

Review

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Review

Evolutionary Game Theory Use in Healthcare: A Synthetic Knowledge Synthesis

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Abstract

Background: Evolutionary game theory (EGT), originating from Darwinian competition studies, offers a powerful framework for understanding complex healthcare interactions where multiple stakeholders with conflicting interests evolve strategies over time. Unlike traditional game theory, EGT accounts for bounded rationality and strategic evolution through imitation and selection. **Aims and objectives:** In our study we use Synthetic Knowledge Synthesis (SKS) that integrates descriptive bibliometrics and bibliometric mapping, to systematically analyze the application of EGT in healthcare. The SKS aimed to identify prolific research topics, suitable publishing venues, and productive institutions/countries for collaboration and funding. Data was harvested from Scopus bibliographic database, encompassing 539 publications from 2000 to June 2025. **Results:** Production dynamics is revealing an exponential growth in scholarly output since 2019, with peak productivity in 2024. Descriptive bibliometrics showed China as the most prolific country (376 publications), followed by the United States and the United Kingdom. Key institutions are predominantly Chinese, and top journals include *PLoS One* and *Frontiers in Public Health*. Funding is primarily from Chinese entities like the National Natural Science Foundation of China. Bibliometric mapping identified five key research themes: Game theory in cancer research, Evolution game-based simulation of supply management, Evolutionary game theory in epidemics, Evolutionary games in trustworthy connected public health, and Evolutionary games in collaborative governance. **Conclusion:** Despite EGT's utility, significant research gaps exist in methodological robustness, data availability, contextual modeling, and interdisciplinary translation. Future research should focus on integrating machine learning, longitudinal data, and explicit ethical frameworks to enhance EGT's practical application in adaptive, patient-centered healthcare systems.

Keywords: evolutionary games theory; healthcare; complex healthcare systems; synthetic knowledge synthesis; thematic analysis

1. Introduction

Evolutionary game theory (EGT) [1] is a powerful tool for understanding behavior in complex healthcare settings, particularly where multiple stakeholders or agents interact with potentially conflicting interests and evolve over time [2]. EGT is originating from the study on Darwinian competition in biology published in 1971 [3]. Unlike traditional game theory, EGT accounts for bounded rationality and how strategies evolve over time through imitation and natural selection [4]. Interesting health topics where EGT is applied are modeling antibiotic resistance [5], developing cancer treatment strategies [6], informing public health interventions [7], analyzing doctor-patient interactions [8], human social interactions in macro-level public health [9], and many other applications as described in the rest of this paper. However, given the multidisciplinary and professionally multilayered nature of applying evolutionary games in healthcare, a holistic and systematic analysis is needed. To bridge this research gap, we conducted a Synthetic Knowledge

Synthesis (SKS), as detailed in [10,11]. SKS utilizes a triangulated approach to knowledge synthesis, integrating descriptive bibliometrics and bibliometric mapping.

This synthesis was aimed to:

- Identify the most prolific research topics and themes.
- Pinpoint suitable publishing venues for researchers to stay informed and disseminate their research work on evolutionary games in healthcare.
- Discover productive institutions and countries for potential collaborations, as well as identify possible funding bodies.

2. Materials and Methods

While SKS framework is extensively presented elsewhere, the description bellow focuses specifically on its application within the present research. The research publications corpus was retrieved from the Scopus bibliographic database (Elsevier, Amsterdam) [12] using the advanced search command

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TITLE-ABS-KEY("evolution* game*" AND ( health* OR medic* OR nursi* ))
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Descriptive bibliometrics was performed using Scopus's built-in functions. Bibliometric mapping was executed using VOSViewer software version 1.6.20 (Leiden University, The Netherlands). The following four steps were undertaken:

1. **Corpus Harvesting:** The literature search was conducted on June 2, 2025.
2. **Descriptive Bibliometric Analysis:** This involved analysing country and institutional productivity, literature production trends, journal analytics, and identifying funding bodies and document types.
3. **Bibliometric Mapping:** Author keywords were mapped to visualize their relationships.
4. **Thematic Analysis:** A thematic analysis was performed on the bibliometric map by examining the proximity and links between author keywords to discern underlying research themes.

