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## APPLICATION OF MARKOV CHAINS AND ARTIFICIAL NEURAL NETWORKS IN THE PREDICTION OF HEPATITIS CASES IN THE SOUTHERN STATES OF BRAZIL

APLICAÇÃO DAS CADEIAS DE MARKOV E REDES NEURAIAS ARTIFICIAIS NA PREDIÇÃO DE CASOS DE HEPATITE NOS ESTADOS DO SUL DO BRASIL

APLICACIÓN DE CADENAS DE MARKOV Y REDES NEURONALES ARTIFICIALES EN LA PREDICCIÓN DE CASOS DE HEPATITIS EN LOS ESTADOS DEL SUR DE BRASIL

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### ABSTRACT

Viral hepatitis is a disease caused by five known types of virus and can be chronic or acute. This study collected historical data on hepatitis in the southern states of Brazil and applied Markov Chains as an input parameter for predicting cases, using Artificial Neural Networks (ANN). A comparison was then made between the method that includes the two methodologies and the prediction made by ANN using only the data from the historical series. The mean absolute error (MAE) and mean absolute percentage error (MAPE) were calculated to determine the best forecasting model for each state. It was not possible to determine a configuration that simultaneously presented the best MAE and MAPE values for each state, but it was found that the lowest errors were obtained by using Markov Chains as an information generator for the ANN models, with a MAPE of 4.45% using the Levenberg-Marquardt training algorithm, with a delay equal to 3 and a number of neurons equal to 60.

### KEYWORDS

Markov Chains; Hepatitis; Artificial Neural Networks

## RESUMO

As hepatites virais são doenças causadas por cinco tipos conhecidos de vírus, podendo apresentar quadros crônicos ou agudos. O presente estudo coletou dados históricos acerca de hepatite nos estados do sul do Brasil e aplicou Cadeias de Markov como parâmetro de entrada para previsão de casos, por meio de Redes Neurais Artificiais (RNA). Comparou-se então método que contempla as duas metodologias com a previsão realizada por RNA considerando apenas os dados da série histórica. Calculou-se o erro médio absoluto (MAE) e erro percentual médio absoluto (MAPE) para determinar qual o melhor modelo de previsão referente a cada estado. Não foi possível determinar uma configuração que apresentasse simultaneamente os melhores valores de MAE e MAPE para cada estado, mas constatou-se que os menores erros foram obtidos com emprego de Cadeias de Markov como um gerador de informações para os modelos de RNA, chegando a apresentar MAPE de 4,45% por meio do algoritmo de treinamento de Levenberg- Marquardt, com delay igual a 3 e número de neurônios igual a 60.

## PALAVRAS-CHAVE

Cadeias de Markov; Hepatite; Redes Neurais Artificiais.

## RESUMEN

La hepatitis viral es una enfermedad causada por cinco tipos conocidos de virus, y puede presentar afecciones crónicas o agudas. El presente estudio recolectó datos históricos sobre hepatitis en los estados del sur de Brasil y aplicó las Cadenas de Markov como parámetro de entrada para la predicción de casos por medio de Redes Neuronales Artificiales (RNA). A continuación, se comparó un método que contempla las dos metodologías con la predicción realizada por ARN, considerando solo los datos de las series históricas. Se calculó el error absoluto medio (MAE) y el error porcentual absoluto medio (MAPE) para determinar el mejor modelo de predicción para cada estado. No fue posible determinar una configuración que presentara simultáneamente los mejores valores de MAE y MAPE para cada estado, pero se encontró que los menores errores se obtuvieron con el uso de cadenas de Markov como generador de información para los modelos de ARN, alcanzando un MAPE de 4.45% mediante el algoritmo de entrenamiento de Levenberg-Marquardt. con un retraso de 3 y un número de neuronas de 60.

## PALABRAS CLAVE

Cadenas de Markov; Hepatitis; Redes neuronales artificiales

## 1 INTRODUCTION

Technological advances, boosted by the evolution of electronic components, have led to the application of methodologies for analyzing data and aiding decision-making, especially those that use computer systems to carry out this analysis. As a result of these advances, numerous models have emerged or have been enhanced (SANTOS *et al.*, 2005; SOUZA FILHO *et al.*, 2020).

