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Simulaciones de modelos estacionales de propagación del covid: estudio de caso en México

Artículo Original

Simulations of seasonal covid spread models: case study Mexico

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SUMMARY

In this work we propose some mathematical models to simulate seasonality behavior of Covid-19 spread; a periodic transmission rate is added to SEIR, SEIRS, SEIRS with vaccination (SEIRSV) ode systems and the models are fitted to reported Covid infected historical data 2021 in Mexico. Numerical simulations reproduce the qualitative seasonality behavior of covid spread and provide an insight to develop strategies to prevent the diseases spread. Nearly all discussed approaches show the possible appearance of a fourth covid wave in Mexico at the end of 2021. Our results suggest that it is mandatory to consider seasonal factors when planing intervention strategies.

Key words: seir, reinfection, vaccination, periodic transmission rate, machine learning, Pearson correlation, seasonality.
Codes: 68U20, 92D30, 65D10,00A71.

INTRODUCTION

COVID-19 is the most recently discovered infectious disease caused by the coronavirus. Both this new virus and the disease it causes in the human body were unknown before the outbreak broke out in Wuhan, China, in December 2019. On March 11, 2020, by analyzing the alarming levels of the spread of the disease and its severity, as well as the levels of inaction, the World Health

Organization (WHO) determined that COVID-19 could be characterized as a pandemic. Since then, the number of victims has not stopped growing. Currently, COVID-19 is a pandemic that affects more than 190 countries on all continents of the world. The number of cases has multiplied daily, reaching almost 21 million, and the number of deaths now exceeds 800,000 (situation report until 2020) [29]. That is why the pandemic caused by the SARS-COV2 virus has been and is a concern for governments around the world [31].

The Covid-19 pandemic has placed epidemic modeling at the forefront of public policy-making around the world [4]. From this point of view, the inter national scientific interest in Covid-19 is of great proportions, as indicated by a large number of publications in specialized journals such as medicine, biol ogy, mathematics, physics, such as, for example [7, 10, 11, 13, 18, 19, 26, 30], among others. Therefore, by studying the dynamic behavior on the evo lution of the SARS-COV2 virus, millions of lives could be saved, since the authorities can use this information to continue preparing and facing this crisis that has not yet ended in more convenient ways by counting with a priori information [1]. In fact, thousands of COVID19 patients arrive ev ery day in need of immediate assistance, which is often not available [31]. Likewise, the impact depends directly on the characteristics of the affected population, such as their social contacts, personal economic and educational levels, and the government's resources to face the crisis [1].

In addition, there exist some other drawbacks typical of each region that complicate the anal ysis and help the spread of the infection (SARS-COV2), such as other types of diseases, for example, the case of Mexico with the A/H1N1 virus. The H1N1 virus is an infection of the nose, throat, and lungs. Incipient forms of the H1N1 virus were found in pigs (swine). Over time, the virus changed (mutated) and infected humans. H1N1 is a virus first detected in humans in 2009 and spread rapidly in Mexico and around the world.

However, although the H1N1 virus is currently considered a regular flu virus, concern increases again as the change of season of the year in Mexico (December 21 to March 20) accompanied by the H1N1 virus points to an increase considerable again of cases of spread in Mexico of the SARS-COV2 virus and likewise a rebound in its transmission, thus triggering a new wave of contagion cases. In this sense, the need has arisen to build technological tools that allow predicting the number of infected people and anticipating the worst scenarios.

One of the tools for this purpose can be mathematical models aided by Artifi cial Intelligence techniques. Mathematical models can be used to trace the progress of an infectious disease; having a probable result allows the health authorities to make interventions to reduce or avoid the spread. The mod els use basic assumptions and mathematics to find parameters related to various infectious diseases, these parameters can be used to calculate the ef fect of possible interventions such as: quarantine isolation, social distancing, sanitary regulations, vaccination, etc.

The foundations of mathematical epi demiology date back to the beginning of the 20th century and are supported by the works of public health doctors and biologists. W.H. Hamer applied the law of mass action to explain the epidemic behavior, R. A. Ross showed that mosquitos were responsible for the transmission of malaria and built a model to study its spread; McKendrick and Kermack propose models of compartments, where the population is located in groups that share relevant characteristics with respect to the transmission of a disease (Susceptible, In fectious, Recovered).

