-\kappa(P_j - P_i)]} \quad (14)$$

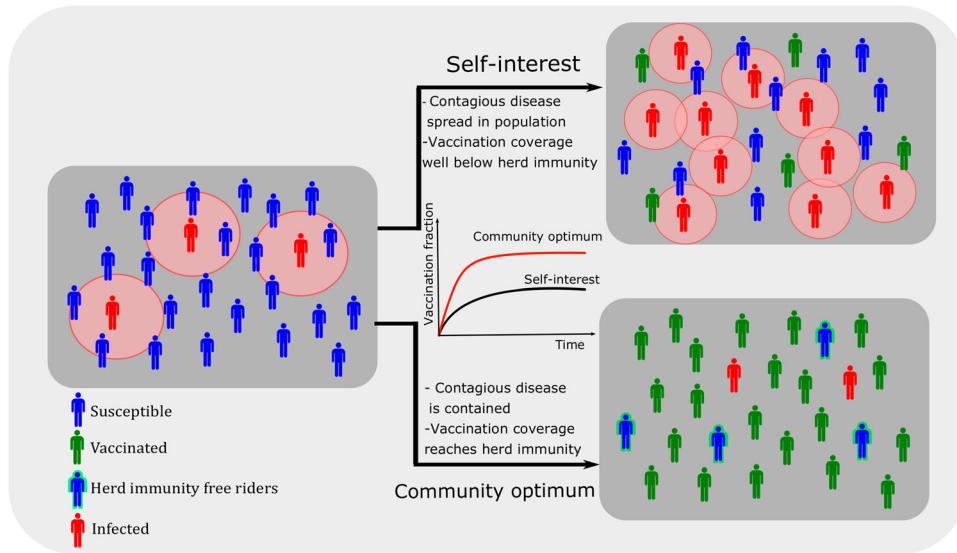
where  $\kappa$  is the strength of selection  $0 < \kappa < 1$  [29]. Li et al. [41] uses non-repeated games which utilize similar imitation game settings at individual level as seen in [29, 44, 76, 77] where individuals imitate the most successful strategy from a randomly chosen neighbour but combine the imitation game with a deterministic network model by grouping population by their number of contacts first, then further divide each subclass into three health compartments. Wells et al. [73] places individuals on a homogeneously distributed network that models the disease transmission and vaccination strategy adoption. The disease spreads if a susceptible individual has an infected contact (known as the index case). Individuals make decision on vaccination by comparing the pay-off between vaccination and non-vaccination while imitating the most prevalent strategy among all contacts. The vaccination decision is finalized on the first day when the infected index case shows symptoms. The game is played continuously until the simulation time is reached. The time window of vaccination is set differently from previously stated papers: there is no fixed time window of vaccination for all individuals to decide on whether to vaccinate or not, as seen in [29, 44, 76, 77]; instead, individuals decide on vaccination on the first day when one of their infected contacts symptomatic, at any time step during the epidemic season. If at that time step they decide not to vaccinate however, they face the same decision when another of their neighbours become symptomatic. Thus, they have multiple opportunities to decide to vaccinate, though a vaccination decision, of course, is not reversible within that season. Hence, [73] use a repeated game, although the iteration does not depend on a fixed time-period.

### 3.3. Key findings

In this section, we present the key findings of the considered studies.

#### 3.3.1. Key finding 1

Despite using different methods, all studies broadly agree, as shown in Figure 4, that (a) it is impossible to eradicate disease spread under voluntary vaccination unless specific conditions are met, and (b) the vaccination level that is best for self-interest is always well-below



