Analysis of Driving Factors Influencing Human Vaccine Development in Iran: a Cross-impact Analysis

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Abstract

Background:

Despite many successes in Immunization programs in Iran, vaccine policymaking has confronted with important weaknesses, and more effort is required to improve progress and prepare for the preferred future. In order to address the challenges facing vaccine development, this study has defined to identify influential factors on the future of development of human vaccines in Iran for strengthening evidence-based policy-making.

Method:

This mixed-method study aimed to analyze the factors affecting the future of human vaccine development using Cross Impact Analysis. Firstly, with a scoping review, the factors affecting the future of human vaccine development were identified. Secondly, a semi-structured interview was carried out with the determined experts in this sphere to add more factors and confirm the identified factors in the Iran context. Finally, a cross-impact analysis (CIA) approach was applied to understand the complex relationships between the given factors. Thematic analysis was used for the qualitative data and MICMAC analysis was applied for characterizing the relationships between factors.

Results:

Seventeen key driving forces factors were first identified through reviewing and interviewing. These factors are weighted from zero-three and analyzed by MICMAC software. The CIA technique characterized the effect of each one of these factors on vaccine development and then elaborated on the interaction between them. The results revealed that strong leadership and governance, innovation ecosystem, and immunization information systems were critical driving forces for developing vaccines in Iran. In fact, the degree of influence of these factors is much stronger than the degree of their dependency in the future. So, the vaccine development system is basically dependent on these key drivers.

Conclusion:

This study explores interactions among factors affecting vaccine development by using cross-impact analysis. It indicates that interactions among the identified factors do have a major influence on the overall system. Understanding the interactions among factors help policymakers formulating successful strategies for shaping a desirable future. Future studies could ratify the findings from this research applying other methodological approaches.

Background

Immunization is one of the cost-effective interventions to prevent diseases and mortality, which has always been in the center of attention in modern medicine (1). Since the invention of vaccines in 1796 by Edward Jenner, the science has consistently witnessed significant advances such as genomics, reverse

vaccinology, computational vaccination, recombinant vaccines, and, more recently, the prospect of "universal vaccines"(2) .

On the other hand, despite considerable developments in the prevention and treatment of infectious diseases, pathogenic microorganisms are still considered a threat to public health(3). Although conventional vaccines have been useful in the treatment or eradication of some diseases, emerging and re-emerging diseases have encouraged developing new vaccines(4).

In fact, in the interconnected world of today, where connections and international travels facilitate the transfer of diseases across borders, the threat of emerging and re-emerging diseases must always be considered and a coordinated, sustainable prevention program including developing the required vaccines and other immunologic agents should be designed to prevent disease occurrence and outbreaks. The vulnerability of the communities to the outbreaks of Zika virus, Ebola virus, and more recently, 2019nCoV virus, and their subsequent social, economic, and political problems support a proactive strategy(5).

Therefore, the world focus on better selection and support of novel vaccines, reassurance on the implementation of vaccines in countries with weak health systems, provision of the vaccines for all age groups, and the global commitment to the sustainable development has always set the development of vaccines at high priority (6).

Furthermore, unprecedented technological advances in genome sequencing, vaccinomics, molecular and cellular immunology, biological systems, bioinformatics, artificial intelligence, machine learning, genomics, epigenetics, computational biology, nanotechnology, and reverse vaccinology have brought a significant paradigm shift in the development of vaccines, shifting the focus from diseases to effective and sustainable immune responses against diseases (7–9). However, the concern about the lag in the world of vaccines in relation to these rapid changes is not yet resolved (10).

Besides, the evidence shows severe obstacles in the development of vaccines despite their proven benefits in immunization (11, 12). Therefore, it requires planning, futuristic vision, and making new strategies for sustainable development and provision of vaccines to achieve immunization and public health goals in the present and future, in addition to preparation for dealing with the emerging infectious diseases and changing trends effectively and at the appropriate time(13).

A review on the upstream documents in the field of vaccination in the Islamic Republic of Iran shows the mentioned innovations are seldom implemented in the process of developing vaccines, while in order to prioritize such issues, we first need to form a political dialogue(14).

Thereby, the present study aimed to investigate the interactive relationship between the effective factors in developing human vaccines in Iran. These interrelationships analysis between the factors are called cross-impact analysis which is a method to diminish the ambiguity and complexity of the system. The

identification of the main factors means that any modification in critical factors will affect the entire system and they should be considered in the future of the vaccine development system.

The history of human vaccines in Iran.

The World Health Organization (WHO) introduced the Expanded Program on Immunization in 1974 in all countries, aiming at vaccinating against measles, polio, diphtheria, tetanus, pertussis, and tuberculosis(15, 16).

Following the adoption of the Alma Ata Declaration on primary healthcare by Iran in 1978, the Expanded Program on Immunization is now a major part of PHC, and the medical university presidents across the country are responsible for its implementation, leading to the rapid development of the primary health network. With the establishment of the immunization development program, remarkable achievements have been made in the prevention and control of vaccine-preventable diseases and the health promotion in Iranian children(17, 18).