Renaults

Descriptive bibliometrics

A comprehensive search identified a total of 539 publications. The distribution of these publications by type was as follows: 418 articles, 66 conference papers, 25 conference reviews, 15 reviews, 6 book chapters, 3 books, and 8 other publication types. One publication was subsequently retracted. The first publication presenting evolutionary game theory employment in the healthcare domain emerged in 2000. This inaugural publication addressed critical issues related to healthcare information security, confidentiality, and privacy in response to the increasing adoption of Electronic Patient Records [13]. Following this initial publication, the scholarly output remained limited, with no more than three publications per year until 2009. From 2009 onwards, a linear growth trend in publications was observed, transitioning to an exponential growth phase beginning in 2019. Peak productivity was recorded in 2024, with 98 publications.

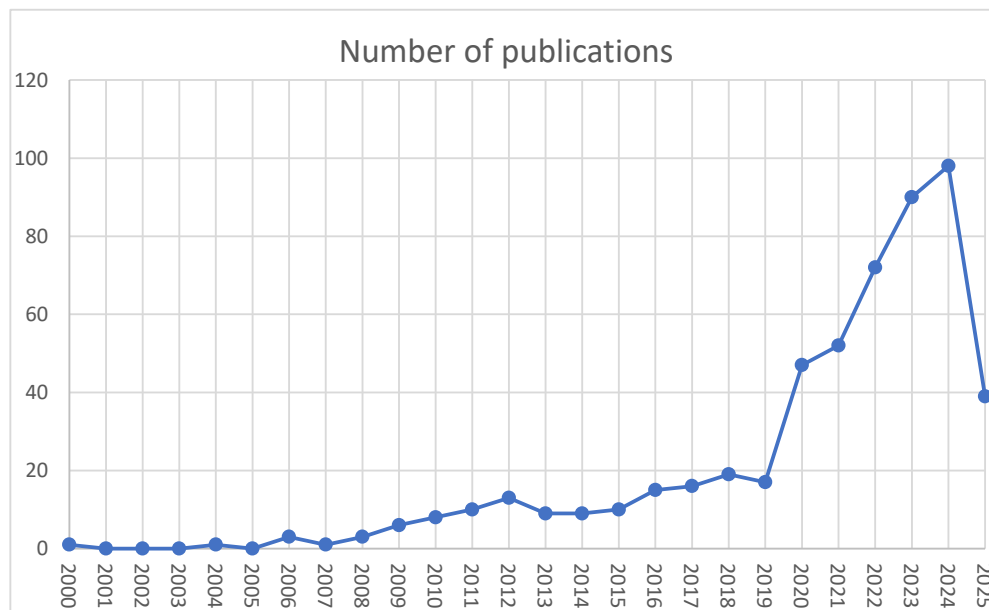


Figure 1. Publication Trends in Evolutionary Game Theory and Healthcare.

China is the most prolific country, contributing 376 publications, which constitutes over two-thirds of the total output. Following China, the most productive countries (with $n \geq 10$ publications) are:

- United States (n=65)
- United Kingdom (n=39)
- Italy (n=107)
- India (n=49)
- Hong Kong (n=11)
- Iran (n=11)
- Canada (n=10)
- Japan (n=10)

A substantial majority of these nations possess robust economies, exhibit high Healthcare Index scores [14], and consistently rank among the top-tier countries in general and medical sciences according to the Scimago Country Rank (Elsevier, Netherlands).

The most productive institutions, each contributing eight or more publications, are predominantly located in China, with one exception:

- Jiangsu University (n=17)
- Ministry of Education of the People's Republic of China (n=14)
- Wuhan University (n=10)
- Beijing Institute of Technology (n=8)
- Bangladesh University of Engineering and Technology (n=8)
- Nanjing University of Information Science & Technology (n=8)
- Tongji University (n=8)

Table 1. Themes and thematic categories in EGT research.