Compartmental models make assumptions about the nature and rate of the transferring time from one compartment to another. The transfer rates between compartments are expressed as the derivatives of the sizes of the compartments with respect to time, thus the models are initially represented by differential equations. Brauer et al [5] provide math ematical modeling and analysis of several disease transmission models. They analyzed SEIR epidemic models and obtained expressions for the reproduc tion number and ways of estimating the initial exponential growth rate, so that the reproduction number may be calculated from parameters that can be estimated.

In this work we defined SEIR, SEIRS and SEIRSV (with vaccination) all of them forced with a periodic transmission rate models to simulate and inves tigate the seasonality behavior of the spread of Covid.

The work is organized as follows: section Methods presents the main assumptions of the proposed SEIR, SEIRS, SEIRSV Covid spread models. Section Results shows some numerical simulations. Finally we include some conclusions of this work.

MATERIAL AND METHODS

Our starting point is the basic epidemic SEIR ode model [5]. The main assumptions are that: homogeneous mixing of the population, not demo-graphics in the human population, thus we neglect birth and natural death rates of humans. We consider a constant total population size N of hosts (humans) divided into S susceptibles, E exposed members, I infectives, and R recovered members. There is a significant latency period during which individuals have been infected but are not yet infectious themselves. During this period the individual is in compartment E. A healthy person (susceptible) makes an average of β contacts sufficient to become exposed to infection in unit time from infected people. Exposed proceed to the infectious class at rate η (inverse of the latent period of infection), and infected host recover at rate γ. The basic SEIR ordinary differential equation model is

$$\begin{aligned} S' &= -\beta \tfrac{I}{N} S \\ E' &= \beta \tfrac{I}{N} S - \eta E \\ I' &= \eta E - \gamma I \\ R' &= \gamma I \end{aligned} \tag{1}$$

where, for the constant transmission rate the basic reproduction number is given by

$$\mathcal{R}_0 = \frac{\beta}{\eta} \tag{2}$$

Based on the ordinary differential equations model, our Covid spread model is defined by the following assumptions

1. Time domain is [1,52] epidemiological weeks of the 2021 year.

2. Initial conditions are obtained from reported covid data retrieved from the official Mexican government health agency [15]. The number of suspected are assumed as exposed. $S(1) = N - I(1) - E(1) - R(1)$ where the total population is assumed $N = 126014024$.

3. The transmission rate β is assumed to be time dependent (non autonomous ode system) with a periodic structure:

$$\beta(t) = \beta_0 + \beta_1 cos\left(\pi \frac{t-\phi}{T}\right) \tag{3}$$

Table 1 summarized the parameter that describe the seir forced periodic transmission ode model. A seasonally-varying transmission rate yields oscillations at periods that are integer multiples of the period of forcing. Field observations and mathematical models show that the strength and mechanisms of seasonality can alter the spread and persistence of infectious diseases, thus population-level responses can range from simple annual cycles to more complex multiyear fluctuations [2], [9]. We are mainly interested in showing how the early identification of a seasonal pattern in the data can give us a warning of the early appearance of new outbreaks of the disease

Table 1: Parameters of the extended seir model

Parameter	Description
β_0	mean contact rate
β_1	cyclic transmission rate
η	reciprocal of latent period
γ	recovery rate
ϕ	horizontal shift
T	period

This has been observed by [8] Engelbrecht and Scholes , if the disease does have a substantial seasonal dependence, and herd immunity is not established during the first peak season of the outbreak (no vaccine is available), there is likely to be a seasonality sensitive second wave of infections about one year after the initial outbreak.

Buonomo et.al. [6] provide a review of some key literature results on the influence of seasonality and other time heterogeneities of contact rates, and other parameters, such as vaccination rates, on the spread of infectious diseases. Surveillance systems that are capable to report the duration and size of these outbreaks can provide important information about the underlying transmission parameter and contact patterns in a given population.

RESULTS

Data análisis

Data corresponding to confirmed covid infected in Mexico at 2021 were retrieved from the official repository of the Mexican government [15]. Table 2 displays biweekly confirmed covid infected in Mexico, here we chose biweekly grouped data due the fact that this grouping reduces data oscillations, two weeks resembles the average covid infectious period of 14 days and when making machine learning projections, few points are translated into a further away look in the future.