Currently, all the Iranian children are vaccinated against tuberculosis, hepatitis B, polio, diphtheria, pertussis, tetanus, Haemophilus influenzae type B, measles, rubella, and mumps. The country has been free of polio for more than 15 years, and neonatal measles, rubella, and measles have been eliminated, and diphtheria, pertussis, and mumps have been controlled. The last vaccine to be included in Iran's national vaccination program is the Haemophilus influenzae type B vaccine, which is a pentavalent vaccine in combination with the DPT vaccine and hepatitis B vaccine and is injected for all Iranian children at the ages of two, four, and six months since late 2014. Recently, two rotavirus pneumococcal vaccines have been approved but not yet produced and implemented, and Iran intends to purchase them; if so, Iran's comprehensive immunization system will include 12 vaccines(17–19). Figure 1 shows vaccine timeline in Iran.

Method

Study design

A mixed-methods design was used for this study. The two-step qualitative phase consisted of 1) a scoping review to identify the factors affecting the future of vaccine development, and 2) a semi-structured interview for adding more contextual factors and confirming previous factors. The quantitative phase consisted of Cross-Impact Analysis by using Cross Impact Matrix Multiplication Applied to Classification (MICMAC) software to explore the relationships between factors. Figure 2 illustrates the study design. In the following, the research method of each phase is described separately in detail.

First Phase: a scoping review was used to identify the main factors affecting the future of vaccine development. the framework of Arksey and O'Malley(20) was used for performing scoping reviews in five stages as follow:

Stage 1: Identifying the research questions. The main question was: what factors affect vaccine development in the future?

Stage 2: Identifying the relevant studies. The related studies were searched in Scientific Information Database includes Scopus, PubMed, EMBASE, Web of Science, the Cochrane Library, World Health Organization, Scientific Information Database (SID) and national Immunization policy documents from various sources. The search was conducted from 2000 till 1 June 2020. The list of references in the selected studies was searched as well.

The searched keywords were “Horizon scanning”, “vaccine development”, “Vaccine Policy”, “next generation”, “driving force” AND “Immunization, “vaccine strategies”, “vaccine production”. The search strategy for PubMed database was as follows and was modified for other databases (Table 1).

Table 1 Search strategy for the main components of

Searched Databases	PubMed, Scopus, Science direct, Web of Science, and Scientific Information Database (SID)
Search strategy	#1 AND #2
#1	“Horizon Scan” OR Foresight OR “Futures Studies” OR “Road Map” OR Driver OR “Driving Force” OR “Key Factors” OR “Policymaking” OR “Strategy” OR “Policy”
#2	Immunization OR Vaccine OR “Vaccine Development” OR “Vaccine Innovation” OR “Vaccine Production” OR “Vaccine Strategy”
Limitations	Language: articles with at least an abstract in English,

Stage 3: Study selection. All studies obtained in the search stage were transferred to Zotero software. Two authors (SG and AA) independently screened citation titles and abstracts, and then reviewed potentially relevant articles in full. All study designs, which provided information on vaccine development were eligible for inclusion.

Stage 4: Charting the data. A charting form was developed by two reviewers (SG and AA) to determine extracted variables. The data extracted from the studies included the general features (author’s name, country), methodological data (type of publication, study design, research objective) and key results.

Stage 5: Collating, summarizing, and reporting the results. Data analysis was carried out based on the data extraction form. Then variables extracted and introduced to further investigation.

Using the search strategy shown in table 1, a total of 4,429 studies were extracted from all mentioned databases. After eliminating duplicate documents, 792 papers were selected for the assessment phase. In order to select relevant articles, we performed an iterative three-step appraisal process; so that in each

step we modified the search strategy, searched the databases, and reviewed new papers. The objective of the appraisal phase was to identify articles that explore the factors affecting vaccine development in the future.

Two reviewers screened the extracted articles independently at three levels. At the first step, they screened titles of the articles independently. At this step, the researchers selected 94 articles for further appraisal. Then, two reviewers scanned the abstracts and excluded those that were not consistent with the objective appraisal process. At this step, 40 full-text articles were selected for further evaluation. Eventually, the reviewers apprised full-texts and 24 studies were included in the final analysis. At all stages of screening, a third researcher reviewed cases of disagreement.

Second Phase: A qualitative study

As mentioned in study design, the focus of the first step of the cross-impact analysis is on identifying a set of comprehensive factors that affect the phenomena from a variety of perspective, to this end, a series of semi-structured interviews were conducted with related stakeholders to explore the main factors of the future of vaccine development in Iran and confirm the factors were explored in the previous step. Interviewees were selected using a snowballing strategy which ensured the selection of who is knowledgeable in the vaccine field.

Sampling and Inclusion Criteria

For in-depth interviews, stakeholders and key informants were selected through purposive and snowball sampling. Interviewees included health policymakers, vaccine researchers both in public and private sectors, academic members from different disciplines, such as Pediatrics, Virology, immunology, epidemiology, pharmacology, infectious diseases, public health, and biotechnology.

Data Collection

In total, 13 in-depth interviews were conducted between December 2018 and June 2019 mostly by S.G. Informed consent was obtained from each interviewee. The interview guide was developed through the literature review and a series of meetings amongst researchers. Prior to the interviews, the main objective of the research was clarified and an information sheet was provided. The interviews were conducted in the participants' offices, or another place that was convenient for the interviewee.