Among the numerous existing methods, one that stands out is the application of Artificial Neural Networks (ANN), which have a certain similarity to the human mind, i.e. a learning stage for subsequent application (KWON *et al.*, 2018; SOUZA FILHO *et al.*, 2020). This mathematical model has great potential, especially because of its wide range of applications. The demand for these decision-making methods is growing in the health sector, in order to help with forecasting and strategic decision-making (NAKAJIMA *et al.*, 2017; RUBIN *et al.*, 2018; ZHANG *et al.*, 2018; HERNESNIEMI *et al.*, 2019; MORTAZAVI *et al.*, 2019).

The synergy between areas of health and data analysis has proven to be of paramount importance and has potential for exploitation, as explained by Hernesniemi *et al.* (2019). Numerous examples of application can be found in the literature, especially in helping to develop new diagnostic means and new prognostic approaches (ZERON *et al.*, 2019; GONÇALVES *et al.*, 2020).

Viral hepatitis, a globally prevalent liver disease caused by various viruses, presents a complex epidemiological profile. Its diverse etiologies, including hepatitis A, B, C, D, and E, each with distinct transmission modes, clinical manifestations, and disease progression, pose significant challenges for public health management (GOULART *et al.*, 2006; FARIAS *et al.*, 2019). The identification of factors influencing the spread of these infections is crucial for developing effective prevention and control strategies. Mathematical modeling offers a powerful tool to analyze epidemiological patterns, predict disease outbreaks, and evaluate the impact of interventions (ZERON *et al.*, 2019; GONÇALVES *et al.*, 2020).

This study aims to construct an optimal Artificial Neural Network (ANN) model, incorporating Markov Chain principles, to forecast hepatitis incidence in the southern Brazilian states of Paraná, Rio Grande do Sul, and Santa Catarina. By leveraging data-driven approaches, we seek to improve understanding of hepatitis transmission dynamics and inform public health policies.

### 1.1 THEORETICAL FRAMEWORK

This chapter is divided into two stages to review the literature on the subjects covered throughout the article: Markov Chains (MC) and Artificial Neural Networks (ANN). The combined application of MC and ANN demonstrates significant potential for enhancing the prediction of viral hepatitis cases. By capturing complex patterns in data, these models can enable more accurate forecasting, leading to improved disease management and public health interventions.

#### 1.1.1 MARKOV CHAINS

The model proposed by Markov is one of the stochastic models (a model that evolves over time, based on a probability), a special property of which is the fact that the future state is linked to the

current state (by probabilistic means), without a dependence on events in the past state (HILLIER *et al.*, 2013; ROSHAN *et al.*, 2018). This is defined as a Markovian property, and a stochastic process with this characteristic has been classified as a Markov chain (HILLIER *et al.*, 2013). A given Markov Chain can be represented by the transition matrix, where the probabilities of changing state ( $i$  to state  $j$ ) over a certain period of time is represented in Equation 1 by  $p_{ij}$  (TAHA, 2007; HILLIER *et al.*, 2013).

$$P = \begin{bmatrix} p_{11} & p_{12} & \dots & p_{1n} \\ p_{21} & p_{22} & \dots & p_{2n} \\ \dots & \dots & \dots & \dots \\ p_{n1} & p_{n2} & \dots & p_{nn} \end{bmatrix} \quad (1)$$

### 1.1.2 ARTIFICIAL NEURAL NETWORKS

A prominent model in Artificial Intelligence, ANNs have been used by mathematical means to reproduce the neurons of the brain, with the aim of acquiring knowledge through experience and storing this learning, making it possible to apply it to a given situation (HAYKIN *et al.*, 2003; TAHA, 2007; BITTAR *et al.*, 2020). Among the various ANN models, the multi-layer ones stand out when it comes to solving non-stationary time series (BRAGA *et al.*, 2007; BORSATO *et al.*, 2019; LIU *et al.*, 2019). This method consists of an input layer of the model, plus an output layer, and may have one or more intermediate layers - these layers help in the design of the learning algorithm and operation (BRAGA *et al.*, 2007; BORSATO *et al.*, 2019).