The Mexican government has already reported in its official site that the peaks (maximum points of the disease in Mexico due to covid 19) correspond to the months of July 2020 for the first wave of infections, the second wave of infections occurred in January of 2021 and the third wave in august 2021. Thus until the end of October 2021, the three covid waves in Mexico.

Table 2: Biweekly confirmed covid infected data Mexico 2021

Biweekly period	Infected reported
1	186,714
2	226,972
3	13,465
4	95,433
5	79,747
6	60,912
7	53,653
8	48,318
9	37,879
10	30,713
11	36,950
12	43,425
13	61,752
14	117,242
15	193,553
16	243,719
17	236,892
18	177,880
19	122,069
20	91,733
21	61,116

They have produced cumulative totals of 3,807,211 infected and 288,365 deaths according to official reports.

Figure 1 shows monthly covid infected in Mexico where we can observe that the three peaks seem to show a periodic behavior. Classical seir models (1) do not present multiple peaks, so in order to capture this behavior we added a periodic transmission rate function as defined by equation (3),[3] [21]. Seasonality in disease incidence is ubiquitous among infectious diseases [23].

Main seasonal drivers include weather variables, such as relative humidity, temperature, and social factors (e.g., contact patterns). Attempts to make long-term predictions of infectious diseases are obstructed by the inability to fully understand the complex interaction of these factors. As reported by Kronfeld et al. [14] human respiratory infections, particularly COVID-19, exert the greatest health care burden during winter months in temperate regions, reflecting high community incidence in these periods as corroborated by the works of Li et al. [17] and Nickbakhsh et al. [22].

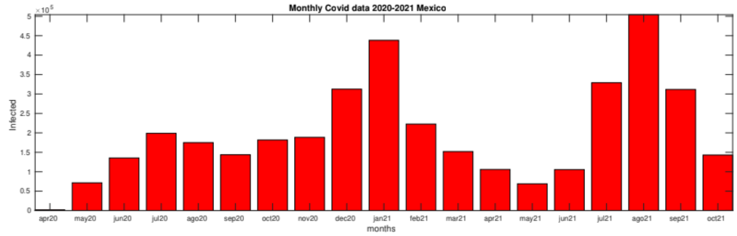

Figure 1: Monthly covid infected official reported data

A visual observation of figure 1 leads us to think that there might be a biannually pattern in peaks. This observation is verified by a simple statistical correlation calculation between infected reported data 2020 (months

April to September) and infected reported data 2021 (may to October). Pearson correlation is 0.834 and correlated graphs are shown at figure 2.

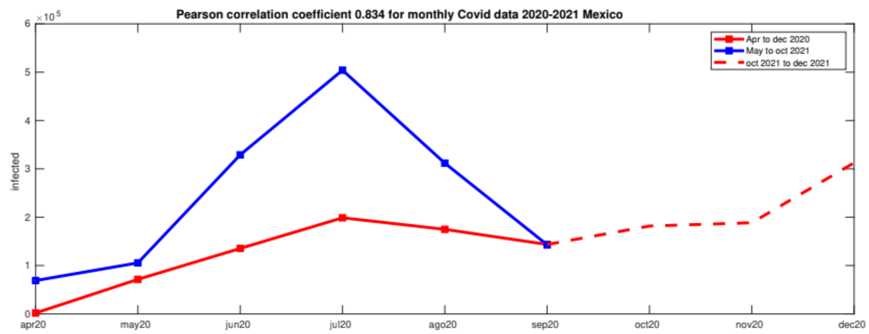

Figure 2: Correlation between monthly infected reported data for 2020 and 2021

At figure 2 the number of reported infected showed a remarkable increase at the end of the year 2020, this suggests that the corresponding correlated data for 2021 would also increase, thus a fourth wave of covid infected could emerge at the end of the year 2021 in Mexico.

Machine Learning

Recently, predictions based on machine learning algorithms have proven to be a useful tool for monitoring and decision making during the course of the covid-19 pandemic. Ghafouri-Fard et al. [12], Lalmuanawma et al. [16] reviewed the use of machine and deep learning approaches in the estimation of COVID-19 spreading trend studies which used these strategies to predict the number of new cases of COVID-19.

Machine learning is an application of artificial intelligence (AI) that provides systems the ability to automatically learn and improve from experience without being explicitly programmed. It manly focuses on the development of computer programs that can access data and use it to learn for themselves.