Cluster Colour	Representative Keywords	Categories	Themes
Violet (6 Author keywords)	Game theory (28), Cooperation (18), Cancer (5)	Game theory in cancer research; Cooperation and evolution in game theory	Game theory in cancer research
Green (11 keywords)	Tripartite evolutionary games (12), Public health emergency (5), Decision making (6), Food supply chain (4), Supply chain management (4)	Evolution game based simulation of public health emergency; Use of evolution stable strategy for decision making; in food supply chain; Numerical simulation of supply chain management using tripartite evolutionary game	Evolution game-based simulation of supply management
Evolutionary games and prospect theory	Evolutionary game theory (107), Covid Vaccination (6)	Evolutionary game theory for covid -19 vaccination management. Evolutionary game theory in SIR development	Evolutionary game theory in epidemics
Red (14 author keywords)	Evolutionary game (157), Simulation analysis (10), Complex network (9), Blockchain (8), Public health (6), Emergency management	Simulation analysis of using blockchain in trustworthy internet of things; Regulation of privacy protection; Evolutionary games in public health,	Evolutionary games in trustworthy connected public health
Blue (9 author keywords)	Evolutionary games (15), Collaborative governance (7), Public health emergencies (6)	Evolutionary games/prospect theory in collaborative governance of public health emergencies; Four party evolutionary games use in collaborative governance	Evolutionary games in collaborative governance

3. Game Theory in Cancer Research

3.1. Game Theory in Cancer Research

Wolfl et al presented an essay in which they suggest that cancer progression is an evolutionary competition between different cell types and can be analysed as an evolutionary game [18]. West et al introduce a prisoners dilemma game model of three competing cell populations which recapitulates prostate specific antigen data from clinical trials The model enables to design and quantify different treatment strategies [19]. Wu et al designed a statistical physics model combining metabolites into interaction networks. By integrate concepts from ecosystem and evolutionary game theory one can model how the health state-dependent alteration of a metabolite is shaped by its intrinsic properties and extrinsic influences [20]. Szasz [21]used evolution game theory to explain the Petos paradox in epidemiologic observations of the six degrees of tumour prevalence.

3.2. Cooperation and Evolution in Game Theory

Cagan and Page used evolutionary game theory for cancer modelling, aiming to explain how cancerous mutations spread through healthy tissue and how intercellular cooperation persists in tumour-cell populations using more realistic spatial models [22].

4. Evolution Game-Based Simulation of Supply Management

4.1. Evolution Game-Based Simulation of Public Health Emergency

Chain et al analysed the role of behaviour and decisions of public and governments in the COVID-19 panic buying event from the perspective of evolutionary games [23]. Similarly Kabir and Tanimoto analysed behavioural dynamics economic shutdowns and lockdowns during COVID-19 dynamics. Rui et al of used evolutionary games to analyse the more general problem of public health emergencies involving local government, social organisations and the public [24] and Fan et al to analyse the combination of punishment and reward mechanisms in the problem how to mobilize the enthusiasm of residents, community and government [25]. Kabir et al used a novel exportation-importation epidemic model mimicking behavioural dynamics to study the impact of quarantine policies, healthcare facilities, socio-economic cost, and the public counter-compliance effect under the evolutionary game theory by considering : a source country of a contagious disease and a neighbouring disease-free country [26].

4.2. Use of Evolution Stable Strategy for Decision Making; In Food Supply Chain

The replicated dynamic equation based evolutionary games were employed to study evolutionarily stable strategies of suppliers and producers for assuring food safety [27]and quality control [28].

4.3. Numerical Simulation of Supply Chain Management Using Tripartite Evolutionary Game

Peng et al employed a tripartite evolutionary game model that simulates the interaction of interests between food raw material suppliers, food manufacturers, and consumers. to identify the key factors that influence the decision-making of each participant [29]. Tripartite games were also used to analyse the influence of blockchain technology on the evolutionary stability strategies for financial institutions, core enterprises and small to medium size enterprises [30] and cold chain supply for fresh agricultural products [31]. In another study Zhang et al used tripartite evolutionary games to analyse the influence of digital twin service on environmental, social, and governance evaluation and analytically investigates the long-term behaviour of sustainability concerned stakeholders in the vaccine logistics supply chain [32].

5. Evolutionary Game Theory in Epidemics

5.1. Evolutionary Game Theory for Covid -19 Vaccination Management

Jia et al employed the stochastic evolutionary game model in combination with the Moran process, to analyse the epidemic prevention and control strategies to maximise the , expected and super-expected benefits taking into account vaccination, cultural differences and irrational emotions [33]. Similar model was studied by Dashtable and Mirzalel however focusing on behavioural changes based on vaccination, hospitalization and recovery status and by Lee et al focusing [34] on vaccine hesitancy and vaccination campaigns.