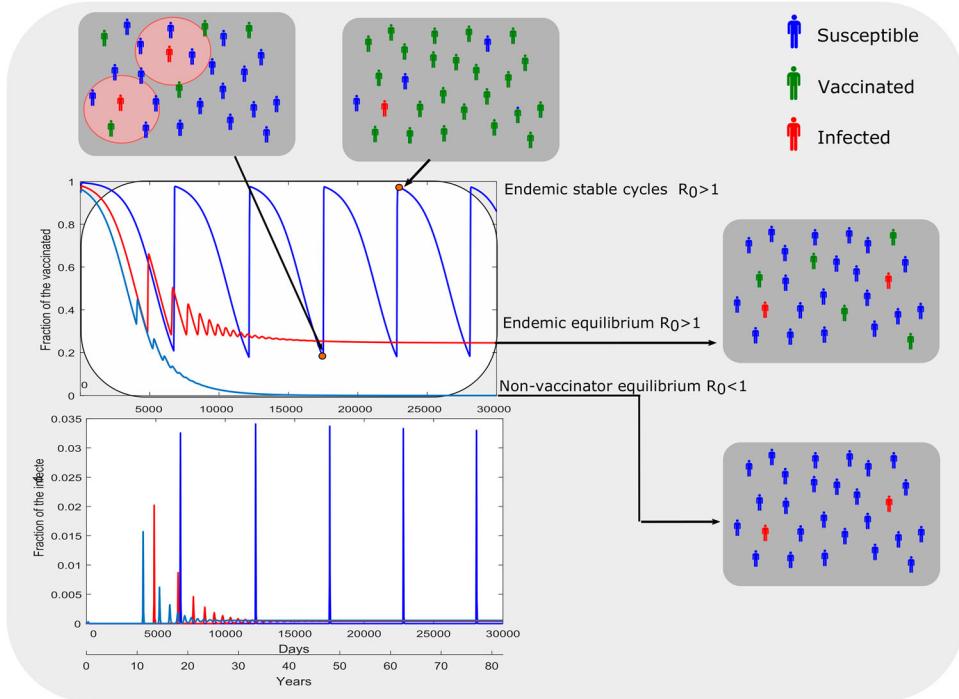
**Figure 4.** Key finding 1: It is impossible to eradicate disease spread under voluntary vaccination schemes without externalities driven by the self interest of individuals: the level of vaccination needed to provide herd immunity to all non-vaccinated individuals, thereby eradicating the disease, is typically higher than the level of vaccination achieved by voluntary vaccination alone.

the optimal level needed by the community to achieve ‘herd immunity’ unless vaccination cost is sufficiently low.

This is because unvaccinated individuals can always hope to escape the infection if the overall vaccination coverage is sufficiently high to curb the epidemic by reaching the ‘*herd immunity*’ threshold – a form of indirect protection against the spread of a contagious disease when a sufficiently high proportion of individuals have immunity. Such a protection requires an extremely high coverage of vaccine uptake (e.g. over 90% for measles) [74] and is difficult to sustain because individuals tend to exploit the temporary herd immunity (i.e. free-riding) and choose not to vaccinate. If each individual is purely selfish, herd immunity is not attainable without externalities (e.g. subsidies, regulation, etc.) [6, 8, 9]. The possibility of vaccination is also dependent on the transmissibility of the disease, and is also proportional to the number of contacts the individuals have if they make decisions based on memories [76]. Generally, self-interest behaviours are not aligned with social optimum [32] unless vaccine is sufficiently inexpensive [43], in which case both self-interest and social optimum converge to herd immunity. Relationship between the cost of vaccine and vaccine uptake is further discussed in Section 3.3.3.

### 3.3.2. Key finding 2

The fraction of vaccinated population can (i) reach zero (at a low level of transmissibility below epidemic threshold), (ii) yield a wave-like vaccination behaviour (above a critical value of transmissibility), or (iii) converge to a stable value (either at low level of transmissibility above epidemic threshold, or at unrealistically high transmissibility), depending on the percentage of prevalence in the population and the value of  $R_0$ .



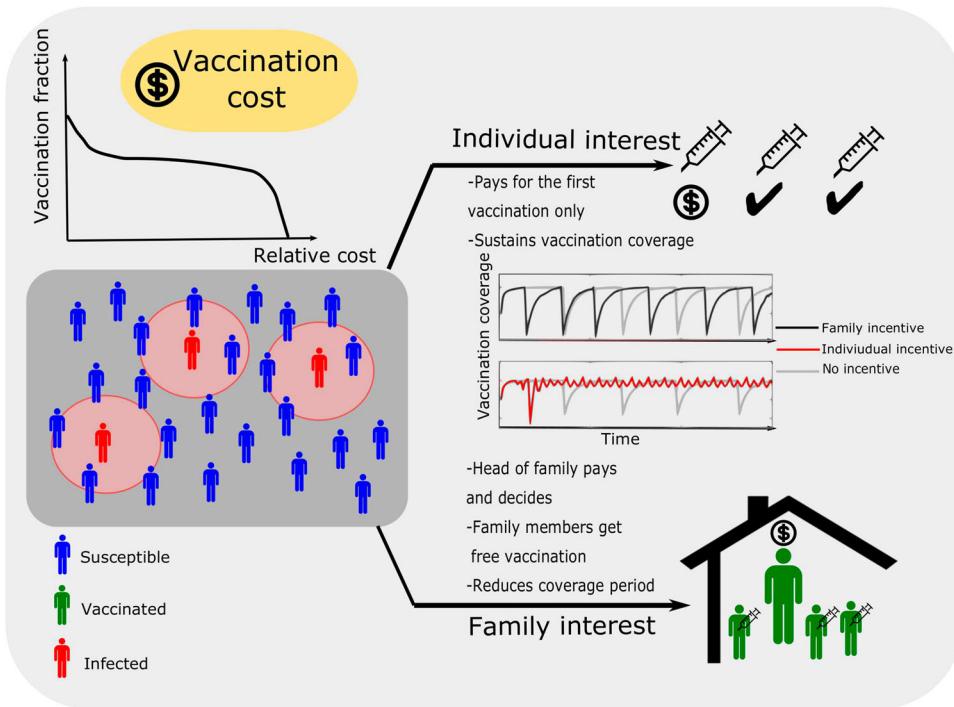
**Figure 5.** Key finding 2: The fraction of the people undertaking vaccination or social distancing may converge into stable values or display inter-dependent oscillatory behaviour with the prevalence percentage, depending on the value of  $R_0$ .