Synaptic weights are also assigned in order to weight this activation function (FERNEDA *et al.*, 2006; BRAGA *et al.*, 2007; OLIVEIRA *et al.*, 2012). For the aforementioned mathematical method, two stages are required: definition of the model's architecture (taking into account layout - layers and neurons - and activation function) and validation (comparison carried out after training with a series not used in the development (OLIVEIRA *et al.*, 2012; FERNEDA *et al.*, 2006). The performance of the ANN model can be verified according to the mean absolute percentage error (MAPE) and the mean absolute error (MAE), represented by Equations 2 and 3 (MAPUWEI *et al.*, 2020).

$$MAPE = \frac{1}{n} \sum_{i=1}^n \frac{|e_i|}{y_t} \times 100 \quad (2)$$

$$MAE = \frac{1}{n} \sum_{i=1}^n |e_i| \quad (3)$$

Where,  $n$  represents the number of evaluation periods,  $y_t$  is the actual value for the period ( $t$ ) e  $e_i$  is the difference between the actual value and the forecast value for the  $i$ -th period. These errors together help in the search for the model with the smallest difference between the expected and actual values.

## 2 METHODS

This work sought to define, using Artificial Neural Networks and Markov Chains, a model for predicting hepatitis cases in the southern states of Brazil. To this end, the steps described in this chapter were followed.

### 2.1 DATA COLLECTION

The data for each state analyzed (Rio Grande do Sul, Paraná, and Santa Catarina) were obtained from the DATASUS database, Brazil's Unified Health System's Department of Informatics. DATASUS is a reliable source for epidemiological studies, collecting, processing, and providing comprehensive health data. Accessing the TABNET system in September 2020, we gathered data from all three southern Brazilian states. This data spanned 12 years (2007-2018), collected monthly from healthcare settings.

Data were collected considering the number of individuals with confirmed infection per month (Jan-Dec), for each year, over the 12-year period. Without distinguishing between hepatitis virus types, we analyzed the total number of cases, providing a general overview of the disease. Annual databases were created for each state, allowing for monthly assessments and tracking the historical evolution of hepatitis cases across these Brazilian states.

### 2.2 MARKOV CHAINS APPLICATION

The following sections describe the method used to apply Markov Chains in order to obtain the transition matrix and then the steady-state probabilities for Rio Grande do Sul, Santa Catarina and Paraná.

### 2.3 DEFINITION OF TRANSITION BANDS AND CONSTRUCTION OF THE TRANSITION MATRIX

The data obtained from DATASUS was grouped together in a spreadsheet, taking into account the percentage variation over time. Subsequently, the ranges used in the study were divided up and defined according to their occurrences. A total of 7 ranges were created in order to provide greater visualization of the changes in intervals. These ranges are shown in chart 1. After classifying the transition ranges for the data obtained, the quantity matrix was constructed by adding up each transition identified in the spreadsheet. The sums are counted in a new matrix, which is named according to its indication, i.e. the quantity of each occurrence (variation).

**Chart 1** – Classification of variations range

Percentage	Range
Below -20,0001%	A
-20 to -10,0001%	B
-10 to -5,0001%	C
-5 to -0,0001%	D

Percentage	Range
0 to 4,9999%	E
5 to 9,99%	F
Above 10%	G

Source: Created by authors.

By providing a measure of the dispersion of the data around a central value, the variation intervals can be applied to the elements of a transition matrix, thus obtaining a better understanding of the dynamics of the system and the uncertainty associated with the transition probabilities. Therefore, this step resulted in the transition matrix, which reflects the probability of a change of state in a given period of time.

## 2.4 ANN APPLICATION

When comparing ANN models that use different approaches to forecasting time series, it is pointed out that single-variable models only consider the historical data of the series in question, while multivariable models incorporate additional information, such as probabilities derived from MC. To optimize the performance of the models, various calculation configurations were tested within the *scikit-learn* library of the *Python* programming language, including the number of neurons, the number of delays and different training algorithms (Levenberg-Marquardt, Bayesian Regularization and Scaled Conjugate Gradient). The main objective is to identify the combination of hyperparameters and algorithm that results in the lowest prediction error for each time series, allowing the most appropriate model to be chosen for each case. In this way, it is possible to verify how useful the model is for use in projecting cases in epidemiology.