5.2. Evolutionary Game Theory in SIR Development

An epidemiological SIR model was proposed combining's social strategies, individual risk perception, and viral spreading to study different strategy adoptions [35]. To characterise this mechanism, we construct a networked SIR model that introduces an evolutionary game framework. Behavioural effects that significantly influence disease dynamics within the coupled disease-behaviour system are captured through sensitivity analysis. Zhang et al [36]used evolutionary based SIR modelling to study the behavioural exchanges on different governmental decision making strategies.

6. Evolutionary Games in Trustworthy Connected Public Health

6.1. Simulation Analysis of Using Blockchain in Trustworthy Internet of Things

Mai et al [37] and Yao and Guizani [38] used a centralized evolutionary game pool selection algorithm to maximise the privacy, security and utility of healthcare IoT network based blockchain and mining pools architectures.

6.2. Regulation of Privacy Protection

Regulation of privacy protection become a significant problem in mobile healthcare systems. Those problems can be analysed using evolutionary games approach. In this manner Zhu et al analysed the influence of economic factors in privacy protection of mHealth systems [39], Jiang et al [40] and Hu et al [41] studied the secure access to big medical data access. In a different kind of context Zhu et al [42] analysed the interaction mechanisms of four parties (patients, medical institutions, smart medical platforms and governments) in maintaining privacy of smart medical care.

6.3. Evolutionary Games in Public Health

Chen and Zhu [43] constructed an evolutionary four partite game model (pharmaceutical enterprises, testing agencies, government regulators, and drug wholesale enterprises) that incorporates rent-seeking dynamics together with a reward-punishment mechanism, to analyse strategies of four players in achieving integrity of pharmaceutical enterprises in the manner to maintain public health, social stability, and national security. Ma and liu [44] developed a tripartite evolutionary game model (government, whistleblowers, and the public) analysing interaction between these subjects under the uncertainty of risk perception to achieve early warnings for public health emergencies.

7. Evolutionary Games in Collaborative Governance

7.1. Evolutionary Games/ Prospect Theory in Collaborative Governance of Public Health Emergencies

Zhao et al [45] analysed the evolutionary paths of stability points, dual-stable states, and unstable states under different government engagement policies during strikes causing public health emergencies. While co-operation is crucial in preventing and controlling emergencies Xu et al [46] proposed an evolutionary tripartite game (government, enterprises, and public) to analyse different factors in combination with different conditions to support decision making of players. On the other hand Shan and Pi [47] used a tripartite game (public, merchants, government) to respond to buying panic events.

7.2. Four Party Evolutionary Games Use in Collaborative Governance

Due to influence from enterprises, local governments might relax environmental regulations, posing threats to public health. Hu et all [48] used four-party evolutionary game model (enterprises, local governments, central government and the media) to seek equilibrium collaborative governance solutions. In another interesting application four party game (government regulatory agency, We Media, vaccine industry groups, and the public) was used in the development of a dual regulatory system of vaccine quality in assessing the stability points of each players strategy [49]. Chen and Zhu [50] used evolutionary games/ prospect theory to assess the collaborative governance in rent seeking dynamics and reward-punishment measures between pharmaceutical industry, drug testing agencies, government regulators and drug selling entities. Zang et al [51] devised a evolutionary game model to analyse integrative coordination mechanisms adopted by humanitarian business partnership (humanitarian organizations, business corporations, impact of public engagement) to prevent, corruption and counterfeit products.

7.3. Research Gaps

Despite its demonstrated utility shown above EGT's potential in healthcare are hindered by several critical research gaps. These include fundamental methodological challenges in model construction, particularly concerning the accurate representation of complex biological and social interactions, and the persistent issues of data scarcity, quality, and parameter estimation. Furthermore, significant barriers exist in real world contextual and behavioural modelling, technical and implementation challenges, in translating theoretical EGT models into actionable clinical tools and validated public health policies, largely due to limitations in interpretability, generalizability, difficulty in interdisciplinary communication) and the absence of robust empirical validation frameworks. Addressing ethical, governance and regulatory considerations, such as algorithmic bias and equity in model outcomes, also remains paramount.