Studies using classical deterministic models with imitation [6, 10, 11, 57] and without imitation [21] both highlighted that the inter-dependent oscillatory behaviours are largely affected by three factors: the percentage of players who choose to intervene (by either taking vaccination or doing some form of social distancing), the degree of tendency and speed of imitation across communities, and the incidence/prevalence percentage in the population. In vaccination games, when vaccination coverage is high, the disease prevalence is depressed; subsequently, people have less incentive to vaccinate, and the prevalence level quickly recovers when the vaccination coverage drops [6]. Similarly, when social distancing is adopted, if the number of susceptible individuals is not adequate to sustain the epidemic, the epidemic peak decreases below the threshold value; while if the reproduction number for people not adopting social distancing  $R_0^a$ , is still greater than 1, the epidemic then picks up, creating wave-like oscillations [57]. Similar oscillatory observations are also found in studies using network models [19, 77]. This is illustrated in Figure 5.

### 3.3.3. Key finding 3

*Incentive-based public health programs are necessary to control epidemics but are not equally effective.*

As illustrated in Figure 6, vaccination cost heavily influences the vaccination decision. There is a cost threshold above which nobody would choose to vaccinate. Such an observation is seen in both network [29, 76] and classical models [43]. A low vaccination



**Figure 6.** Key finding 3: there is a cost threshold above which nobody would choose to vaccinate. Different incentive-based public health programs need to be evaluated carefully. For example, free vaccination schemes are more effective if individuals are allowed to decide based on their self-interest. If the head of the family decides on behalf of the family, such free vaccination programs are less effective.

cost generally encourages the vaccination uptake until it reaches an intermediate range where individual decisions become insensitive to the cost change. A high cost threshold exists above which nobody would choose to vaccinate [29, 76]. Interestingly, however, if correlating the risk evaluation model with vaccination cost, even for a small vaccination cost, the epidemic prevalence for the risk evaluation model is higher, compared to the original model without risk evaluation. The explanation is that the evaluation process creates a threshold in risk assessment, and individuals with a high risk threshold have a low possibility of getting vaccinated. The vaccination behaviour of the individuals in such models is not driven by the vaccination cost as strongly as in the models without risk evaluation. This suggests, firstly, that a lower vaccination cost does not necessarily suppress the epidemic level and/or encourage more vaccination, and secondly, that an individual's decision-making produces distinct outcomes if different conditions are applied [76].

Different public health programs also affect the epidemic and vaccination dynamics in a different fashion. In classical deterministic models using non-repeated, minority games [15, 69], if free subsequent vaccinations are given to individuals who pay for their first vaccination, the critical vaccination coverage is achieved more rapidly, and the threshold for epidemic spread is not reached. However, if the population is divided into families and the head of the family pays for his/her vaccination while the family members receive free

