Modelling by Generation of Poisson Distributed Numbers of First Historical Zika Outbreak in Salta, Argentina.

Abstract

Scopes and Objectives: In this work we describe the first historical Zika virus outbreak recorded in Salta, Argentina, in the year 2017, through Monte Carlo-type simulations using the Poisson model. Later we made comparisons with previous results.

Study design: Retrospective-descriptive studies and stochastic computational experiment analysis.

Place and Duration of Study: Department of Mathematic, Faculty of Exact Sciences. National University of Salta, Argentina, from March 2021 to December 2023.

Methodology: Descriptive and computational experiment analysis. Parameter estimation by Maximum Likelihood and Simulation of type Monte Carlo.

Results: We describe the probabilistic behavior through Monte Carlo simulations of the first historical outbreak of Zika in Salta Argentina, 2017. Based on the data of registered Zika cases, we estimate a probabilistic Poisson model with parameter $\widehat{\lambda} = 13.092\, cases\, week^{-1}$ and confidence interval $95\%\, CI\, [11.889 - 15.110]$. Finally, by computational experiments we generate epidemic outbreaks with 20 runs. The computational experiments shows that, from a qualitative point of view, the descriptions of the outbreak are qualitatively acceptable and they were not better than the probabilistic model obtained in a previous study. However, from the statistical point of view, carrying out computational experiments of 10 comparative runs in each model, the models provide simulations of epidemic outbreaks by Zika virus, for this region of Salta, Argentina, that do not differ significantly at a confidence level of 5%.

1 Introduction

The Zika virus (ZIKV), was identified in Uganda in 1947, its name comes from the Zika forest located near Entebbe, where it was first isolated. Similar to the Dengue and Chikingunya viruses, the ZIKV is mainly spread in tropical and subtropical regions by *Aedes aegypti* mosquitoes. Besides, the ZIKV has the particularity of being transmitted sexually. The symptoms of the disease are mild fever, rash, conjunctivitis, muscle and joint pain, malaise or headache. Symptoms usually last 2 to 7 days [1].

The interest in knowing the spread of the disease has generated social and medical alarms due to the evidence of a causal link between the ZIKV and various congenital lesions, such as microcephaly, when the infection occurs during pregnancy; as well as its association with neurological disorders in adults and children, such as Guillain-Barré syndrome, neuropathy and myelitis. Its rapid global geographic expansion with explosive outbreaks causes concern to the Ministries of Public Health of the different affected countries. In America, this is a new virus, so the entire population is susceptible, with no defense against ZIKV. At the same time, the Aedes mosquito is widespread in the Region, given the climatic conditions, temperature, and humidity in tropical countries [1],[2].

In Latin America, Chile and Brazil were the first countries to report cases in 2014 and 2015 respectively [1]. In Argentina, in 2016 the first case of local transmission of ZIKV through sexual contact was reported in the province of Córdoba. Subsequently, in the province of Tucumán, the first outbreak of vector transmission registered in Argentina took place. In addition, the first case of congenital syndrome associated with ZIKV infection in Argentina was confirmed in the city of San Miguel de Tucumán [2].

In 2017, ZIKV circulation was confirmed in the province of Salta in the towns of Embarcación, General Mosconi, Tartagal, Orán and Rivadavia. In 2018, the province registered a new outbreak that affected the same localities, no cases were registered in pregnant women, and a case of congenital syndrome associated with ZIKV was confirmed [3]. During the 2019/2020, 2020/2021, 2021/2022, and 2022/2023 seasons, although there were people with symptoms compatible with those of ZIKV, this possibility was later ruled out, with which, since then, ZIKV has remained in a phase of silence in this region of Argentina [4],[5],[6] and [7].

Rosales *et al.* (2021)[8], following the ideas that the theoretical concept of the basic reproduction number, R_0, of infectious diseases, could be related to the initial growth of an epidemic outbreak, carry out implementations in Matlab, in order to be able to estimate values for the basic reproductive number based on the data referred to the Province of Salta, Argentina. They qualitatively describe this first historical ZIKV outbreak in Salta using Monte Carlo simulations. Also, they estimate a classic measure of the frequency of a disease, the prevalence ratio. These researchers build a heat map with the estimated values of prevalence in the departments affected by ZIKV infection in this region of Argentina.

In addition, they estimated R_0 with the expression of Begon Harper [9], using a generation time that includes both the human being and the mosquito. These estimates were affected by the simulation type factor, which correspond to 10 runs. However, when 20 or 30 runs were carried out, the scenarios obtained were quite acceptable and can generate rates to be applied to deterministic models of the SIR and SEIR type [8]. In that work, the values of the estimates of the infection forces and R_0 indicated that the first ZIKV outbreak in Salta was of relatively low intensity and short duration, coinciding with patterns that generally present emerging diseases.

In the case of Salta province, Argentina, the situation of cases Zika is new, the first cases were reported in 2017 and provide research opportunities of vital importance in different epidemiological aspects. On this occasion, it is intended to carry out an analysis using the Poisson distribution, estimating the corresponding parameter for said distribution. It is then modeled the epidemic outbreak based on Poisson model and comparing results with the simulations mentioned above.

2 Materials and Methods

In this section, we briefly comment on different aspects of the methods applied in this work. First of all, we present some definitions that were used in the present study, in order to highlight their

application to the situation under analysis.

