Analysis of SEIR-type models used at the beginning of COVID-19 pandemic reported in high-impact journals

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Abstract

Introduction

The Susceptible-Exposed-Infected-Recovered (SEIR) mathematical-epidemiological model has been exhaustively used since the beginning of the COVID-19 pandemic. These models intended to predict hospital burden and evaluate health measures to contain its spread. In this sense, flaws have been evidenced in the predictions of the first published models. It is considered necessary to evaluate the differences in the approach and verification of the models.

Objectives

Categorize the scientific publications of high-impact journals that proposed SEIR-type models to represent the COVID-19 pandemic in its early days.

Methods

We carried out a systematic review of the articles published in journals indexed in the Web of Science, of the first quartile and with an impact factor greater than two, that met the selection and inclusion criteria following the PRISMA-ScR standards. We included a total of 32 articles, which were evaluated according to demographic characteristics such as the month of receipt and publication, the country of origin of the information, the subject matter of the journal, and the characteristics of the modeling such as the presence of additional compartments, graphical analysis, conceptual model approach, interpretation of the basic reproductive number, and estimation of parameters.

Results

Articles published in medical and health journals were predominant from February to July 2020. These articles most frequently used data from China and mostly focused on SEIR or full quarantine compartment models. The articles published in journals in mathematics were predominant from August to December 2020. Models used data from different world regions, considering a greater diversity of compartments such as asymptomatic patients or partial or complete quarantine.

Conclusions

The articles analyzed mostly use SEIR-type models expanded with additional compartments. There are discrepancies in the breadth and methodological quality of the articles published according to the journal’s subject matter. The unification of quality criteria for describing the models in any journal is recommended.
INTRODUCTION
Throughout history, infectious diseases have immensely impacted the population’s morbidity and mortality. Multiple studies on projections of the behavior of epidemics have been known for centuries [1]. Currently, increased access to mobility leads to a rapid spread of epidemics [2,3]. COVID-19 is an infectious pandemic caused by the SARS-CoV-2 pathogen, first detected during the 2019 epidemic in Wuhan, China, which was reported as an emerging pneumonic coronavirus disease with high morbidity and mortality rates [4,5]. Unlike other epidemics with a shortage of investigators, many scientists are now studying this pandemic globally and regionally. In this regard, the Susceptible-Exposed-Infected-Recovered (SEIR) model approach is widely used to represent this epidemiologic phenomenon [1,3].

This work aimed to categorize scientific publications from high-impact journals that proposed SEIR-type models to predict the COVID-19 pandemic spread in its early stages when obtaining reliable sources on the risk of COVID-19 disease. Moreover, essential elements in the analysis of the models were evaluated. These elements included the quality of the modeling and the parameters that compose them, to provide tools for decision-makers and determine which published models have relevant information and are appropriate to their particular situation.

FIRST EPIDEMIC MODELS
The first mathematical models related to infectious diseases were carried out in 1761 by D’Alambert, who developed a method to analyze the competing risks of death [6] and in 1766 by Daniel Bernoulli, studying the age-specific equilibrium prevalence analysis of individuals who were immune to chickenpox [7]. Approximating the number of contagions through mathematical expressions has a long history, motivated by infectious outbreaks that prompted its appearance. These were the cases of John Snow in 1855 in a Cholera outbreak and Daniel Bernoulli in 1760 in a smallpox outbreak [6]. Then, Pyotr Dimitrievich En’ko published the epidemic model in 1889, studying successive measles outbreaks of previous decades [8].

At the beginning of the 20th century, the physician and mathematician Anderson G. McKendrick considered that the probability of a new person suffering from a contagious infection is directly proportional to the number of susceptible and infected people at an instant [9]. This reasoning took on a more general approach, leading him to publish the system of differential equations in 1927, together with the biochemist and mathematician William O. Kermack. Decades later, this model would be the basis of the Susceptible-Infected-Recovered (SIR) model [10], which would be the protagonist of the modeling of several epidemics in the following decades [11]. However, unsolved problems and mathematical curiosity motivated changes to the SIR model. Thus, the Susceptible-Exposed-Infected-Recovered (SEIR) model was born [1,9], which subdivides the total size of the human population at time t, denoted as $N(t)$, into susceptible $S(t)$, exposed $E(t)$, infected $I(t)$ and recovered $R(t)$. Therefore, for the human population we have: $N(t)=S(t)+E(t)+I(t)+R(t)$.