Data Analysis

Data were analyzed based on thematic content analysis and key emerging themes were identified and consolidated in a framework that was checked and refined iteratively. The authors read the transcripts several times to capture meaning units that are related to the subject. Second, data were coded by AAK, SG in order for the initial codes to be reviewed jointly to create the final set of codes by consensus. The codes were merged into larger categories that lead to a set of themes. These themes were revised jointly by two of the investigators to ensure that they sufficiently answered the research questions. In the final

stage of the analysis, the second author of this study identified the key characteristics and made the final interpretation of the data set as a whole.

Trustworthiness

To enhance dependability, data collection process was done mostly by the SG; an interview-guide was applied to ensure all key informants were asked the similar queries. To strengthen credibility data analysis process was accomplished by two authors (SG and AA). To improve transferability of the data, Interview texts along with the extracted codes were sent to participants for verifying.

Phase Three: Cross Impact Analysis

The CIA technique is one of the most prevalent foresight methods(21,22) developed to identify the relationships among the key variables defining the vision of the future. The method reveals the structure of relations of dependence and influence between variables and points out the key variables in the evolution of the system. Finally, the method determines which of these variables the most important role are in the future. CIA comprises the following steps:

Variable definition: The results of the previous steps are aggregated into variables that affect the future of vaccine development.

Interactions analysis: Variables entered into the interaction matrix and the relationship between these variables is determined by experts. Row variables affect column variables. In other words, row variables are influenced and column variables are dependence. These variables are weighted according to the degree of influence from 0 to 3 (0 = non-existent, 1 = weak, 2 = medium, 3 = strong).

Chart analysis and visual representation of the interactions: this step identifies the roles played by the variables. An influence–dependence value is prepared to interpret the results. Each factor is assigned to a unique position on the graph according to its influence and dependence scores. Then, the chart is classified into 4 quarters reveals its individual role in relation to the system. In fact, the location of each factor in the map reflects its impact on the investigated issue. Figure 3 visualizes the graph and typology of variables described as follows.

- **Determinant/factors** also called influential are factors which located in the north-west quarter of the graph. The influent factors are the most critical factors since they can act on the system depending on how much we can control them as a key factor either of inertia or of movement. These factors considered as input variables in the system.
- **Relay variables** which situated in the north-east quarter are very influent and very dependent. These variables are divided two groups: stake variables which suited around the diagonal which will have strong chances to arouse the lust of major actors, since, given their unstable character, they are potential fracture points for the system; and target variables which located under the diagonal are more dependent than influent.

- **Depending variables**, located in the south-east position of the graph, are little influent and very dependent. Subsequently, they are principally sensitive to the evolution of influent factors.
- **Autonomous variables**, are situated in the south-west quarter which have little influent and dependent.

Selection of key variables: Considering chart analysis the variables with both high influence and high dependence are selected as key variables. In fact, variables which located on determinant position are key and critical.

Results

In this study, at the first phase of the study we conducted a literature review and semi-structured interview in order to identify the factors affecting the future of vaccine development in Iran. Using thematic content analysis approach, results from 26 related studies in addition 13 semi-structured interview, lead to emerging 17 main components. Table 2 displays the results of thematic analysis. At the second phase, we applied CIA method with the participation of 13 vaccine filed experts.

Based on number of variables, a matrix with dimensions of 17 x 17 is used. In this matrix, effect of each of these factors on each other was recognized by weighting scales (from 0 to 3). All factors involved in vaccine development are considered as a system with intertwined elements and in the form of one structure and the relationship between these factors is measured so as to extract superior factors with higher effects.

For pair-wise comparison of the factors, each expert completed a cross impact matrix and we entered the mean of results to MICMAC software and develop the interaction chart (Fig. 3**).** Based on the results of the CIA model presented in the Fig. 4, the main components of vaccine development located to the chart. These results show that strong leadership, immunization information system and innovation ecosystem have the highest influence in the shaping the future among the main components of vaccine development respectively.

Table 2
Final factors from interviews and literature review

#	Main Components	Sources
1	National Vaccine Research link to NITAG	(23)
2	International Collaboration and partnership	(24–28)
3	strong & multidisciplinary leadership and governance	(29–31)
4	Vaccine Advocacy and Communication	(32–34)
5	Private sector partnerships	(24,25,35)
6	Sustain and Innovative financing	(36,37)
7	Surveillance and monitoring system for diseases impact and vaccine coverage	(34–36)
8	Immunization Information Systems	(27,38)
9	research and development in vaccine vaccinology	(4,7,9,39–43)
10	Developing Vaccine Manufacturers' Network	(44,45)
11	life course immunization approach	(23,38,46–48)
12	Skilled and motivated workforce	(34,36,49–51)
13	Supply Chain Management	(34,36,44)
14	Convergence in science and technology	(9,37,44)
15	Vaccine Innovation Ecosystem	(10)
16	Social Marketing	(52,53)
17	Equitable Immunization Services	(34,36,37)

The number of repeated interactions between variables was considered two times. From a total of 270 evaluable relationships in this matrix, 19 relationships are zero, 44 relationships are 1, 130 relationships are 2 and 96 relationships are 3. As displayed in Fig. 3 in MICMAC analysis, the variables are categorized into four categories. The factors having low influence and low dependence are known as autonomous factors. Based on the results, Advocacy and communication, social marketing and convergence in sciences and technology are considered as autonomous which are relatively disconnected from the system. Supply chain management, life course immunization, vaccine manufacture networks and equitable immunization services are dependent variables having low influence but strong dependence.

