SYSTEMATIC REVIEW



Innovation ecosystems in health: countries and theoretical

models used [version 1; peer review: awaiting peer review]

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Abstract

This article sought to analyze the innovation ecosystems in health, countries that develop them and the theoretical models they resort to. To this end, three databases carried out a systematic review through a bibliographic search in English, Spanish and Portuguese. 40% of health innovation ecosystems are in the USA, 13% in South Africa, 10% in the UK, 6.67% in Namibia, and 30% in various countries. Of the theoretical models used, 13% resort to the quadruple helix, open innovation 13%, the triple helix 10%, and ehealth 7%. The USA concentrated the development of innovation ecosystems. Quadruple helix and open innovation, were the theorical models frequently used, both includes society as part of its implementation.

Keywords

Innovation systems, health innovation, health, health ecosystem



This article is included in the Health Services gateway.

Open Peer Review

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Any reports and responses or comments on the article can be found at the end of the article.

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Introduction

Innovation generates knowledge and comprehensively addresses solutions of all kinds, including health, environment, poverty, and security.¹ Innovation can become a solution for health equity,² this becomes tangible through medical devices, care models, health processes, and medications, where scientific and technological health knowledge is critical.³

Innovation ecosystems are today considered the most prominent driver to be built and nurtured to reap innovation's benefits. It reflects a paradigm shift, where innovation is becoming a centerpiece of a socioeconomic development model for cities and regions.⁴

Several authors have defined this structure, Walrave *et al.* conceive it as a network of interdependent actors that combine specialized but complementary resources or capabilities in the quest to co-create and deliver a global value proposition to end users and receive the derived gains in the process.⁵ For his part, Gobble indicates that "they are dynamic and purposeful communities with complex and intertwined relationships based on collaboration, trust, and co-creation of value and specialized in the exploitation of a shared set of complementary technologies or competencies".⁶

Different theoretical models have been proposed in the literature to structure or manage innovation ecosystems: quadruple helix, triple helix, open innovation, and digital systems, among others. They differ in the conformation of the actors involved and the methodology for the approach to developing innovation projects. Nevertheless, the above ends up being relevant at the moment of knowing the dynamics, not only of the components that interact within it, but also from the perspective of the actors that integrate it.

This article aims to analyze health innovation ecosystems to learn about the countries where they are developed and the theoretical models to which they resort.

Methods

This systematic review was conducted by searching PubMed, IEEE, and Science Direct databases for articles focused on health innovation ecosystems, published from January 2010 to December 2020, relevant to some types of health innovations articulated in an ecosystem.

Identification

MeSH validated search terms were used: "innovation", "ecosystem", "politics", "Health", "Process", "System". In addition, additional articles were identified by performing similar searches in Google Scholar and reviewing references identified in relevant publications.

The search strategy used for the databases was ALL (("Innovation" AND "Ecosystem" AND "Health") OR ("Politics" AND "Innovation" AND "Health") OR ("System" AND "Innovation" AND "Health") OR ("Process" AND "Innovation" AND "Health")).

Screening

We excluded articles related to innovation ecosystems in fields other than health. Conference presentations, congresses, or trials on innovation were excluded. The authors applied inclusion and exclusion criteria independently (abstract and full article), and consensus resolved uncertainty.

Inclusion

At least two authors independently extracted data using an excel template designed for this systematic review. In addition, the included results reviewed by an external reviewer.

The quality of evidence assessed using the Standard Quality Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields and the SANRA (Scale for the quality Assessment of Narrative Review Articles) guidelines. It was established that quantitative papers with a score equal to or higher than 10 would be taken into account; for qualitative papers, the score would be equal to or higher than 8, and for systematic reviews, the score would be 6.

The ROBIS tool was used to assess the risk of bias in the systematic review, using a rigorous methodology for the different research domains: study eligibility criteria, identification and selection of studies, data collection, evaluation of the study, synthesis, and findings.

The results were plotted in a structural network diagram considering the relevance, intermediation, and relevance of the different nodes (innovation ecosystem actors and innovation models), identifying the relationships between nodes according to the results to analyze the models with the best connections and the most relevant actors.

The included studies were evaluated with the screening instrument "PRISMA" and the main results met the inclusion criteria.