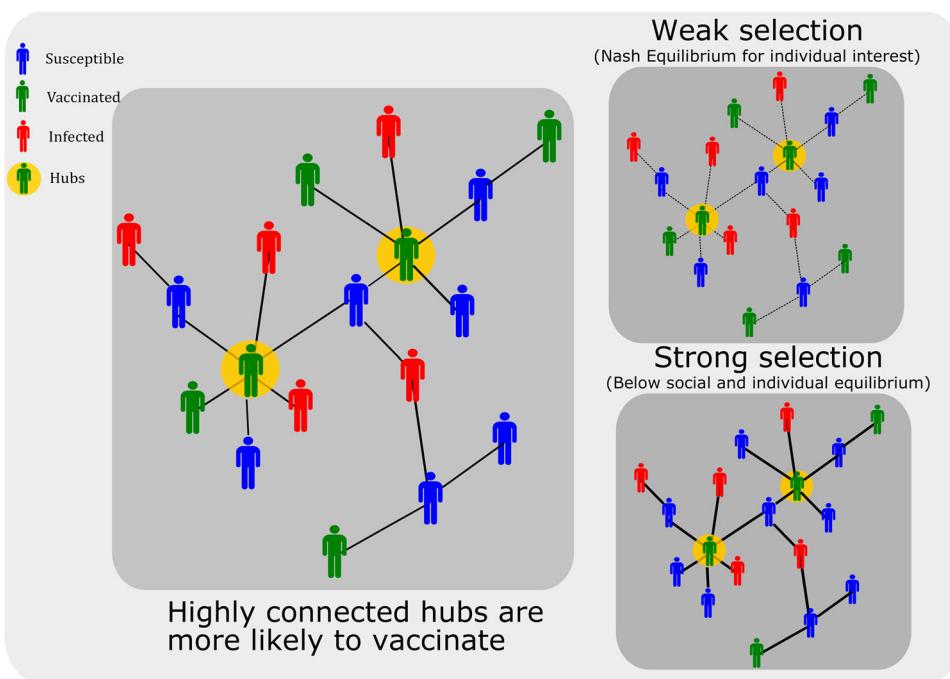
vaccinations, the epidemic is more likely to develop. The reason for this is that such incentive programs reduce the number of players in the population and the head of family makes the decision on behalf of his/her entire family unit. Such vaccination programs have been found to increase the frequency of influenza epidemics and reduce the duration of coverage. If no incentives are offered, the availability of epidemiological information plays a role in suppressing the epidemic severity. Assuming that (a) each individual is aware of an epidemic breakout, and (b) the media broadcasts information about the incidence and the vaccination coverage, or both, it was found that providing more epidemiological information does not necessarily improve the vaccination coverage, compared to broadcasting only the minimal information. As individuals become more knowledgeable about epidemiology, they could either become more attracted to vaccination, or more able to rely on herd immunity – if they perceive that the current vaccination coverage is adequately high [14].

### 3.3.4. Key finding 4

*Contact network topology plays an important role in affecting the level of vaccination coverage within a community.*

Notably, the model proposed by [29] found that highly connected individuals (network hubs) are more likely to be vaccinated because of the significant risk of infection. As illustrated in Figure 7, the strength of selection (the responsiveness to pay-off difference) also affects the vaccination coverage to a great extent. With strong selection and incomplete information, the vaccination coverage is well below both the social optimum and the Nash equilibrium (for individual's interest) because rational individuals are drawn to the success of free-riders after a single observation. Weak selection, by contrast, converges to Nash equilibrium in a well-mixed population. This is generally the case with over-exploitation of herd immunity, which in return delivers higher disease prevalence and lower vaccination coverage. Different topological structures are studied to investigate how topology affects the epidemic quantifiers [29, 44, 76, 77]. It is found that contact network topology can influence voluntary vaccination coverage and herd immunity but this effect is sensitive to the increase in the vaccination cost. A cost threshold exists beyond which small topological changes cause a significant reduction in the vaccination coverage and a rise in the infected cases, compared to homogeneous populations. This threshold-related effect is observed in both random and scale-free networks [29].

The behaviour-prevalence dynamics in populations modelled as random networks indicate that the epidemic spread is very sensitive to a change of risk assessment made by the individuals facing a vaccination decision. The overall impact is exhibited on the population level: for example, in the final epidemic size and number of vaccinated persons. Another interesting finding is that voluntary vaccinations can contribute to disease eradication when individuals act for their own interest under certain conditions (e.g. low vaccination cost, weak selection and on random network) [29], contradicting the common conclusion that voluntary vaccinations cannot stop an epidemic outbreak. Furthermore, [77] builds on this behaviour-prevalence system by drawing comparisons with a scale-free network. Findings show that the scale-free network topology suppresses the epidemics more compared to random networks, as the hubs tend to vaccinate, and their high connectivity encourages the higher overall vaccination coverage.



**Figure 7.** Key finding 4: Contact network topology plays an important role in affecting the level of vaccination coverage within a community. Highly connected people are more likely to get vaccinated.

### 3.3.5. Summary

Although using different modelling approaches, the existing literature appears to arrive at the consensus that human behaviour and decision-making at the individual level have a significant impact on epidemic spread at the population level. Two such behaviours, social distancing [55–57, 60] and vaccination [6, 11, 20, 32, 52, 76], have been widely studied. It has been found that voluntary vaccination decision-making can curb the disease prevalence and reach Nash equilibrium under some conditions, but that such an equilibrium is not able to eradicate diseases, or achieve herd immunity for the entire community [8, 9], unless specific restraints are applied [29, 43].