ADVANTAGES OF SEIR MODELS
As the disease spreads, the susceptible individual $S(t)$ moves first to the exposed population $E(t)$ [10], and considering an incubation period in between, the exposed individual moves to the infectious population $I(t)$. After ending the disease, the infected individuals move to the recovered population $R(t)$, where the deceased individuals are also represented. This model recognizes the biological existence of incubation time in infectious diseases, allowing a more realistic approach [11,12]. Adding more realistic elements to the mathematical model requires more parameters and assumptions. Unfortunately, in many real-world circumstances, reliable data are unavailable to perform the required parameter quantifications, resulting in model predictions with considerable error. Therefore, model results should be treated with caution.

Although many mathematical models cannot make accurate predictions, mainly due to a lack of data, they are handy for estimating the effect of control measures even before the start of the epidemic [1,9]. Through these models, it is also possible to predict thresholds in the density of infected individuals above which an epidemic is triggered, final values of the number of individuals that will be affected by the disease, the influence of external or seasonal factors, and, in some cases, the spatial spread of epidemics [1,3]. In addition, SEIR-type models help forecast a disease’s evolution, obtain estimates of its
characteristics (such as mortality and hospitalization rates), and know the impact of interventions to predict the evolution of COVID-19.

Each compartment represents a group of individuals in the same health state, e.g., susceptible or infectious. The connections between the compartments indicate the direction and rate of passage from one health state to another. It should be emphasized that there is no natural birth and mortality due to the short coverage time of the model and its incidence of mass action [1,3,9].

**LIMITATIONS OF SEIR MODELS**

Since the first Susceptible-Infected-Recovered (SIR) model was published for the initial SARS-CoV-2 outbreak in Wuhan (China) [12], at least 18 papers describing the behavior of the epidemic through SIR or SEIR-type models had already been published by April 2020. For example, by February 20, 2020, Zhan C et al. published a preprint of one of the first Susceptible-Exposed-Infected-Recovered (SEIR) models based on parameters fitted with data on the spread of the virus in 367 cities in China [13].

An essential aspect of SEIR models is assessing an intervention’s impact. However, it is difficult to consider all possible interactions between interventions in the same model and find parameters close to reality through simulations [1,3,9]. Moreover, these models do not involve the variability of the sources of the information nor the possible errors and biases. In this way, two parameters from different contexts could be used in the same model. Mathematical models have had hits and misses during the COVID-19 pandemic. For example, at the beginning of the pandemic and after the first cases of infection in the United Kingdom, several mathematical models were published, some of which postulated the possibility of a more benign outcome by overestimating the idea of the protective effect of rapid herd immunity [14,15].

**METHODS**

Systematic reviews used in the epidemiological context are frequently applied to clinical trials or observational studies to summarize, through a meta-analysis, the estimates made for comparable populations [12]. Heterogeneity among the populations included in the review may introduce biases in the overall estimate obtained after condensing the results.

On the other hand, a systematic review of mathematical models does not intend to collect studies measuring the same set of variables in comparable populations. They aim to collect modeling works under the same set of assumptions (in our case, underlying SEIR-type models) with parameters that characterize an epidemic at different times and places by the same infectious agent and host.

Frequency tables were used in this work to compare modeling approaches that successfully represent the population's data distribution characteristics and, therefore, predict their sample realizations. However, statistical comparison of mathematical models is only possible when two or more different models seek to predict data from the same population. When the same modeling strategy (in our case Susceptible-Exposed-Infected-Recovered) is applied to predict different populations, even if they are similar in terms of the infectious agent, comparisons are not possible. Consequently, this review aims to measure differences in approaching Susceptible-Exposed-Infected-Recovered (SEIR) models. The choice and evaluation of data sources and processes of verification of adequacy were analyzed. Likewise, as the source of information regarding each model comes from published articles, we establish to what extent the reading of the article allows us to evaluate each model with the information provided.