The process of learning begins with observations or data, such as examples, direct experience, or instruction, in order to look for patterns in data and make better decisions in the future based on the examples that we provide. Several libraries and computer algebra systems include implementations to allow us to obtain a prediction function trained by our input data.

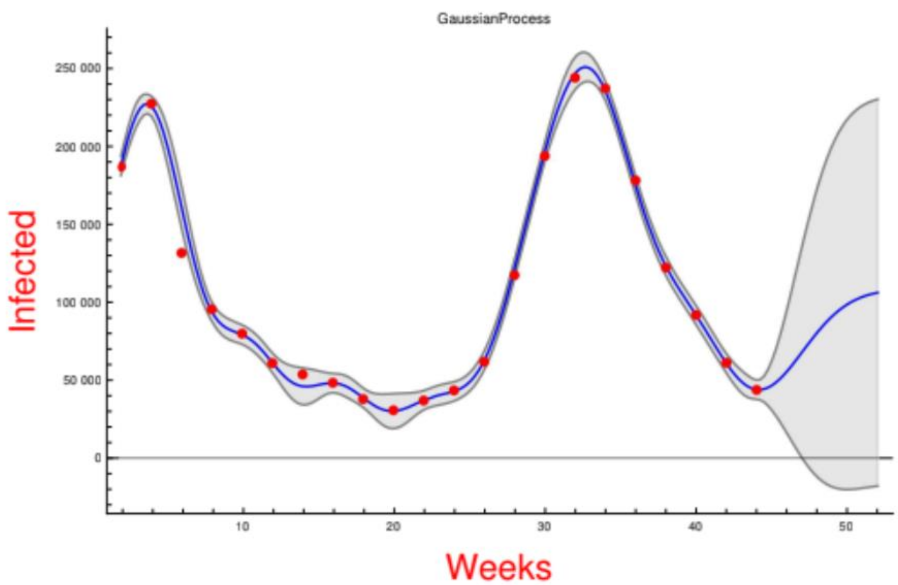

Figure 3: Machine Learning projection for reported covid infected 2021 in Mexico

Figure 3 shows a machine learning projection for confirmed infected cases by using the Predict function of Wolfram Mathematica 12.3 with a Gaussian Process method[25]. The mean projection (blue line) shows an increase in the number of cases for the final eight weeks of 2021.

Forced Periodic SEIR

The seir ode model (2) forced by the periodic transmission function (3) is least squares fitted to biweekly confirmed cases data in Mexico. $T = 13.0$ is assumed corresponding to biannual waves while γ, η, $\beta 0$, $\beta 1$, φ are obtained by using the optimize.curve_fit option of the optimize scipy python library.

Figure 4 shows the seir with periodic transmission rate fitted to officially reported covid infected data in Mexico.

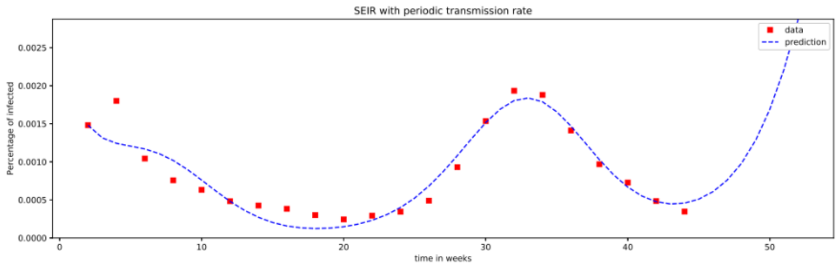

Figure 4: SEIR with periodic transmission rate fitted to reported covid infected data 2021 in Mexico

Forced periodic SEIRS (reinfection)

Here we consider the seir ode model (2) with periodic transmission β(t) (3) but this time we consider reinfection, thus an amount of rR leaves the recover compartment R and returns to the susceptible compartment S.

$$\begin{aligned} S' &= -\beta(t)\tfrac{I}{N}S + rR \\ E' &= \beta(t)\tfrac{I}{N}S - \eta E \\ I' &= \eta E - \gamma I \\ R' &= \gamma I - rR \end{aligned} \tag{4}$$

Moreover we assume that the rate of reinfection has the structure of sigmoid function.