Search

For this, a peer review is applied, blindly and independently, who must review the list of studies thrown by title or abstract for a first sieve, following a checklist (inclusion criteria) to make the decision if the study is included/excluded. In the first stage, controversies (contrary decisions between the two evaluators) were resolved by consensus; in case of not achieving it, a third evaluator made the decision. Items included in the first sieve were equally divided for full-text reading for the purpose of evaluating the usefulness of the article and extracting the information of interest defined in the domain of analysis.

Rayyan was implemented as a tool to manage evaluation and inclusion of the studies organized by labels according to the inclusion and exclusion criteria. Once the title had been read, and the abstract was classified into labels according to the criteria, if the article was excluded, the reason was related according to already established labels.

The protocol rests on the research and innovation committee at the Faculty of Medicine and the Graduate School of Universidad CES.

Results

The variables taken into account in the results are: year, city, theory or model used in the innovation ecosystem, health area involved, type of health professionals who participated.

The initial search yielded 285 articles; after eliminating duplicates, 278 articles remained; after reading the titles, 94 articles were selected; after reading the abstracts, 56 articles were selected, and 20 papers focusing on information technologies were not taken into account. Finally, the articles were read applying the defined inclusion criteria, and 32 articles were selected.

According to the SANRA guide (scale for the quality assessment of narrative review articles), 30 articles were analyzed for review of quality criteria; two articles were excluded since the qualification according to the defined guide was lower than indicated (Figure 1). The data is available in the dataset called Ecosystem in health located in the DOI https://doi. org/10.7910/DVN/NKFCKF

The possible causes of the heterogeneity between the results of the study are that the studies were classified in terms of: Emerging technologies, Innovation and research, and Information technology, these were included; Conferences, Smart cities, Other health issues, Education, and Ecology, were excluded due to the focus of what is intended in the objective of the study.

Regarding the health innovation ecosystems reviewed, 40% are located in the USA, 13.3% in South Africa, 10% in the UK, 6.67% in Namibia, and the remaining ecosystems represent 30% (Figure 2).

Concerning the models used in the analyzed health innovation ecosystems, we observed that the quadruple helix is equivalent to 13%, open innovation represents 13%, the triple helix corresponds to 10%, and ehealth (use of information and communication technologies for health) corresponds to 7%. In addition, the review shows other models which were the basis for this design.

The innovation ecosystems found in the literature were specialized in the health area. Thus, six models were widely applied to health areas; eight were about digital health and other specialized ecosystems (Table 1).

Actors involved in these ecosystems, which also promote healthcare, have primarily supported the concept that new, emerging innovations and technologies can transform healthcare into an increasingly patient-centered and transparent model, thus improving outcomes and reducing costs.

One of the analyzed categories was the functioning of the ecosystem in terms of its processes in certain relevant aspects such as ethical, political, and legal components. As well as management of ideas, involvement of users in usability



Figure 1. Article selection algorithm.



Figure 2. Countries where health innovation ecosystems are developed.

Ecosystem name Country Theory	Country Theory	Theory		Actors	Health area	Quality of the
						of the paper
Digital health United States SI innovation cr ecosystems	United States SI cr	5 2	DL focuses on how value eation occurs	Company - consumer, co-creation, consumer - consumer	Broadly applied to the entire health sector	23
Digital Health South Africa Qu Innovation Ecosystem for South Africa	South Africa Qu	nờ	adruple-helix components	Government, industry, NGOs, community	Digital health broadly applied to the entire healthcare sector	20
Ecosystem of mHealth Malaysia Pe Ve	Malaysia Pe Ve	Ve Ve	rsonal Health Record (PHR) - ry Small Aperture Terminal	Patients, hospitals/clinics, mHealtrh developers, caregivers, physicians, ministry of health, other allies	Digital health broadly applied to the entire healthcare sector	20
Digital health South Africa Tri innovation ecosystem	South Africa Tri	T	ple Helix systems	University - Company - State, based on the triple helix model.	Digital health broadly applied to the entire healthcare sector	20
Innovation ecosystem England ST of regenerative ad medicine ini	England ST ad ini	ad in	RATIS (Strategic planning of lvanced technological novation systems)	Small businesses, hospitals, pharmaceuticals, government	Regenerative medicine	20
Ecosystem of medical Germany eC. care for patients with Parkinson's disease (PD).	Germany eC. Per	e Co Per Pat	are for Moods from Kaiser manent - Digital Health thways (DHP).	Patient, caregiver, physician, hospital	Parkinson	20
Personalized Belgium Trip medicine innovation ecosystem	Belgium Triț	Trip	ole Helix systems	Physicians, health care facilities, public payer	Personalized medicine	20
Healthcare South Africa Qu Innovation Ecosystems	South Africa Qu	ηQ	adruple-helix components	Workforce, information, medical technologies, health, financing, leadership and governance	Digital health broadly applied to the entire healthcare sector	20
Advanced United States Re. manufacturing (RI innovation ecosystems	United States Re((RI)	(RI)	gional Innovation Systems S)	Original Equipment Manufacturers (OEMs), SMEs, Startups, Universities)	Advanced manufacturing - medical devices	20
Entrepreneurial England De ecosystem health Orr	England ecc Or	De O	finition and dimensions of system health: Vigour, ganization, Resilience:	University of Cambridge, consumers and focal companies drive entrepreneurship clusters such as Silicon Valley, governments and industry associations	Broadly applied to the entire health sector	19