**SEARCH STRATEGY AND IDENTIFICATION**

In this review, an advanced search for publications was performed through the Web of Science (WoS) integrated online scientific information service provided by Clarivate Analytics, between May 21, 2020, and April 30, 2021, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews (PRISMA-ScR).

The search terms for titles and abstracts by subarea in medicine or mathematics used were: ALL= (covid* OR SARS* OR coronavirus*) AND ALL= (model* OR SEIR OR math*) AND PY= (2020) AND IS= (Issn OR Issn), where ISSN corresponds to the journals according to subject category. Additionally, the journals' first quartile (Q1) ranking for 2019 and impact factors greater than or equal to two were considered (See Figure 1). There were no restrictions on languages, publishers, countries of publication, or types of documents.

**SELECTION AND ELIGIBILITY OF STUDIES**

The tabulation of records was performed in Microsoft Excel, proceeding to the elimination of duplications and initial review of the title and abstract. Three of our authors extracted the information independently in order to avoid errors. The records of potentially eligible articles were reviewed independently by three of our authors to confirm their relevance. Any discrepancies were resolved by mutual agreement.

**INCLUSION CRITERIA**

Studies had to meet the following predetermined criteria for inclusion:

- Does the basic structure contain a population SEIR-type mathematical model?
- Does it study the dynamics of people with SARS-CoV-2 infection?
- Is the methodology based on mathematical modeling of these dynamics?
Figure 1. Articles inclusion flowchart.

Source: Prepared by the authors of this study.
EXCLUSION CRITERIA

Studies were excluded if they did not provide information to measure differences in the mathematical modeling approach. Letters to the editor, case reports, review articles, and news reports were also excluded. Articles in which the full text was not available were also excluded.

DATA EXTRACTION

The following information was extracted from the articles selected from the SEIR-type models related to COVID-19 and published on the dates defined in the search strategy, as well as from those selected and included in this analysis: first author, journal name, the month of publication, subject category, and reference (Table 1). Three of our authors extracted the data independently to avoid errors in this process.

ASSESSMENT OF INCLUDED ARTICLES

Three of our authors independently performed quality assessments of the articles to ensure their relevance to our objective, according to the following checklist:

- Do they propose compartments for the population additional to those corresponding to the classical SEIR model?
- Is the mathematical modeling based on a conceptual model suitable for COVID-19?
- Does it include graphical analysis?
- Is the location and time-period for which the study was conducted documented?
- Is the basic reproductive number (R0) found and interpreted?
- Are the values of the parameters considered and their sources of information presented?

Two authors independently verified the information obtained to avoid errors in its inclusion. Differences were resolved by mutual agreement.

DATA ANALYSIS

The variables were recategorized to delimit the description of the results. The following regions were defined: China, Asia (comprising all Asian countries except China), North America (the United States and Canada), Europe, Latin America, Africa, Oceania, and combined (when the information used came from sources in different regions).

The study months were grouped into February to July 2020 and August to December 2020, as shown in Table 2. The subareas of medical and mathematical journals correspond to the following subject categories classified by the Web of Science as public health, environmental and occupational health (Med. PHEOH), infectious disease (Med.ID), pulmonary and respiratory (Med.PR), applied mathematics (Mat.A), computational mathematics (Mat.CM), mathematical physics (Mat.MP), and modeling and simulation (Mat.MaS). The information collected in each of the phases was tabulated using spreadsheets. Absolute and relative frequencies were extracted for each category, and corresponding contingency tables were made (tables 1–3).

RESULTS

STUDY INCLUSION CHARACTERISTICS

The identification, selection, eligibility, and inclusion process is shown in Figure 1. We selected 331 articles for COVID-19 analysis through SEIR-type models that met the search criteria. The title, abstract, and methodology were read, and 78 articles were selected to read the full text and review the inclusion criteria. Thus, a total of 32 articles were obtained for subsequent evaluation, excluding articles that did not meet these criteria. All articles were retrospective. Those with insufficient information based on the inclusion criteria were excluded. The characteristics of the included articles are summarized in Table 1 and Figure 2.