$$r(t) = r_1 + \frac{r_2 - r_1}{1.0 + exp(-r_3(t - r_4))} \tag{5}$$

Here constants r1, r2 describe the asymptotic lines (lower and upper plateau respectively), r3 is the curvature of the growth pattern and r4 is the inflection point. Parameters T = 13, γ and η are assumed given (literature reports average values of 10 and 4 days respectively), while β0, β1, φ, r1, r2, r3, r4 are obtained by fitting the model (4), (5) to reported infected data. Figure 5 shows the curve of infected of the SEIRS model fitted to covid confirmed cases in Mexico. In general reinfection models produce a qualitative endemic behavior. Mandal et.al. [20] examined four potential mechanisms for a new wave to arise: (i) waning immunity restores previously exposed individuals to a susceptible state, (ii) emergence of a new viral variant that is capable of escaping immunity to previously circulating strains, (iii) emergence of a new viral variant that is more transmissible than the previously circulating strains, and (iv) release of current lockdowns affording fresh opportunities for transmission.

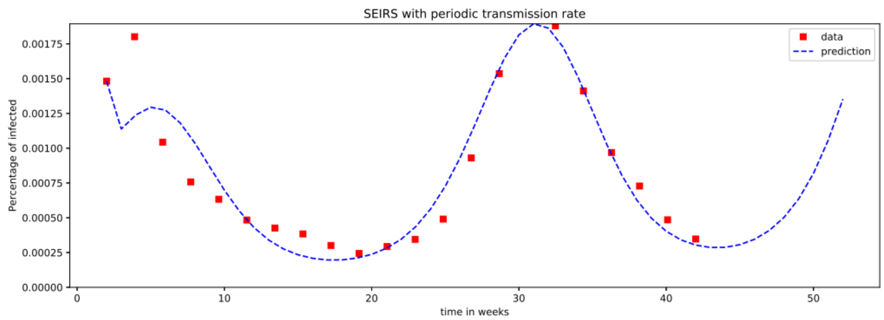

Figure 5: SEIRS with periodic transmission rate fitted to reported covid infected data 2021 in Mexico

Forced Periodic SEIRS with Vaccination (SEIRV)

$$\begin{array}{l} S' = -\beta(t)(1-v)\frac{I}{N}S - (1-c)v\beta(t)\frac{I}{N}S - cvS + rR \\ E' = \beta(t)(1-v)\frac{I}{N}S + (1-c)v\beta(t)\frac{I}{N}S - \eta E \\ I' = \eta E - (\mu+\gamma)I \\ R' = cvS + \gamma I - rR \end{array} \tag{6}$$

We consider the SEIRS ode model and the assumption that susceptible individuals are vaccinated at a constant per capita rate v (vaccine coverage rate) with $0 \leq v < 1$. Due to the partial efficiency of the vaccine, only a c fraction of the vaccinated susceptibles ($0 \leq c \leq 1$) goes to the recovered class, here c is the vaccine efficacy. The remained $1 - c$ fraction of the vaccinated susceptibles has no immunity at all and goes to the exposed class after infected by contact with the infectives. Thus $c = 0$ means that the vaccine has no effect at all, while $c = 1$ implies that the vaccine is perfectly effective [27]. The parameter μ is the constant rate of disease-related death.

We assume the values of the parameters $\gamma = 1.4$, $\eta = 3.5$, $v = 0.025567$ (average value of the data percentage with at least one dose vaccine for Mexico obtained from our world data [24]) $T = 13.0$ (biannual waves) while β0, β1, φ, r, c, μ are obtained by fitting the model 6, 3 to reported infected covid cases in Mexico. Figure 6 shows the SEIRS model with vaccination fitted to confirmed infected cases in Mexico.

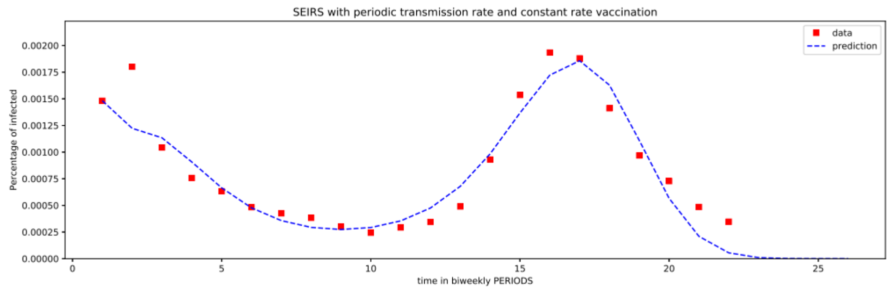

Figure 6: SEIRS with periodic transmission rate, constant vaccination rate fitted to reported covid infected data 2021 in Mexico

Table 3 reports the values of the parameters obtained by fitting data to the models SEIR, SEIRS and SEIRV and their respective 95% confidence intervals, while table 4 reports R-squared value which is used to measure the goodness of the fits.