Monovariate ANN models were developed, considering only the historical series, while multivariate models incorporated both the historical data and the probabilities derived from the application of Markov Chains. The optimal number of neurons was then determined by creating ANNs with the number of neurons varying from 10 to 100 in increments of 10. Tests were then carried out with delay numbers from 2 to 10, in order to obtain the lowest error for each time series, and then 3 training algorithms were tested. These are *Levenberg-Marquardt* (LM), *Bayesian Regularization* (BR) e *Scaled Conjugate Gradiente* (SCG). The LM model can be described using the following Equation 4 (HAMZA-ÇEBI *et al.*, 2017; LIMA *et al.*, 2020):

$$x_{k+1} = x_k - (J^T J + \mu I)^{-1} J^T e \quad (4)$$

Where:  $J$  is the Jacobian matrix that receives and controls the first errors of the ANN and  $\mu$  is the learning rate. The BR model is described by Equation 5, where  $M$  is the practical form of the model and  $D$  is the training data set. This model is based on Bayes' rule (LIMA *et al.*, 2020):

$$p(\emptyset|D, M) = \frac{p(D|\emptyset, M) p(\emptyset|M)}{p(D|M)} \quad (5)$$

The SCG technique described in Equations 6 and 7 is suitable for solving large-scale problems (LIMA *et al.*, 2020).

$$s_k = E''(\theta_k) d_k \approx \frac{E'(\theta_{t,k}) - E'(\theta_k)}{y_k} \quad (6)$$

$$\alpha_k = \frac{-d^T E'_q(\theta_1)}{d^T s_k} \quad (7)$$

Subject to:

$$0 < y_k \ll 1$$

Considering  $s_k$  as second-order information,  $\alpha_k$  step size,  $E''$  and  $E'$  are the second and first derivatives of the error function with reference to the weight vectors,  $dk$  represents the temporal weight vector, with variation over the period  $k$ , being  $d^T$  the tranpose matrix of  $d_k$  (HAMZAÇEBI *et al.*, 2017).

## 2.5 METRICS EVALUATION

In order to determine the best of the methods presented in the study, the MAPE and MAE were used, applying Equations 2 and 3 respectively. The results of the application, the best models found and their errors are presented in Chapter 4.

## 3 RESULTS

To create and develop the ANN models, training models were evaluated for the data from each state, varying the number of neurons and delays, as presented in the methodology. The historical data series was taken into account, as well as data from the application of Markov Chains. As a result, 231,660 data points from this simulation were analyzed - 143 data points for each of the 270 different configurations tested per state (two predictions are added to these, considering the application of Markov Chains and ANN or just the latter applied to the historical series), for a total of 1620 different configurations.

Tables 1 and 2 show the MAPE and MAE results, considering the model evaluation metrics, for the three lowest values in each state. It can be seen that in no case was a model found that obtained the lowest values for both metrics simultaneously. The tables show the configurations used in the algorithm, as well as the metric values obtained for each one. The Model column shows the training algorithm used: LM, BR and SCG. It can be seen that the *Levenberg-Marquardt* model showed the lowest MAPE and MAE values for the three states, always varying the number of neurons and *delays*.

**Table 1** – Lowest MAPE values for each state, including models, delays and neurons used

State	MAPE							
	Model	Delay	Neurons	MAPE no Markov	MAPE with Markov	Model	Delay	Neurons
Rio Grande doSul	LM	10	30	12,2%	4,4%	LM	3	60
	LM	9	70	12,3%	5,3%	LM	4	80
	SCG	8	90	12,7%	5,5%	LM	4	30
Santa Catarina	LM	3	80	7,4%	4,4%	LM	6	70
	LM	3	60	7,6%	4,8%	LM	7	90
	BR	4	70	8,4%	4,8%	LM	6	40
Parana	LM	2	100	6,4%	5,5%	LM	4	20
	BR	2	50	8,7%	5,8%	LM	5	30
	LM	2	80	8,8%	5,8%	LM	5	40

Source: Research data.

**Table 2** – Lowest MAE values for each state, including models, delays and neurons used

State	MAE							
	Models	Delay	Neurons	MAE no Markov	MAE with Markov	Model	Delay	Neurons
Rio Grande do Sul	LM	10	30	28,7%	21,9%	LM	8	100
	LM	8	30	31,6%	22,1%	LM	4	30
	LM	2	100	42,5%	22,7%	LM	8	40
Santa Catarina	LM	3	80	17,4%	12,7%	LM	6	70
	LM	3	60	18,3%	13,5%	LM	6	40
	LM	3	70	20,5%	13,6%	LM	7	90



State	MAE							
	Models	Delay	Neurons	MAE no Markov	MAE with Markov	Model	Delay	Neurons
Parana	LM	2	100	17,5%	15,1%	LM	4	20
	LM	2	80	23%	15,4%	LM	5	40
	BR	2	50	23,9%	15,9%	LM	5	30

Source: Research data.