Figure 2 shows a conceptual model representing the main compartmental findings of the articles included in this review, as shown below:

- Susceptible (S), exposed (E), infected (I), and recovered (R) compartments were shared in all articles and represented the classic SEIR model.
- Three articles included an Sq compartment corresponding to individuals who temporarily cease to be susceptible due to quarantine. One of these articles also included a B compartment corresponding to suspected cases of infection, which were subsequently confirmed to be in full quarantine or returned to susceptibility.
- Compartment E traditionally involves infected but non-infectious people. However, in 13 articles, this compartment had an infecting character, although more limited than compartment I.
- Compartment A was evident in nine articles and consisted of asymptomatic infected people, usually with lower infectivity, except in one article where the infectivity was similar to compartment I.
- Compartments P and Q mentioned partial quarantine (with low infectivity) or complete quarantine (no infectivity). Of the 15 articles that included quarantined compartments, seven involved hospitalized people.
- Compartment R included those recovered, while deaths in the different articles occurred in any of the compartments, being more frequent in I, P, and Q.
- Three articles included the possibility of reinfection of recovered persons.
- Two articles considered vaccinated people, representing individuals moving from susceptible to recovered populations. No articles were found that considered reinfection of vaccinated people.
- Compartment V referred to reservoirs. Two articles dealt with the virus’s presence in the environment, while three others represented the virus in the Wuhan seafood market.
Table 3a and b describe the absolute and relative frequencies by row for the thematic categories, region, and general models. Table 3a shows 14 (44%) articles on mathematical models based on data from China. Of these, 64% were published from February to July and 36% from August to December. It is
worth noting that, of the nine articles published in medical and health journals, 89% used data from China, in contrast to 26% from mathematical journals. [c2] [c3] Table 3

Table 3b shows that 12 included articles corresponded to classic Susceptible-Exposed-Infected-Recovered (SEIR) models, with no asymptomatic or quarantine compartment. However, in four of these, the E compartment had individuals who were partially infecting. Within the Susceptible-Exposed-Infected-Asymptomatic-Partial Quarantine-Infected-Recovered (SEAIR) models, we found five articles, three of which included reservoirs. In Susceptible-Exposed-Infected-Partial Quarantine-Recovered (SEIPR) models, there were two with partially infecting E compartments. In Susceptible-Exposed-Infected-Complete Quarantine-Recovered (SEIQR) models, nine articles were located, five of which had partially infecting E compartments. Only one article involved a Susceptible-Exposed-Infected-Partial Quarantine-Complete Quarantine-Recovered (SEIPQR) model, which included a viral reservoir. Finally, two articles were Susceptible-Exposed-Asymptomatic-Infected-Complete Quarantine-Recovered (SEAQR) and one was Susceptible-Exposed-Asymptomatic-Infected-Partial Quarantine-Complete Quarantine-Recovered (SEAPQR).

There are relevant differences between the model classes and subject categories of the journals in which the articles were published.

Table 3a. Table 3 Descriptive analysis of articles included according to geographical area (a) and generalization of analyzed models (b).

| Subject category | Month of article submission | Month of article publication |
|------------------|----------------------------|-----------------------------|
|                  | January to June | July to December | February to July | August to December |
| Mat.A | 14 (67) | 7 (33) | 6 (29) | 15 (71) |
| Mat.MaS | 2 (100) | 0 (0) | 2 (100) | 0 (0) |
| Total Mathematics | 16 (70) | 7 (30) | 8 (35) | 15 (65) |
| Med.ID | 2 (100) | 0 (0) | 2 (67) | 1 (33) |
| Med.PHEOH | 6 (100) | 0 (0) | 4 (67) | 2 (33) |
| Total medicine | 8 (100) | 0 (0) | 6 (67) | 3 (33) |
| Total | 24 (75) | 7 (22) | 14 (44) | 18 (56) |

Table 3b. Table 3 Descriptive analysis of articles included according to geographical area (a) and generalization of analyzed models (b).