The factors that have strong influence as well as strong dependence are included in third cluster and are called stake factors. The fourth category contains the independent factors which have strong influence

but low dependence. Since these factors are strong influence, they may be considered as the root causes of all the factors and are the “key factors” that affect the vaccine development process. Identification of these factors assist the policymakers to develop comprehensive approach for the future of vaccine development. The cluster of factors is shown in Fig. 4.

After determining the status of each factor affecting the vaccine development, the relationships of these factors were explored in the MICMAC software and the relationships of the effects of factors were shown in the Fig. 5.

Discussion

A better understanding of the future of a system is possible when it is deeply analyzed, and the contributing factors to it are identified. In the present study, based on the existing theoretical knowledge and intuitive and tacit knowledge of key scientists in vaccinology in Iran,

We identified seventeen key factors contributing to the development of human vaccines in Iran, and by analyzing the interaction between the factors, we depicted the relationship between them.

The results of the present study show that developing a human vaccine necessitates the existence of a comprehensive and efficient planning system in content and process. Countries have distinct and sometimes unique characteristics in terms of input, process, and output, and identifying these factors is a critical step in understanding the system accurately and helping the stakeholders and all those involved in the development.

As shown in Fig. 3, the MICMAC analysis showed that four variables, namely, research and development, expert human resources, monitoring system, and international collaboration, had the highest influence and dependency in vaccine development, and are the Intermediate variables. Four variables, leadership and strong governance, comprehensive security information system, innovation ecosystem, and sustainable and innovative financial resources, had a higher influence than dependency; they are located on the upper left side of the map and are considered the leading variables or key driving forces. The variables such as immunization industry infrastructure, quality, and reliable immunization delivery, and full vaccination coverage for all age groups are in the lower right area of the map and have a high dependency from the system. The three factors of advocacy, marketing, and convergence in science, were the independent factors.

In Levin's study, the diseases with epidemic potential, targeting regional needs, strengthening the vaccine delivery system, safety vaccine safety, the element of money, and individual behaviors were determined as the most important leading variables affecting the future of global immunization in the era of great convergence by 2035. This study showed that although these factors are still considered by the decision-makers, they will play a more prominent role in the future(5).

WHO Immunization Agenda 2030 has identified immunization to achieve the goals of universal health coverage, equal vaccine coverage for all ages, vaccine commitment and demand, considering the outbreaks and emergencies, sustainable vaccine supply, and research innovation in vaccine research as seven key strategies for all countries of the world by 2030(54).

One of the leading variables identified in this study was the establishment of a network of researchers inside the country and the development of international interactions in this regard. Desai and kamet(55) also state in their article that since a world free of vaccine-preventable diseases needs a global alliance, each country, depending on its capabilities and free from political contradictions, must act in this field. Access to the suburbs, remote areas, and politically unstable areas is still a barrier in reducing the immunity gap. The Global Vaccination Action Plan also emphasizes a global coalition in removing the existing inequalities. The outbreak of Ebola, Zika, and Coronavirus 2019, and the economic and social effects of them show that our world needs unity and solidarity more than ever before, regardless of political conflicts(56–58). The creation of the Solidarity Trial (which the Islamic Republic of Iran is a part of) concurrent with the COVID-19 pandemic shows a promising prospect(59).

Another influential factor extracted in this research was the strengthening of the research and development process in vaccinology in Iran. In this regard, the study of Kieny and Girard (60) showed that low- and middle-income countries should have the power to actively participate in the development and introduction of new vaccines according to their national priorities.

According to the study results, sustainable and innovative financing was one of the most important and influential variables in the matrix and is indicative of its prominent role in vaccine development. Considering that vaccine development is time-consuming and costly, sustainable financial support would be an incentive for knowledgeable investors. According to GBD estimates, approximately 60% of the total burden of infectious diseases in all ages belongs to those without vaccine (61), with more than 90% of the deaths in countries with low and medium incomes (62) The improvement of existing vaccines and the development of new ones is essential to reduce the gap between low-income and rich countries. The most important obstacle in this process is financing. G-Finder estimated that before COVID’19 pandemic, 938 million $- 75% of all vaccine resources in …..- was spent on three major diseases, AIDS, malaria, and tuberculosis (62, 63), while the world needs more resources and investments in the development of vaccines for neglected diseases, especially in low-income countries (20). A part of this negligence is due to its low return on investment. Plotkin et al. proposed the creation of an international vaccine development fund to overcome existing barriers and support scientists. This strategic investment, especially in times of crises such as Ebola, COVID-19, and the like, can save millions of people around the world (64, 65).

Another sub-factor identified in this study is the importance of prioritizing vaccines both in the Research and Development process and in the decision-making process to enter the immunization program; Bloom suggested that policymakers should work together at the national, regional, and global levels to identify priorities and plan for the development of vaccines. The US Institute of Medicine has recently developed a

new tool, Strategic Multi-Attribute Ranking Tool (SMART), to prioritize vaccines according to 28 features (66). The important factors in the decision-making process of introducing a vaccine to the national program in Iran are the epidemiology of diseases, feasibility, and cost-effectiveness, which is consistent with most parts of the world. In Saul's study, the element of cost-effectiveness and funding of vaccines was proposed as a critical element in prioritizing vaccines over the features of Smart tools.