7.4. Methodological and Theoretical Limitations

Many models are based on oversimplified assumptions like static payoffs and perfect rationality, failing to capture the dynamic nature of healthcare systems where parameters (e.g., disease prevalence, resource availability) constantly evolve [52,53]. Furthermore models often remain theoretical without real-world testing [54] or Existing frameworks struggle to incorporate heterogeneous stakeholders (e.g., patients, providers, insurers) with conflicting incentives[55].

Additionally models rarely account for regional disparities in resource access or patient behavior. Some urban-rural healthcare competition studies show that efficiency gains from cooperation depend heavily on unaddressed contextual variables like income levels or education [56,57]. Evolutionary games also assume gradual strategy shifts, but real-world crises (e.g., pandemics) trigger rapid behavioral changes [58]. EGT also faces technical, implementation and regulatory challenges. Due to exponential rise in using IoT and artificial intelligence in healthcare few studies address interoperability with existing systems or data privacy constraints [59]. Current regulatory frameworks are modeled as static inputs, however, policies evolve in response to stakeholder strategies, creating feedback loops that are rarely incorporated [60]. Furthermore fraud detection systems or third-party entities may collude with hospitals systems. In addition to above EGT research faces interdisciplinary translation problems, For example cancer therapy models using evolutionary games (e.g., adaptive therapy) are mathematically robust but face implementation barriers due to clinicians' limited familiarity with game-theoretic concepts [62]. Furthermore gamified health interventions often prioritize engagement over clinical outcomes. For instance, serious games for chronic disease management rarely integrate evolutionary game mechanics tailored to patient motivation profiles [63]. But, by addressing above research gaps through in a multidisciplinary and multiprofessional way EGT might still become powerful and useful analytical tool in developing component, adaptive, personalized, patient centered and equitable healthcare systems.

7.5. Future Research Directions

Based on above described gaps and using a bibliographic based approach [64], following future research directions have been induced:

- Incorporating machine learning into EGT design and execution to enable dynamic parameter settings
- Integrating data from longitudinal studies and regulatory feedback mechanisms into EGT construction and validation forming advanced ecosystems
- Developing shared ontologies between health profesionist, data scientists, and game theorists.
- Solvig scalability issues with investment in computationally efficient and scalable EGT algorithms and platforms

- Developing explicit ethical frameworks and methodologies to integrate ethical considerations, such as fairness, equity, and patient autonomy, directly into the design, parameterization, and evaluation of EGT models.

8. Conclusions

This Synthetic Knowledge Synthesis underscores the escalating relevance of Evolutionary Game Theory (EGT) as a vital analytical tool in comprehending and addressing complex dynamics within healthcare systems. Our analysis reveals a robust and rapidly expanding body of literature, with an exponential growth trajectory since 2019, heavily driven by research from China. We identified key research themes, including EGT's application in cancer research, supply chain management, epidemics, trustworthy public health systems, and collaborative governance, demonstrating its versatile utility across diverse healthcare challenges.

Despite EGT's proven potential, its broader impact is currently constrained by several critical research gaps. These include fundamental methodological limitations, such as oversimplified assumptions and the need for more realistic contextual and behavioral modeling, particularly during rapidly evolving crises. Furthermore, challenges in technical implementation, governance, and interdisciplinary translation hinder the conversion of theoretical EGT models into actionable clinical and public health solutions. Bridging these gaps necessitates addressing issues of data scarcity, interpretability, and the absence of robust empirical validation frameworks.

To unlock EGT's full transformative potential in fostering adaptive, personalized, and equitable healthcare systems, future research must adopt a multidisciplinary and multiprofessional approach. Key directions include integrating machine learning for dynamic parameter settings, incorporating longitudinal data and regulatory feedback loops, fostering shared ontologies among diverse professionals, investing in computationally efficient algorithms to solve scalability issues, and developing explicit ethical frameworks to guide model design and evaluation. By proactively addressing these areas, EGT can evolve into an even more powerful instrument for navigating the intricate landscape of modern healthcare.

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