| Subject category | Region | SEIR | SEIQR | SEIPR | SEIPQR | SEAIR | SEAIPQR | Total |
|------------------|--------|------|-------|-------|--------|-------|---------|-------|
| Mat.A | China | 6 (29) | 5 (24) | 5 (24) | 5 (24) | 2 (10) | 2 (10) | 21 |
| Mat.MaS | Asia | 2 (10) | 1 (5) | 1 (5) | 1 (5) | 2 (10) | 1 (5) | 2 |
| Total mathematics | North america | 2 (10) | 1 (4) | 1 (4) | 1 (4) | 2 (10) | 1 (4) | 23 |
| Med.ID | Europe | 3 (13) | 1 (4) | 1 (4) | 1 (4) | 2 (10) | 1 (4) | 23 |
| Med.PHEOH | Combined | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 3 |
| Total medicine | Not reported | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 6 |
| Total | Total | 16 (70) | 5 (24) | 5 (24) | 5 (24) | 2 (10) | 2 (10) | 21 |

| Subject category | General models | SEIR | SEIQR | SEIPR | SEIPQR | SEAIR | SEAIPQR | Total |
|------------------|----------------|------|-------|-------|--------|-------|---------|-------|
| Mat.A | China | 9 (43) | 5 (24) | 1 (5) | 1 (5) | 2 (10) | 2 (10) | 21 |
| Mat.MaS | Asia | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 |
| Total mathematics | North america | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 3 |
| Med.ID | Europe | 1 (4) | 1 (4) | 1 (4) | 1 (4) | 2 (10) | 1 (4) | 23 |
| Med.PHEOH | Combined | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 6 |
| Total medicine | Not reported | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 9 |
| Total | Total | 12 (38) | 9 (28) | 2 (6) | 1 (3) | 5 (16) | 2 (6) | 32 |

Mat.A: applied mathematics. Med.PHEOH: public health, environmental and occupational health. applied mathematics; Mat.MaS: modeling and simulation. infectious disease. modeling and simulation; Med.ID: infectious disease.

Values in parentheses indicate percentage (%).
Source: Prepared by the authors of this study.
In contrast, Susceptible-Exposed-Infected-Recovered (SEIR) models include "latent infections" in the exposed compartment (E). This model considers individuals exposed to contagion and whose ability to infect other individuals has not yet developed but eventually will move to the infectious compartment (I) [1,9].

The exposed compartment (E) represents the existence of latent infection periods, i.e., incubation periods, which are usually pre-symptomatic and described in most infections affecting humans [10–12]. This approach allows a more realistic representation of the contagion dynamics of SEIR models. Although some models had an exposed compartment, some articles were excluded since they did not meet the definition of such a compartment.

We found that 40.6% of the included articles contemplated the possibility of infectivity to persons represented in the exposed compartment (E), even if this was low. Interestingly, of the 32 articles based on the SEIR model, only eight (25%) of these consisted of a classical SEIR model, with no additional compartments and no partial infectivity in the exposed compartment.

Data reported by different studies showed that both asymptomatic and symptomatic infected persons spread SARS-CoV-2 to susceptible individuals once they are in contact [28,30,41,45]. Thus, it is possible to establish transmission in two ways: from person to person and from the environment to the person [48–50].

The measures implemented to prevent the spread of COVID-19 mean that once infected persons sneeze or cough, the virus spreads in the environment [4,51]. In addition, terminating restrictions imposed on international travel around the world led to an increase in the transmission of COVID-19 [5,51]. SARS-CoV-2 survives in the environment for a few days, so this would increase the probability of contagion for susceptible individuals in contact with such an environment. This is especially noticeable in the first days of the COVID-19 outbreak, even before biosecurity and hygiene protocols were applied [4,19,52].

**CONCLUSIONS**

The SEIR-type mathematical-epidemiological model has been employed in several published articles based on available information to predict pandemic behavior. Initially, the data used came from China and other Asian countries affected early, which allowed them to obtain the first estimates of the contagion rate, latency time, and infectious time, thus improving the predictions' quality. Most of the first articles were published in medical and health journals, although later articles published in mathematical journals predominated. It should be noted that most of the available graphical analysis descriptions come from articles published in mathematical journals, even though the methodological approach to the same problem is similar.

**DISCUSSION**

This paper presents the variations in the categorization of scientific publications according to diverse approaches to compartmental models. These models have been widely used to study the behavior of infectious diseases in the last three decades [1–3,6]. The Susceptible-Infected-Recovered (SIR) models are suited to different scenarios, assuming that individuals, once infected, can start infecting other individuals [10,11].