Table 1. The innovation ecosystems found in the literature were specialized in the health area.

Author	Ecosystem name	Country	Theory	Actors	Health area	Quality of the paper
Hudes M. K. 2017 ¹⁷	The Health Care Ecosystem	United States	Prediction and verification model	Healthcare providers, government, patients, medical technologies, devices and diagnostics (MedTech), biologic drugs and pharmaceuticals (BioPharma)	Digital health broadly applied to the entire healthcare sector	19
Tripoliti et al. 2019 ¹⁸	Hearten KMS	United States	New York Heart Association (NYHA) estimate.	Public health researchers, policy makers, clinicians, regulatory agencies, and the general public to monitor the effects of change in the patient space	Heart failure	19
Fan Li et al. 2014 ¹⁹	Tuberculosis vaccination innovation ecosystem	South Africa	Open innovation	Traditional centers of knowledge production, such as corporate pharmaceutical R&D laboratories, research institutes or universities, entrepreneurial companies or government	Tuberculosis	19
Chong N. K. et al. 2020 ²⁰	Digital Child Health Ecosystem	England	Learning health care system	Patient, pediatrician, health care institutions, community	Children's health	18
Ejehiohen et al. 2017 ²¹	Digital Health Innovation Ecosystem for the Namibian	Namibia	eHealth Ecosystem that connects different health institutions together	Physician, systems analyst, research professor, project manager, system administrator	Digital health broadly applied to the entire healthcare sector	18
Goldman M. 2012 ²²	Pharmaceutical innovation ecosystem	United States	Quadruple-helix components	European Federation of Pharmaceutical Industries and Associations, academia, hospitals, patient organizations, regulators, small and medium sized companies	Pharmaceuticals	18
Kerr D. et al. 2018 ²³	Digital diabetes ecosystem	United States	The drivers towards a technology focused system of care are multifactorial	Patient, care team	Diabetes	17
Catarinella F. S. et al. 2016 ²⁴	Digital health assessment in rheumatology	The Netherlands	Model of patient-oriented outcome assessment	Patient, physician, rheumatologist, scientific community, nurse, laboratory, society, funders	Rheumatology	16
Hesse B. W. et al. 2011 ²⁵	Oncology Health Information Ecosystem	United States	Health Information Technology for Economic and Clinical Health (HITECH) Law of 2009.	Patient, caregiver, physician, hospital	Cancer	16
Mitra S. et al. 2020 ²⁶	Surgical innovation ecosystem	India	Conceptual model to health hackathons in low-resource settings.	International academic institutions, students and professors	Surgery	16