Since 2010, 116 countries have introduced vaccines against major killers, such as pneumococcal pneumonia, rotavirus diarrhea, cervical cancer, typhoid, cholera, and meningitis, into their immunization program(67). Among these countries, Iran has not introduced vaccines such as pneumococcal, rotavirus, and HPV vaccines to its national immunization program despite several cost-efficiency studies(68, 69). The introduction of new and expensive vaccines to the health market intensifies the debate over who should pay and how much should be paid. The role of public-private partnerships is important in ensuring the provision of the best vaccines to the community with the least barriers (70). The most important challenges faced by vaccines that have utilized over the years and proved their effectiveness, is the continued implementation in low-income countries, especially when devoured by war and political turmoil. However, achieving global vaccination coverage requires serious cooperation and commitment from the public and private sectors around the world(71).

The costs of producing new generation vaccines have increased in comparison to most of the old vaccines due to new technologies and regulatory requirements. This has inhibited the introduction of some of the new vaccines to the national vaccination program in Iran. Therefore, new and sustainable financing methods should be utilized in vaccine development. Batson et al. have proposed the subsidy-based advanced market commitments method that can be used to consider a specific return on investment for the vaccine industry(72).

The analysis of the results identified the research and development factor as a key influential factor. The research and development processes of vaccines are mainly governmental in Iran. In many developed countries, in addition to the government, the pharmaceutical industry also supports the vaccine research and development process. In low-income countries, the supply and development of vaccines are conducted by institutions such as Gavi, Melinda Gates, Welcome Trust, and Path(73). Evidence suggests that vaccine development in the future is heavily dependent on public-private partnerships, and the public sector alone could not afford the costs of vaccine development. In addition to vaccine research and development, the coverage and access to vaccines also require the participation of the private and public sectors(74, 75).

Improving the quality of immunization data using an integrated immunization system was one of the topics in this study. In this regard, the study of Chopra et al. regarded the use of machine learning knowledge and satellite imagery to identify children in difficult-to-reach areas, along with information technology systems as an essential innovation in improving vaccination coverage(74).

Another influential factor is the role of vaccine development companies. In addition to the prominent role of vaccine production and distribution, companies involved in the vaccine production process play an

important and often unknown role in the field of global health management. These companies are involved in the identification of pathogens, clinical trials, and collaboration with regulatory agencies and related scientific academies. The social responsibility of these companies in the cost-effective distribution of vaccines in areas that need life-saving vaccines is undeniable(76). The main vaccine producers in Iran are the Razi Vaccine and Serum Research Institute and the Iran Pasteur Institute, both of which have more than 80 years of experience in this field. Vaccine production complexities, high costs, and the monopoly in the vaccine supply market were the key factors of the low presence of vaccine manufacturing companies in this study. In this regard, Gordon's study(76) showed that 80% of the world vaccine market is owned by five major companies, Pfizer, Sanofi, Merck, GlaxoSmithKline, and CLS, two of which are in the United States and the rest in Europe. Cuba, India, Indonesia, and China are the emerging vaccine markets(76).

The government has numerous political leverages to encourage the vaccine innovation ecosystem, which can encourage the national coordination between industrial, research, and educational projects and renovate the university-industry relationship.

The results of this study showed that capable and multidisciplinary human resources are a highly effective factor in the development of vaccines. The creation of specific and joint training courses and programs with reputable international institutions, the transfer of new knowledge and skills from university to industry, and the development of biotechnology and vaccination disciplines were the sub-categories of this research. In the study of Traicoff et al.(49), they divided the human resource competencies in vaccine development into five areas and four sections.

Conclusion

The present study has recognized the critical driving forces which affect the vaccine development by conducting a scoping review and semi-structured review. A total of seventeen factors were finally identified and visualized by using the CIA approach. The position of the 17 influential factors and their characterization using MICMAC analysis is key to understanding how they affect the vaccine development process and can be used for directing policy making in this sphere. Identification of the factors and considering the relationship between them will have a remarkable effect on the vaccine development plans in the future.

We believe that the study findings support these recommendations. The first and most important decisive intervention of the Iranian health system should be on full coverage of vaccinations and the elimination of shortages of essential vaccines. This may be by strengthening the public sector or encouraging the private sector to provide safe and effective vaccines at reasonable prices. The strategy of importing vaccines such as rotavirus, pneumococcus in the short term, and technology transfer and in-house production should be considered as a medium-term strategy. Even with a strong will and coherent planning, Iran can play a key role in eliminating the shortage of essential vaccines in the region.

Iran should also strengthen its disease monitoring and pandemic forecasting system and continue to prioritize its public health-based immunization program. Strategic collaborations with institutes, scientists, and vaccine companies and manufacturers are also an issue that has been overlooked in Iran. Finally, the government must actively encourage independent policies, cost-benefit studies, and broader national research and development on various aspects of vaccines and public health in order to make more informed decisions. Given all this, Sustained and coordinated efforts should be done to bring the Iranian vaccine into an era of global leadership.

Limitation

Notwithstanding some contributions arising from this study, there are definite limitations. First, the method of analysis is directed by a literature review and interview that yields a set of variables and the cross-impact analysis through interviewing experts. Although the researchers try to review the literature comprehensively and conduct the interviews with strong domain knowledge of experts, future studies could conduct with using conventional approaches to validate as well as improve the generalizability of results. Second, the CIA approach is based on the participant's mental models and perceptions. In this study, experts are chosen from diverse fields to consider more perspectives. Third, this study concentrated on the unique Iran context, which has been unexplored in past studies hence, is only limited to seventeen factors. In future research, more than these factors would be explored.