## 4. Discussion: the emerging trends in game-theoretic modelling of interventions

In preceding section, we presented a possible taxonomy of literature that focuses on game theory and epidemic modelling. Here we consider the temporal evolution of the research studies, and observe the emerging trends. The quantitative investigations of vaccination dynamics have achieved prominence in early 1980s [27, 28]. Here, we focus on the more recent development on the relations between individual decision-making and overall epidemic from 2000s onwards. Figure 8 shows the distribution of the papers covered in this review over time. It can be seen that the modelling efforts in the early stages focused on the use of deterministic models with self-learning game settings. This combination dominated early investigations, which generally only examined mass human behaviour. These

	Cornforth, D. M. and et al., 2011 [19]	<u>Li, Q. and et al., 2017 [41]</u>		
Network model deterministic				
Network model stochastic	Perisic, A. and Bauch, C.T., 2009 [52] Perisic, A. and Bauch, C.T., 2009 [53]  Wells, C. R. and et al., 2011 [73]  Fu, F. and et al., 2010 [29]	Zhang, H. and et al., 2010 [77] <u>Ndeffo Mbah, M.L. and et al., 2012 [47]</u> Bhattacharyya, S. and et al., 2019 [12] Fukuda, E., 2015 [30] <u>Zhang, H. and et al., 2012 [76]</u> Liu, X. and et al., 2012 [44] <u>Zhang, Y., 2013 [78]</u> Eksin, C. and et al., [23]		
Modelling structure	Bauch, C.T., et al, 2003 [9]  <u>Bauch, C. T., 2005 [6]</u>	Poletti, P. and et al., 2011 [55] <u>d'Onofrio, A. and et al., 2011 [20]</u> Breban, R. and et al., 2006 [15] Vardavas, R. and et al., 2007 [69] Breban, R., 2011 [14] Reluga, T. et al., 2006 [58] Bhattacharyya, S. and Bauch, C. T., 2010 [10] <u>Bhattacharyya, S. and Bauch, C. T., 2011 [11]</u> Poletti, P. and et al., 2009 [57] <u>d'Onofrio, A. and et al., 2007 [21]</u>		
Classical model deterministic	Bauch, C.T. and Earn, D. J. D., 2004 [8]	Feng, X. and et al., 2018 [26]  <u>Bauch, C. T. and Bhattacharyya, S., 2012 [7]</u>		
Classical stochastic		Reluga, T.C. and Galvani, A. P., 2011 [61] Reluga, T.C., 2010 [60] Reluga, T.C., 2009 [59] Reluga, T.C. and Galvani, A. P., 2011 [61]		
	Early 2000s	2005-2012	2012 Onwards	Year

**Figure 8.** Research trends in game-theoretic decision-making in infectious disease dynamics. Where the game used does not involve social learning, the author names are not underlined; where social learning by imitation is used, the author names are underlined.

earlier studies were built on the assumption of well-mixed population – an assumption that quickly fell out of favour due to its inability to capture nuances in an individual's social life. Later on, still using deterministic models, attempts were made to divide the population into finer compartments based on demographic characteristics. More sophisticated models quickly emerged, incorporating networks into the epidemic modelling to capture different contact patterns. It was also found that the topology of networks plays an important role in controlling epidemics, further motivating the search for a realistic representation of mixing patterns as networks. While abstract complex network topologies (e.g. small world network, scale-free network, etc.) are still being widely studied, research efforts continue to develop model networks with topological properties that mimic real-world contact networks even better [17, 18, 49]. Stochastic network models have also gained in popularity in recent years, aimed to model epidemic spreads on diverse contact networks.

Turning our attention to the type of health strategies considered on intervention decision-making, we note that studies of social learning by imitation have seen substantial development. Although self-learning and imitation games would continue to co-exist for their competing merits, imitation games enabled researchers to include flexible windows of opportunity in decision-making, as well as social influences on all individuals within a population. Non-repeated self-learning population games with a simple induction of self-learning on pay-off assessment were widely studied in the early years. These represented the ideal case in which every individual is perfectly rational with complete information about current epidemic prevalence and other people's behaviours [8, 9], however, may be

lacking memories or previous experiences. Later studies distinguished between the perceived and actual epidemic prevalence. In making intervention decisions for an upcoming epidemic season, these studies [14, 15, 69] model the individuals which consider not only the current benefit from vaccination, but also the ‘weighted memories’ of previous vaccination experiences, including the memories of strategy adoption in previous seasons, and a fitting parameter to adjust the weight of memories. For instance, the adaptability parameter of memory,  $\epsilon$  ( $0 < \epsilon < 1$ ), controls how memories of strategy affect the strategy adoption in the next season, where  $\epsilon = 0$  means individuals will take the same strategy as in previous years, and  $\epsilon = 1$  means the strategy adoption is solely based on current pay-off assessment, independent from previous experiences [69].