Author	Ecosystem name	Country	Theory	Actors	Health area	Quality of the paper
Pombo- Juárez et al. 2017 ²⁷	Multi-layer innovation ecosystem	Austria	Multi-layer foresight	Government, companies, universities	Broadly applied to the entire health sector	16
Rucinski A. et al. 2013 ²⁸	Disruptive Innovative e-Health Ecosystem for Regenerative Medicine	Poland	Smart Specialization and Cohesion Policy the Commission	Universities, research institutions, healthcare institutions, ICT companies, market-oriented companies: Data Techno Park Ltd. and Wrocaw Research Center EIT + Ltd.	Regenerative medicine	15
Chen S. C. et al. 2020 ²⁹	Connected health ecosystem	China	Triple Helix systems	Software developers, hardware manufacturers, clinical and care service providers, internet and telecommunication companies	Digital health broadly applied to the entire healthcare sector	12
Stephanie L. & Sharma R.S. 2020 ³⁰	Digital healthcare ecosystem	United States	Network of digital health communities	Patient, hospital, practice, physician, shared resources, government, laboratories, researcher, organizational mediator	Broadly applied to the entire health sector	12
Iyawa G. E. et al. 2019 ³¹	Namibian Digital Health Innovation Ecosystem framework	Namibia	frameworks of Prat et al.	Patients, stakeholders, local and global networks of experts, health care institutions, etc.	Broadly applied to the entire health sector	11
Ejehiohen G. et al. 2016 ³²	Digital health innovation ecosystems	United States	Digital ecosystems	Community, content, practice, technology, biological species, economic species, digital species, digital environment, security, trust, confidence	Broadly applied to the entire health sector	11
Park A. et al. 2019 ³³	Personalized medicine innovation ecosystem	Canada	Open innovation and Model the Moore	University of British Columbia, industry liaison office, simon fraser university, list of spin-offs, lifesciencies BC, list of science clusters BC	Personalized medicine	10
Silva P. J. et al. 2018 ³⁴	Omics innovation ecosystem	United States	Open Innovation	Clinic, academy, biopharmaceutical industries	Precision Medicine - Genomics	8
Tseng et al. 2018 ³⁵	Brigham and Women's Hospital Digital Health Innovation Group (DHIG)	United States	Quadruple-helix components	All hospital staff	Broadly applied to the entire health sector	7

Table 1. Continued



Figure 3. Graph of relationship nodes of the actors in the framework of innovation ecosystems.

processes, all centered on protocols, guidelines or care models, confidentiality or privacy in the handled information, staff training and education, culture management, and in some cases, investors are included in the ecosystem. All always have healthcare at the center or as a relevant topic.

The innovation ecosystems' functioning, processes, and tools vary according to the model used and the actors involved, as shown in Table 1. The cooperation of the actors is essential for articulating and generating the expected results for the developed ecosystem. Synergy is presented to achieve joint actions of the ecosystem elements and to give better results. Cooperation among several actors allows for more significant overall effects than the sum of the benefits each would achieve individually. This is why an innovation ecosystem determines the evolving set of actors, activities, artifacts, and institutions, including complementary and substitutive relationships, which are essential for the innovative performance of an actor or a population of actors. It is where these structures' different actors' connections must be recognized.

A network diagram was used to identify which innovation models were most relevant in this systematic review and which actors were most connected (Figure 3).

When analyzing the trends or critical nodes in the health innovation ecosystems and the actors that are part of them (Figure 2), the first most relevant trend or node is that of hospitals/clinics, which are considered as the "enterprise" and cover different levels of care, and for the present review, are of a medium or high level of complexity. This trend or node is related to 13 theories presented in this work and the different actors (state, academia, and community).

In second place is the tendency or node of patients who are part of the community and are people who have different pathologies or are related to their country's health system in different ways. This node has 11 connections with the theories, and the theory of the triple helix systems presents the most significant relationship.

Regarding the nodes with the highest relevance according to the quadruple helix theory, in the community helix, the patients' node has a relevance of 0.917/1; in the state helix, the government node has a relevance of 0.739/1; in the company helix, the pharmaceuticals node has a relevance of 0.661/1, and in the academy helix the researchers' node has a relevance of 0.470/1.

The node of the actors had the highest intermediation with hospitals/clinics with a value of 367.17, indicating that this is a cut-off vertex for many geodesics between actors. Likewise, the node of models with the highest intermediation was the

triple helix system with a value of 279.14, showing that this node had the highest frequency among the geodesics or the shortest paths of other actors.

Nodes with the highest relevance or importance were hospitals/clinics, with a value of 1/1, patients with a value of 0.917/1, and the triple helix system with a value of 0.851/1. In fourth place was the government node with 0.739/1, and in fifth was the digital health community network with a value of 0.729/1. These nodes were the most involved in many ties, being the most popular.