In contrast, Susceptible-Exposed-Infected-Recovered (SEIR) models include "latent infections" in the exposed compartment (E). This model considers individuals exposed to contagion and whose ability to infect other individuals has not yet developed but eventually will move to the infectious compartment (I) [1,9].

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The differences in editorial requirements, as well as the training and experience of the peers, may have influenced the fact that articles in the medical and health journals more often have a conceptual model, usually broader and more detailed. Meanwhile, journals in the mathematical area usually describe the stability and validation of the model. In addition, articles published in the mathematical area also use extensions of the Susceptible-Exposed-Infected-Recovered (SEIR) model more frequently.

Finally, it is recommended to establish more general guidelines to ensure quality in the description of modeling in an article related to the mathematical modeling of epidemics, in particular with SEIR-type models. This measure would improve comparability between the different results. It is also encouraged to use appendices for publications to expand the analysis if required.

**Notes**

**Contributor roles**

LCH: conceptualization, methodology, formal analysis, research, writing (revisions and edits), supervision, research, data management, and manuscript preparation (development of original draft). LP: methodology, research, and writing (revisions and edits). FCL: methodology, research, and writing (revisions and edits). ADA: methodology, research, and writing (revisions and edits). HTM: methodology, research, data management, data presentation, and writing (reviews and edits). JPGJ: methodology, research, and writing (reviews and edits).

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**Competing interests**

The authors declare no competing interests.

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This work did not receive funding.

**Protocol registry**

This review study was not included in the PROSPERO registry because our work does not contemplate studies in humans or animals. Instead, we analyzed scientific publications from high-impact journals that proposed SEIR-type mathematical models to model the COVID-19 pandemic in its beginnings.

**Ethics**

The present study did not require evaluation by an ethics committee because it was secondary source research.

**Data sharing statement**

The authors declare their willingness to make research data available upon request.

**Provenance and peer review**

Not commissioned. Peer-reviewed externally by three double-blind referees.

**Language of submission**

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Resumen

Introducción
El modelo matemático-epidemiológico Susceptible-Expuesto-Infectado-Recuperado (SEIR) ha sido empleado exhaustivamente en el contexto actual de la pandemia COVID-19. En sus inicios de una manera prevalente, donde se buscaba predecir la carga hospitalaria y evaluar las medidas sanitarias para contener su propagación. En este sentido, se han evidenciado fallas en las predicciones de los primeros modelos publicados. Se considera necesario evaluar las diferencias en el planteamiento y verificación de los modelos.

Objetivos
Categorizar las publicaciones científicas de revistas de alto impacto que propusieron modelos tipo SEIR para modelar la pandemia COVID-19 en sus inicios.

Métodos
Realizamos una revisión sistemática de los artículos publicados en revistas indexadas en Web of Science, de primer cuartil y con factor de impacto mayor que dos, que cumplían con los criterios de selección e inclusión siguiendo los estándares PRISMA-ScR. Incluimos un total de 32 artículos que fueron evaluados según características demográficas como el mes de recepción y publicación, el país de origen de la información, la materia temática de la revista, y las características del modelamiento como la presencia de compartimentos adicionales, análisis gráfico, planteamiento de modelo conceptual, interpretación del número reproductivo básico y estimación de los parámetros empleados.

Resultados
Los artículos publicados en revistas del área médica y salud fueron predominantes en los meses de febrero a julio de 2020. Estos artículos emplearon con mayor frecuencia datos procedentes de China y se centraron mayoritariamente en modelos SEIR o con compartimento de cuarentena completa. Los artículos publicados en revistas del área matemática fueron predominantes en el periodo de agosto a diciembre de 2020, y emplearon datos procedentes de diversas regiones del mundo, considerando mayor diversidad de compartimentos como pacientes asintomáticos o en cuarentena parcial o completa.

Conclusiones
Los artículos analizados en su mayoría emplean modelos tipo SEIR ampliados con compartimentos adicionales. Existen discrepancias en la amplitud y calidad metodológica de los artículos publicados, según la materia temática de la revista. Se recomienda la unificación de criterios de calidad para la descripción de los modelos en cualquier revista.