Another set of studies using imitation quickly attracted interest by connecting decision-making to a learning process of not only individuals, but the whole population. Consistent with the observed trend, imitation studied in later years focus on the individual level by limiting the learning process to people who have contacts with each other. Network-based modelling constrains individuals to play the deductive games only with their connected neighbours. Some studies [29, 30, 44, 76, 78] incorporated imitating contacts in the pay-off assessment. While imitating neighbours, individuals also use memories of pay-off, from previous vaccination experiences, to evaluate the total pay-off for the current vaccination decision. For instance, model seen in [76] the total pay-off for a strategy may combine the current pay-off and the historical pay-offs using the ‘weight of memory’ parameter  $w$  ( $0 < w < 1$ ). While  $w = 0$  means that the previous vaccination experiences are omitted,  $w = 1$  means the historical pay-offs are given equal weight to the current pay-off. In other words, the pay-off functions include the parameters governing self-decision-making (e.g. memory, perception of risk, etc.) and those reflecting learning processes (e.g. strength of selection).

## 5. Conclusion

We reviewed game-theoretic studies modelling both (a) an epidemic spread and (b) the decision-making of individuals, contemplating a number of intervention options to protect themselves from the epidemic spread.

The systematic review, based on PRISMA search process, was followed by a succinct categorization of the research works, allowing us to summarize key findings and identify research trends.

Specifically, the classification distinguishes (a) modelling structure, (b) the frequency of the games played, and (c) the type of strategy adoption. The ‘modelling structure’ contrasts between classical and network-based modelling. The classical models such as SIR (Susceptible-Infected-Recovered), and SIS (Susceptible-Infected-Susceptible) are further divided into deterministic and stochastic models. They focus on the aggregate behaviour of sections (compartments) of the population, whereas the individual-based network models focus on individual behaviour.

The ‘frequency of game’ separates non-repeated and repeated games. Non-repeated games are used where the decision can be made only once in the lifetime of an individual or only once during a season: for example, deciding to have the triple-vaccine administered must be done at a certain age, confers a lifelong immunity, and thus cannot be reversed.

Similarly, deciding to have a flu-vaccine is a decision which, while can be made multiple times within a person's lifetime, nevertheless must be made within a particular time-window before every flu season and cannot be reversed once the flu season begins. Both these scenarios lend themselves to non-repeated games. On the other hand, repeated games are used to model decisions which can be changed during the course of an infection-spread. Most decisions regarding social distancing, for example, can be changed during the course of the epidemic, and thus such decisions can be modelled using repeated games. The 'type of strategy adoption' differentiates between self-learning and imitation. An individual who uses self-learning only considers knowledge, information, or their past strategies and their pay-offs in making decisions, whereas an individual adopting imitation imitates the strategies of other successful members of the population. If a classical model is used, such choice imitates (the average of) the entire population, whereas when a network-based model is used, only the neighbours of a player would be imitated.

The resultant taxonomy highlights that the choice of model depends on many factors such as the strength of the immunity conferred by either the vaccine (seasonal or life-long) or the disease itself, the structure of population considered (well-mixed or on spatial structure), and the level of mixing in the population, among others.

Furthermore, we found that several studies used models with memory of previous experiences, including memory of previous strategies, as well as memory of previous pay-offs, in both self-learning and imitation. In other words, players have been modelled to use both their own memories and the memories from the rest of the population (either memories of only the player's neighbours, or the entire population). Often, models utilized weighting mechanisms to limit the influence of memory in comparison to contemporary pay-offs.

Finally, we considered the current trends within the research field. We have shown that while classical models continue to retain their prominence since early studies, network-based models are attracting research interest in recent years. The reason for this is that the network-based models are more realistic in scenarios where global information about the epidemic spread is limited and is not available in time, thus forcing players to depend on their own interactions to make decisions. Nevertheless, classical models are still widely used, possibly due to their simplicity and the ability to capture meta-population dynamics. In terms of game frequency, however, we have observed that non-repeated and repeated games both continue to be used, depending on the nature of the time window available to make intervention decisions.

We believe that the presented review reduces a gap in literature, providing a useful summary of key findings and research trends in an expanding area of behaviour-coupled models in epidemiology.

## Disclosure statement

No potential conflict of interest was reported by the authors.

## Funding

This research was funded by the Australian Research Council (ARC) Discovery Project grant DP160102742. In addition, S. L. C was supported by an Australian Government Research Training Program (RTP) Scholarship.