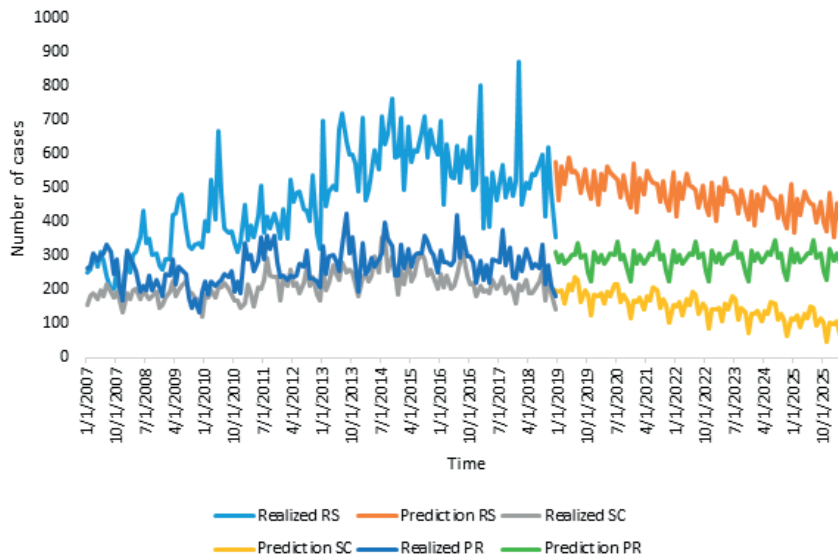
It can be seen that the lowest values are found in the models that took Markov Chains into account ('with Markov' in the table). This shows that the use of this input parameter did in fact improve the forecast result. Table 3 shows the results obtained with the models, considering the average MAPE for each state and a comparison between the methods (with the application of Markov Chains, or considering only the historical data series). The values given in brackets in the figure legends refer to the configuration used: number of *delays* and neurons. The LM training algorithm was used for these models (as it showed the best results among the configurations).

**Table 3** – Comparison of average errors

Average MAPE for training algorithm									
	Rio Grande do Sul			Santa Catarina			Paraná		
Model	LM	BR	SCG	LM	BR	SCG	LM	BR	SCG
No Markov	19,3%	14,4%	18,1%	15,5%	12,8%	15,9%	23%	21,3%	28,1%
With Markov	18,5%	9,7%	17,9%	16,7%	7,6%	15,8%	25,8%	12,1%	27,7%

Source: Research data.

An analysis of the average errors shows that they are closer to the real values when we look at the models using Markov Chains. One detail that stands out is the constant incidence of lower errors in the Bayesian Regularization model, although the lowest MAE and MAPE values were not achieved by this configuration, which corroborates the data presented above and reinforces that different models should be analyzed for studies of this type. Figure 1 shows the graphical diagram relating the number of people diagnosed with viral hepatitis in each state in southern Brazil (RS, SC and PR) over the time horizon considered.

**Figure 1** – Graphical representation of the forecast of new cases of viral hepatitis

Source: Research data.

The lowest mean absolute percentage error values, considering the use of Markov Chains, were 4.45%, 4.46% and 5.58% for Rio Grande do Sul, Santa Catarina and Paraná. In turn, for the same sequence of states, the models without Markov Chains showed MAPEs of 12.27%, 7.47% and 6.46%. These values were obtained using the Levenberg-Marquardt training algorithm, but each with a different configuration.

The variability observed in the data, characterized by peaks and falls, is the result of the interaction of various complex factors, such as epidemic outbreaks, changes in the population's behavioral patterns and fluctuations in climatic conditions. The heterogeneity between states, in turn, reflects the particularities of each context, including vaccination coverage, access to health services and the habits of the population. The analysis of the prediction errors (MAPE and MAE), which were low, suggests that the prediction algorithm was successful in evaluating the artificial intelligence models on the existing data, so the projections are considered effective. However, it is important to note that the effectiveness of public health interventions depends not only on the accuracy of the forecasts, but also on the responsiveness of health systems and the implementation of appropriate control measures.