Declarations

Ethics approval and consent to participate

Ethical approval for this study was obtained from the Ethics Committee of the National Institute for Medical Research Development in Iran (IR.NIMAD.REC.1395.8874). Participation in this research was voluntary. All participants were informed about the study objective and design and they confirmed the written informed consent to participate. All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and materials

The transcripts and datasets analyzed during the current study are not publicly available in order to maintain confidentiality of participants. Only the investigators are granted access to these datasets. Further information is available from the corresponding author on reasonable request.

Competing interests

None of the investigators involved in this study have a conflict of interest.

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Authors' contributions

MML, SG, and AAK conceptualized the study. All authors contributed to the study design. SG, AAK, ATB, and SMZ conducted the data collection. SG and MML conducted the data analysis. SG wrote the first draft, with significant contributions from MML, AE, ATB, and SMZ. All authors contributed to manuscript revisions. All authors read and approved the final version before submission.

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Figures

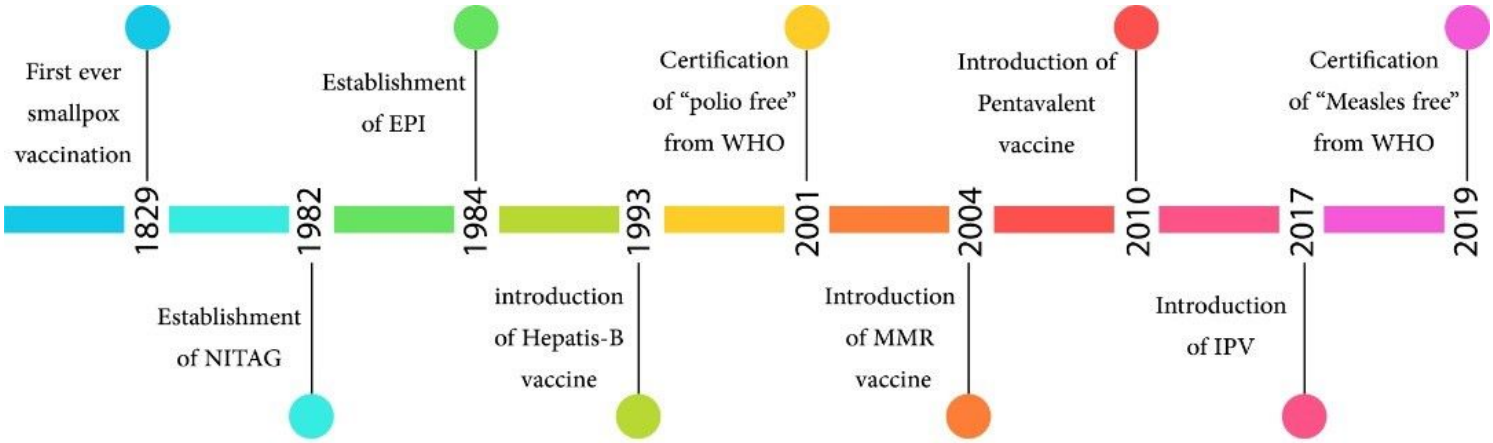

Figure 1

Vaccine Time-Line in Iran

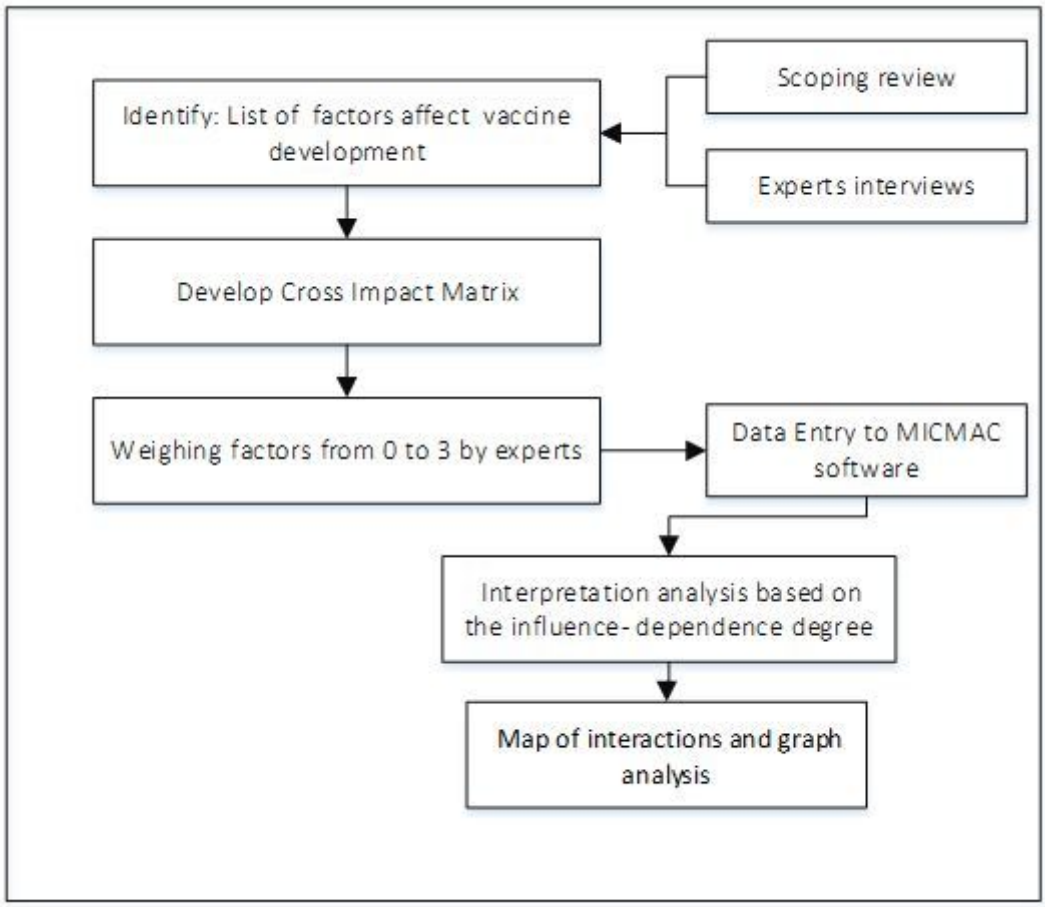

Figure 2

The Study Design

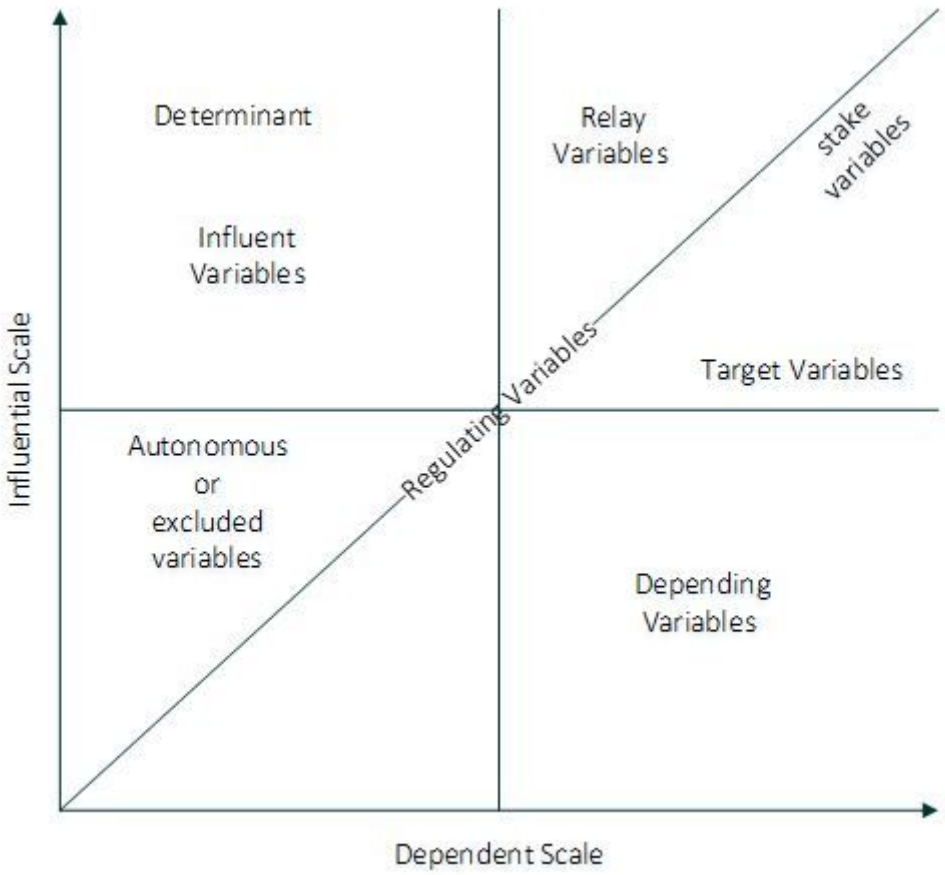

Figure 3

Different types of variables on the matrix

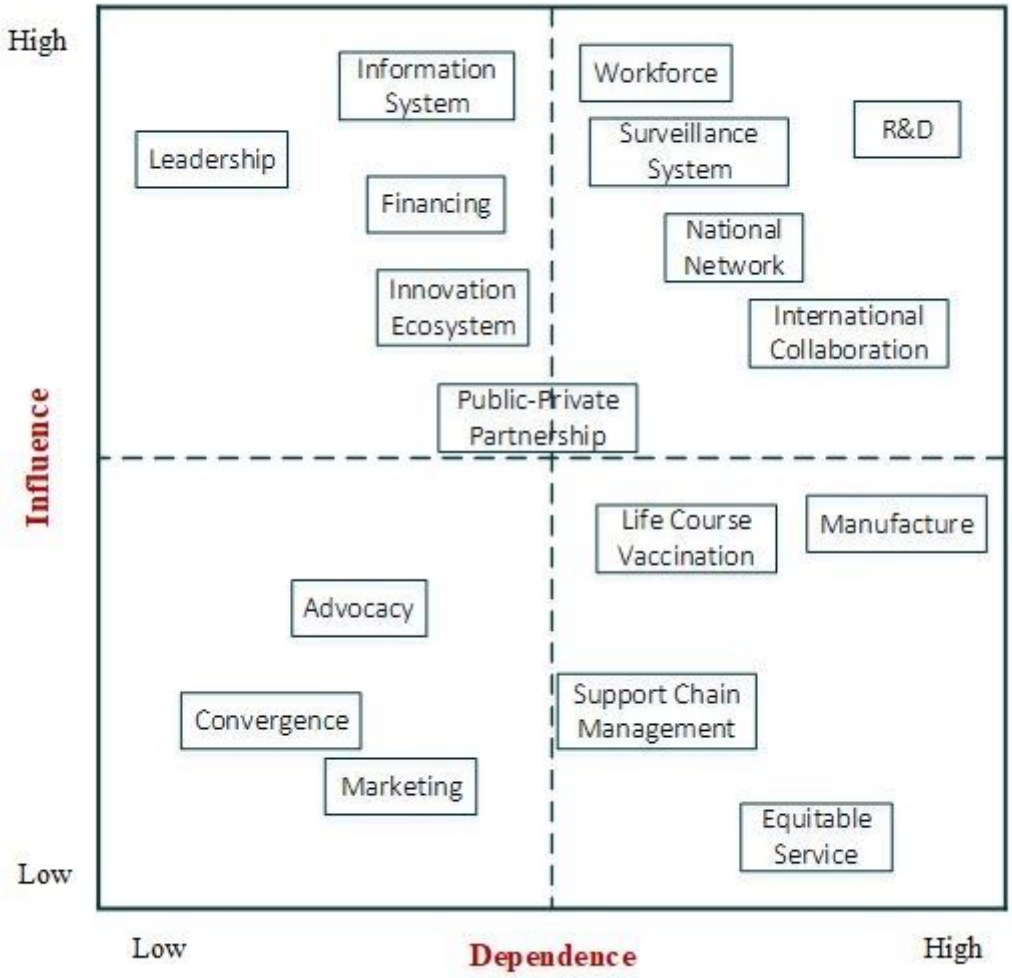

Figure 4

Positioning of factors based on their status

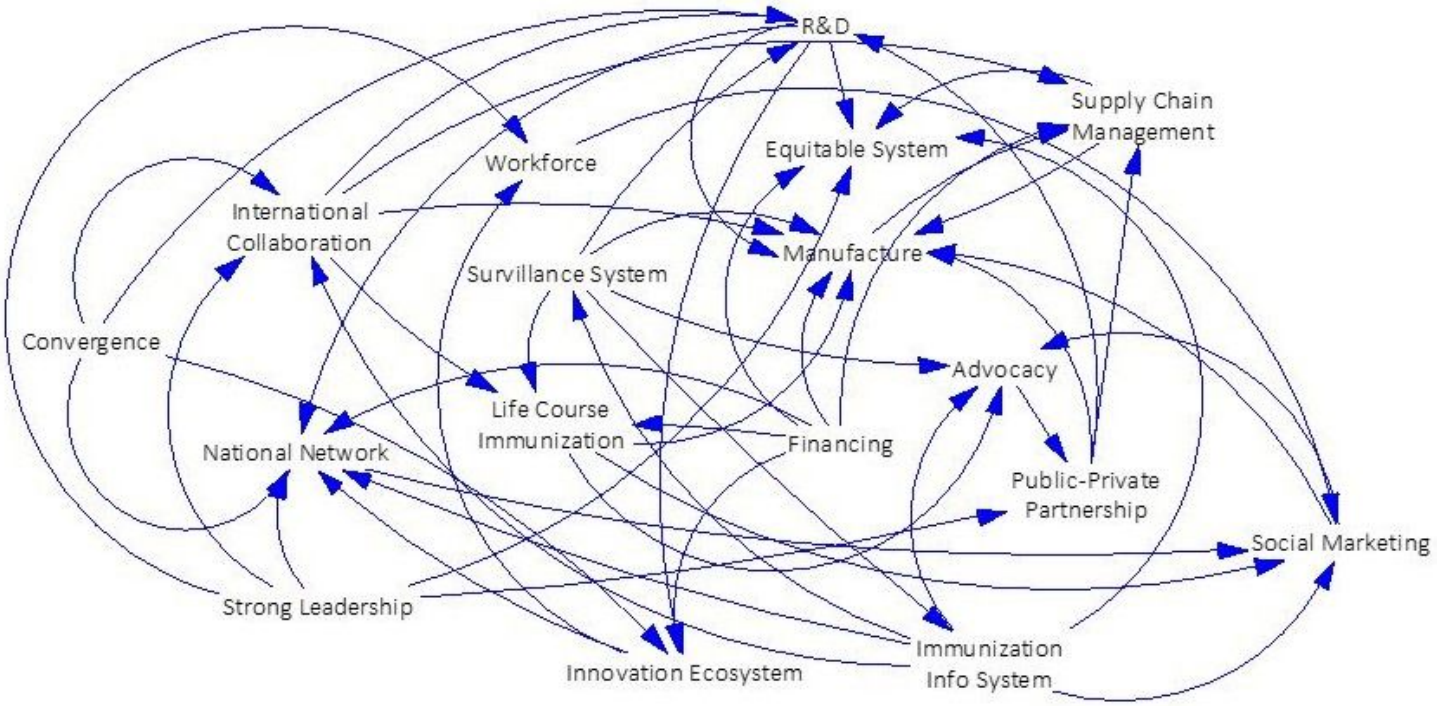

Figure 5

Interaction between factors