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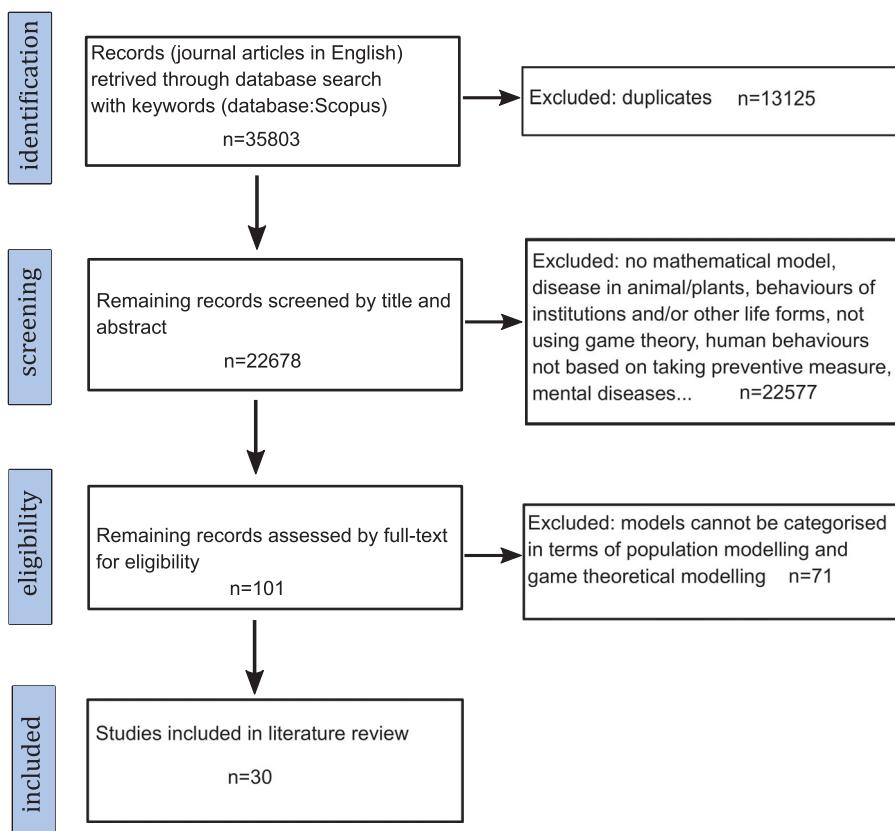
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## Appendices

### Appendix 1. PRISMA flow chart of systematic search process



**Figure A1.** PRISMA flow chart. Refer to Section 2 for details.



## Appendix 2. Game context in epidemic modelling

In the context of epidemic spread, individual decision-making is driven by two main types of pre-emptive measures:

- Vaccination: an individual has the choice of vaccinating or not vaccinating in the face of an epidemic.
- Social distancing: also referred to as behavioural change, this refers mainly to prophylactic actions that reduce the chance of infection. An individual has the choice to either change their behaviour in order to minimize contact (for example, drive rather than taking the train), or live normally.

In a population, each individual is seen as a player who faces the trade-off between perceived benefits and perceived costs of protection. By adopting protective measures, the probability of infection is reduced but some financial/social cost, or even health risks, is increased. However, one might succeed in avoiding infection without any cost if they do not take protective measures but every potential contact has taken them. Therefore, an individual's decision is influenced by the behaviour of others, similar to classical scenarios considered in game theory.

In vaccination games, individuals opt to vaccinate with the hope of gaining immunity and avoiding the infection. From a modelling point of view, the core concept of vaccination games is to change individual's health status by moving susceptible individuals into the vaccinated (or recovered) class. Social distancing games, on the other hand, only have the ability to modify infection-related parameters; for example, individuals who adopt protective measures will have a lower transmission rate but are still prone to infection due to remaining in the susceptible class.

### A.1 Vaccination

In vaccination games, three conditions affect the epidemic model and, consequently, the pay-off construction. These are:

- Length and coverage of immunity
- Risks associated with the vaccination
- Vaccine efficacy

Length of immunity could be broadly categorized as 'lifelong' or 'temporary'. Lifelong immunity by vaccination can be achieved for some diseases, such as measles, mumps and rubella, while immunity obtained by vaccination for other diseases, such as influenza, would be partial and/or only last until the end of the epidemic season. The length of immunity affects how frequently the vaccination game is played. If the vaccination offers lifelong immunity, an individual only gets to play the game once in his/her life, whilst if the vaccination confers temporary immunity, the individual gets to decide whether to get vaccinated every season, thus playing the game every season. Coverage of immunity defines the level of protection that a vaccine can provide. Full immunity may be granted for vaccines that are clinically proven to be fully effective and thus a vaccinated individual will be removed from the susceptible class and no longer exposed to the risk of infection. Where only partial immunity is granted (for example, in the case of influenza), a vaccinated individual is still placed in the susceptible class but with a reduced probability of infection.

Vaccination comes with some risks to individuals who get vaccinated, such as vaccine-induced morbidity or other side effects, though such a risk materializing is typically extremely unlikely. The risk of vaccination will nevertheless affect the expected pay-off of vaccination, since this is a potential 'cost' of vaccination [9].