## 4 DISCUSSION

The tools used in this study demonstrate the potential to analyze vast data sets, uncovering complex patterns and providing accurate predictions about the occurrence of new cases. The scientific literature already recognizes the value of mathematical models in predicting infectious diseases and

optimizing the management of health systems. Nucita *et al.* (2013). presents a similar innovative approach to the epidemiological study of HIV using tools from artificial intelligence, whose main contribution lies in the application of MC to real data from electronic medical records to simulate the dynamics of the HIV epidemic at district level.

By analyzing large volumes of data from electronic medical records and other repositories, these models make it possible to identify patterns, predict trends and assess the impact of different interventions. However, there are limitations regarding the quality of the data collected in order to build robust and reliable models. Collecting accurate and complete data, free from bias, is a complex challenge, especially in health systems with varied infrastructures. Incomplete, inconsistent or faulty data can lead to inaccurate results and impair decision-making.

The application of MC in epidemiological studies, though not as common as traditional methods like Poisson regression, Age-Period-Cohort (APC) models, ARIMA, and Bayesian APC, has shown promise in capturing the temporal dynamics of disease spread. For example, studies such as Roshan *et al.* (2018) have utilized Markov Chains to assess extreme heat stress probabilities, demonstrating the model's applicability to public health data. Similarly, Nucita *et al.* (2013) has highlighted the effectiveness of MC in modeling HIV spread in specific districts. However, its application to Brazilian public health data, especially for diseases like hepatitis, is still underexplored, representing an area ripe for further research.

Markov Chains differ from other epidemiological models in several ways. For instance, unlike Poisson models that assume event independence and constant rate over time, Markov Chains explicitly model the probability of transitioning from one state to another, which can be more appropriate for diseases with clear stages or states. ARIMA models, on the other hand, are designed for time series data but may struggle with non-linear dynamics where MC could offer better insights. Bayesian APC models incorporate prior information, which can be powerful, but may require more extensive data than MC models. The flexibility of MC to handle different types of transitions makes it a valuable tool in the context of epidemiological modeling, though it may not always capture the full complexity of age or cohort effects as well as APC models.

## 5 CONCLUSIONS

This study successfully constructed and evaluated an optimal Artificial Neural Network (ANN) model that incorporates Markov Chain principles to forecast hepatitis incidence in the southern Brazilian states of Paraná, Rio Grande do Sul, and Santa Catarina. By applying these advanced data-driven approaches, the research has significantly improved our understanding of the transmission dynamics of hepatitis in these regions. The results indicate that the integration of Markov Chains with ANNs enhances predictive accuracy compared to models relying solely on historical data, as demonstrated by the reduction in Mean Absolute Percentage Error (MAPE) and Mean Absolute Error (MAE) values.

Transition matrices were obtained for each state, and multiple models were simulated to determine the best forecasting method, confirming that no single model consistently performed best across

all metrics. However, the use of Markov Chains as input parameters for ANN clearly led to superior forecasting outcomes. This improvement in forecasting capability has important implications for public health, as it can lead to more informed decision-making and the development of more effective policies aimed at controlling and preventing hepatitis outbreaks in these states.

The models obtained can be used to predict cases of the disease studied for each state, helping to understand current and future scenarios, allowing for a more assertive approach and development of public health policies, since the impacts of maintaining current control and prevention measures can be better measured.

Despite its potential, the MC approach has limitations. The accuracy of the predictions depends heavily on the quality and granularity of the data. In health systems with varied infrastructures, like those in Brazil, data may be incomplete, inconsistent, or biased, leading to challenges in building robust and reliable models. Furthermore, while Markov Chains can effectively model state transitions, they might oversimplify the underlying processes, especially in the presence of complex interdependencies between variables that are better captured by other methods like ARIMA or Bayesian models.

For future studies, it is recommended that this analysis be extended to other states and regions, as well as being broken down by type of virus, in order to help prevent and combat/prepare treatments for the types most associated with chronic or acute hepatitis, making it possible to reduce the number of cases and reduce this public health problem. It is also suggested that an approach be taken to determine, by means of the symptoms presented, the likelihood of a person having or contracting hepatitis, in order to implement targeted vaccination campaigns based on risk.

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