Table 3: Fitted Parameters

Model	Parameter	Value	confidence interval
SEIR$\beta(t)$	γ	0.16912	(0.04422 , 0.29403)
	η	0.13388	(0.05405, 0.29403)
	β_0	0.55042	(0.14389 , 0.95694)
	β_1	0.87470	(0.22147 , 1.52793)
	ϕ	-2.67228	(-6.29594 , 0.95138)
SEIRS$\beta(t)$	β_0	2.00766	(0.35236 , 3.66297)
	β_1	-1.42314	(-3.60891 , 0.76262)
	ϕ	-3.64983	(-6.12099 , -1.17868)
	r_1	-11.8699	(-26.2676 , 2.52775)
	r_2	0.12166	(-0.28769 , 0.53103)
	r_3	1.16047	(-0.40109 , 2.72203)
	r_4	0.95939	(-1.65968 , 3.57848)
SEIRSV$\beta(t)$	β_0	2.73344	(2.679010 , 2.78787)
	β_1	1.59930	(1.43314 , 1.76547)
	ϕ	17.7941	(17.7404 , 17.8478)
	r	0.57722	(0.50372 , 0.65073)
	c	0.29666	(0.22343 , 0.36988)
	μ	0.04731	(0.01183 , 0.10645)

Table 4: R^2 Fitted Models

Model	R^2
Machine Learning	0.98904
SEIR$\beta(t)$	0.90465
SEIRS$\beta(t)$	0.87174
SEIRSV$\beta(t)$	0.88577

DISCUSSION

For the considered SEIR and SEIRS (reinfection) models, the infected curves are influenced by the oscillatory behavior of the proposed time dependent transmission rate, showing in these cases the possible appearance of a fourth wave at the end of 2021. On the other hand a SEIR ode model withconstant vaccination rate suggests the end of the epidemic in Mexico at the end of 2021.

At the closing of epidemiological week 45, Mexico reports a 57.8 % of the total population vaccinated with at least one doses and the mobility restriction measures have been relaxed with all the Mexican states in green traffic light except Baja California with epidemiological traffic light in orange. However,

United states as well as some European countries with a higher percentage of vaccinated than Mexico have already experienced this situation where, after an apparent decrease in confirmed cases and a relaxation of mobility measures, they have faced the appearance of fourth and fifth covid waves. The SEIRSV model assumes both a constant vaccination rate and a constant vaccine efficiency which is not the best approximation to reality. In fact, supply and demand in the acquisition of vaccines has generated ups and downs in vaccination rates coupled with the fact that Mexico has used different types of vaccines with different effectiveness: Pfizer-BioNTech, AstraZeneca, Sinovac, Janssen, Moderna, Sinopharm approved by the world health organization (WHO) and Sputnik with CanSino not approved by WHO.

CONCLUSIONS

We have proposed the use of SEIR, SEIRS and SEIRSV ode models, all of them forced with periodic transmission rate in order to model and simulate the seasonality behavior of Covid spread. Models are fitted to covid infected cases reported by the Mexican secretariat of health. Values for the fitted parameters, intervals of 95% of confidence and R2 metrics are reported. A visual inspection of the bar plot of confirmed infected cases grouped by months shows an apparent correlation between the months April to September 2020 and months may to October 2021. A Pearson coefficient of 0.834 is calculated and the correlation of the graphs for the confirmed covid cases in 2020 and 2021 suggests that a fourth wave could occur at the end of 2021 in Mexico.

A machine learning projection (Gaussian Process) for confirmed covid cases grouped biweekly also suggests that a fourth wave could occur at the end of 2021 in Mexico. Nearly all discussed approaches show the possible appearance of a fourth covid wave in Mexico at the end of 2021. Thus, it is important to consider the seasonal behavior that the covid is starting to show, especially now that the return to school is announced just at the beginning of the flu season in Mexico (October 2021 to February 2022).

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