The most relevant model was the triple helix system with 0.851 out of 1, with 11 relationships and intermediation of 279.14. On the other hand, the least relevant model was the so-called learning healthcare system with 0.163/1 with three relationships and intermediation of 27.49.

Discussion

The analyzed health innovation ecosystems recognized the complexity and importance of the interactions of the different actors in the innovation process. They had very accentuated factors in health, facilitated the understanding of the dynamics of health in the city where they were installed, some supported the formulation of public policies, and facilitated the identification of regulatory failures. Also, they recognize the role of users/patients/citizens, companies, organizations, and government as essential factors for creating social value.

The models had components consisting of university, industry, and government spheres. Each with a range of actors, such as individual and institutional; innovators in R&D and between institutions hybrids. Relationships between components technology, transfer, collaboration, conflict moderation, collaborative leadership, substitution, and networking. Performance systems generate diffusion and utilization of knowledge and innovation in business, social, cultural, and political environments seeking consensus.

Starting from the notion of Walrave *et al.*⁵ on an innovation ecosystem and throughout this review, it can be understood that the actors identified in said ecosystems are diverse but have a common goal, to enhance an aspect of health in which the region or country wishes to advance due to its impact. Health areas with this development range from pediatrics, urology, and surgery, among others. Ultimately, these ecosystems integrate actors, processes, tools, and resources, generating an impact on patients. All ecosystems aim to improve citizens' quality of life and medical care.

The most used model in these ecosystems is the quadruple helix, based on the approach of Etzkowitz and Leydesdorff. These authors conceptualize innovation ecosystems as "inclusive because the university leads the generation and transfer of knowledge to society through reciprocal and continuous relationships with industry".³⁶ This model increases the probability of innovation regardless of the type (product, process, services, or a combination of these). Furthermore, the greater the number of agents that cooperate in the model, the greater the chances of business innovation, confirming a synergistic effect between agents.³⁷

In particular, the quadruple helix model was identified in the review as one of the most frequent in the included publications. This model focuses on taking advantage of the learning processes and dynamics that allow the hierarchical policies of the university, industry, government, and society's priorities to interact with each other. In this way, and taking into account the current dynamics of societies and, in line with including inclusive models, their increased frequency can be explained.³⁸

The growing potential to benefit from innovations highlights a significant problem faced by health systems: how to take advantage of the knowledge developed in these solutions that generally face many resource challenges in reaching patients.³⁹ Access to health services through hub-and-spoke service delivery models that as drivers of diffusion have complementarity with the existing medical infrastructure of institutions and reduce barriers to solution-mediated access with solutions such as the implementation of telehealth and other approaches.

The impact of innovation processes has been widely explored in the public health literature, and there is a consensus among the innovation ecosystem actors and public health policymakers that adopting innovation in its different types promotes an increase in the population's health status.

However, the frameworks, models, and tools used by the different innovation ecosystems in the world and identified in this review correspond only to those that have been the subject of academic analysis and are published in scientific journals. Thus, gray literature may have left out other ecosystems presented to the community in general. Therefore, the results of this review should be considered in this sense.

Future studies suggest evaluating ecosystems in terms of integrity, efficiency, effectiveness and robustness, fragility, and evaluation of medium and long-term impacts and from other perspectives.

Conclusions

Innovation ecosystems are today considered the most prominent driver to be built and nurtured to reap innovation's benefits. This reflects a paradigm shift, whereby innovation is becoming a centerpiece of a socioeconomic development model for cities and regions.

This paper provided the results of a systematic literature review to identify the variety of health innovation ecosystems in developed and developing countries. Also, the present work identified models, methodologies, and tools in these structures. Different themes emerged from the selected literature on health innovation, clinical application areas, and institutions involved.

Quadruple helix and open innovation, the theorical models most frequently used, both include society as part of their implementation.

Data availability

Underlying data

Havard Dataverse: Underlying data for "Innovation ecosystems in health: countries and theoretical models used", https://doi.org/10.7910/DVN/NKFCKF.⁴⁰

Reporting guidelines

OSF: PRISMA reporting guidelines for "Innovation ecosystems in health: countries and theoretical models used", https://doi.org/10.17605/OSF.IO/M8H2Z.

Data are available under the terms of the Creative Commons Zero "No rights reserved" data waiver (CC0 1.0 Public domain dedication).

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