Vaccines, whether granting full or partial immunity, do not always meet their expected level of efficacy. Manufacturing defects have been considered in previous studies [52]. As a result, a small percentage of vaccinated individuals do not receive any protection (full or partial), and should be treated as unvaccinated individuals who are still prone to infection.

## A.2 Social distancing

Also known as behavioural change, social distancing generally refers to adoption of prophylactic measures to reduce physical contact between individuals, thereby minimizing the likelihood of infection spread. Susceptible individuals who choose this strategy face some form of compromise, represented by extra cost, such as forfeiting on travel plans, or avoiding crowded environments in their daily lives. For those who do not adopt any change in lifestyle, the risk of infection remains relatively high but they are spared the extra cost related to social distancing. Individuals can switch between ‘social distancing’ or ‘social non-distancing’ depending on the pay-off for each strategy by conducting cost-benefit assessments [55–57, 60].

## A.3 Pay-off construction

Assuming all players in the game are rational and their best interest is to obtain maximum gain, their decision-making relies purely on the outcome of cost-benefit assessments. They weigh up the pay-off for each strategy, and at the end of each game, a net pay-off is obtained. This is defined by a numerical value according to the strategy the individual adopts [67, 72]. In the epidemic context, there are several approaches to measure pay-offs, such as:

- Risk assessment: a qualitative measurement that often poses as a reflection on the risks of death from the infection [6–8, 11, 20]
- Monetary value: expected costs expressed as the true financial cost of choosing a certain strategy; this can be either a realistic quote or an estimate based on previous epidemic breakout, or a purely indicative index [32, 43, 64, 66]
- Others: years to live, etc. [5, 40, 52, 68]

A widely used approach to constructing pay-offs is to quantify risks, which can be specifically stated as morbidity (i.e. risk of death) or simply as the risk of infection as shown in [8, 9]. In vaccination games, the risk of vaccination is often defined as the morbidity the vaccine induces; and the risk of non-vaccination is defined as the risk of infection, both simplified as a constant as seen in [2, 8, 29, 44, 76, 78], and in Equation (A1):

$$\begin{aligned} E_v &= -r_v \\ E_i &= -r_i \\ r_v &< r_i \end{aligned} \tag{A1}$$

where  $r_v$  represents the risk of vaccination and  $r_i$  the risk of infection, with the constraint that the risk of infection is always greater than the risk of vaccination.

More sophisticated expressions for the risk of infection are not uncommon. These usually depend on the prevalence of infection, as seen in [6, 55–57]. For example, in vaccination games, given that the pay-off is measured by risks of morbidity, the pay-off for non-vaccination increases when the epidemic propagates and there are greater numbers of cases with infection. In this scenario, the pay-off for not vaccinating is required to reflect the increasing risk of infection and thus defined as a function with variables relating to the size of the infected population [6, 55–57]. Some studies also use a modified form to distinguish between the actual infection prevalence and the perceived prevalence, where the latter is meant to mimic the scenario in which individuals do not necessarily grasp the full extent of the current epidemic breakout. Perceived prevalence is thus built on current observation (force of infection  $\lambda$ ) and memory of previous vaccination history [15, 69, 76].

Some studies constructed pay-offs by assigning monetary costs to each strategy [32, 43, 64, 66]. In vaccination games, if individuals choose to vaccinate, they need to pay a price for the vaccine itself and the related efforts are associated with a cost, financial and otherwise (e.g. time consumed). If individuals choose not to vaccinate, the cost may consist of the treatment cost and/or other consequences of getting infected (e.g. absence from work). For diseases with well-documented epidemic history and available vaccines, the financial cost of vaccination is calculated by estimating costs of

vaccines and health-related utilities [5, 43]. In social distancing games, the cost or pay-off for each strategy (i.e. change behaviour or not) is less clear as this may include a myriad of factors and would vary significantly depending on individual circumstances. A common approach to solving such a problem is to use an indicative index value rather than the true financial cost in pay-off construction so that the generality is maintained [5, 40, 68]. One popular measure is the quality-adjusted life year (QALY), which incorporates both the duration and magnitude of the effects on reduced health on patients to measure the disease burden [40]. QALY is calculated as follows:

$$\text{QALY} = Y \times U$$

$$0 \leq U \leq 1 \quad (\text{A2})$$

where  $Y$  and  $U$  represent *years of life* and *utility of life* respectively.

If one lives for a year in perfect health, one QALY is awarded (utility is equal to 1). A lower utility is assigned when one lives out a year in less than perfect health condition. Because the estimate of utility often comes from patient-based surveys, QALY remains an index for data-rich epidemics such as HPV [5] and measles [68].

When each individual's expected pay-off is calculated, an aggregate pay-off for the entire community can be obtained, as shown in [9, 43, 60].