We first perform the estimation of the parameter that characterizes a Poisson distribution by the Maximum Likelihood Method, for this, we propose the maximum likelihood function and maximize it to find the expression of the Maximum Likelihood Estimator. Following Freund & Walpole [10][FreundWalpole1990], we know that,

Definition 2.1. Let $(X_1, X_2, ..., X_n)$ be a random sample from a population with parameter λ, the Maximum Likelihood Function of the sample is given by

$$L(\lambda) = p(x_1, x_2, ..., x_n; \lambda) = \Pi_{i=1}^{n} p_i(x_i, \lambda) \tag{2.1}$$

In this particular case, we suppose that the marginal probabilities mass functions are

$$p_i(x_i, \lambda) = \begin{cases} \frac{e^{-\lambda} \lambda^{x_i}}{x_i!} & x_i = 0, 1, ... \\ 0 & a.o.c \end{cases} \tag{2.2}$$

maximizing the maximum likelihood function with respect to the λ parameter, the maximum likelihood estimator of the λ parameter of the Poisson distribution is obtained.

$$\widehat{\lambda} = \frac{\sum_{i=1}^{n} x_i}{n} \tag{2.3}$$

We accompany the punctual estimate with the estimate by intervals corresponding to the parameter λ of the Poisson distribution, for a 95% confidence interval we use the expression

$$CI = \left[\ \widehat{\lambda} \pm z_{\frac{\alpha}{2}} \sqrt{\frac{\widehat{\lambda}}{n}} \ \right]$$

see [QuesadaIsidoroLopez1993][11] for more details.

For our situation we consider, $Z(t)$ be equal to the number of cases per ZIKV at time t. Let the probability of occurrence of a human case of Zika in a time interval Δt is equal to $\lambda \Delta t + o(\Delta t^2)$, if the occurrence of cases is a continuous stochastic process, the probability of n cases in time t results.

$$P(Z(t) = n) = \begin{cases} \frac{e^{-\lambda t}(\lambda t)^z}{z!} & z = 0, 1, ..., n, ... \\ 0 & a.o.c \end{cases} \tag{2.4}$$

The process $Z(t)$ is a continuous-time stochastic process which is discrete-valued. Specifically, $Z(t)$ is a Poisson process with intensity $\lambda > 0$.

For computational simulations we generate the sequence $\{Y_n\}$ to be Poisson distributed with parameter λt, i.e., $E(Y_n) = \lambda t$, see by example [12][Allen2007]. It is assumed that we have the sequence $\{U_n\}$ of uniformly distributed numbers on [0, 1]. We know that

$$F_Y(y) = e^{-\lambda t} \sum_{k=0}^{m-1} \frac{(\lambda t)^k}{k!} \ \ for \ \ m \le y \le m+1$$

Therefore, to find Y_n given U_n, the sum is computed until m is found such that

$$e^{-\lambda t} \sum_{k=0}^{m-1} \frac{(\lambda t)^k}{k!} < U_n \le e^{-\lambda t} \sum_{k=0}^{m} \frac{(\lambda t)^k}{k!}$$

Then Y_n is set equal to m.

$$Y_n = \begin{cases} 0 & \text{if } 0 < U_n \le 1 - \alpha \triangle t \\ 1 & \text{if } 1 - \alpha \triangle t < U_n \le 1 \end{cases}$$

For the modelling by simulations of the epidemic curve of the first outbreak, we will define the random variable in a certain probability space.

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Regarding the probability space, we proceed similarly to what was done in a previous work, so for more details we refer the reader to reference [8][JCR2021].

Here we recall the definition related to the triplet $(\Omega, \mathcal{A}, P)$ consisting of the sample space Ω, the $\sigma - algebra$ $\mathcal{A}$ of subsets of Ω, and a probability measure P defined on $\mathcal{A}$ is called a probability space [12][Allen2007]. In this sense, we present the slightly modified the following definition for the case.

Definition 2.2. Let $(\Omega, \mathcal{A}, P)$ a probabilistic space associated to random experiment ε, with $\Omega = \{\omega_i \mid i = 1, 2, ..., m; \omega_i =$ i-th epidemiological week, in which the cases registered that occurred in localities of Department San Martín, Orán and Rivadavia in the first historical outbreak of Zika in Salta}. Let X a discrete random variable defined by $X : \Omega \to \mathbf{R}, X(\omega_i) = n_i$, number of times a case of Zika has occurred in the i-th epidemiological week, ω_i. Let $\mathcal{A} = \{\emptyset, \{\omega_1\}, \{\omega_2\}, ..., \{\omega_m\}, ..., \Omega\}$, be the σ-algebra of events generated by assuming that $\{\omega_i\} \in \mathcal{A}$ for $i = 0, 1, 2, ...$ and $P(\omega_i) = P_{n_i}(\omega_i) \approx p_i(\omega_i)$ be the probability of n_i cases results in the interval *i-th epidemiological week*, w_i , where p_i is the corresponding probability provided by the model obtained of the adjustment to the data of the number of cases of the outbreak.

For the simulations we carry out implementations through scripts in the MATLAB environment [13][Matlab2022]. We also make comparisons with the epidemics simulated with the model found in the present work and with the empirical model found in the work [8][JCR2021]. To do this, we performed several experiments of 10 runs of each model and carried out a multiple comparison analysis of the stochastically generated epidemics. The statistical analysis was performed in the statistical software Statgraphics Centurion (version 16.1.03) [14][Statg2010].

3   Results

The first historical outbreak of ZIKV in Salta, Argentina, occurred in the departments of Orán, General San Martín and Rivadavia, de la provincia de Salta, Argentina, in el año 2017. The total number of Zika cases registrados in this outbreak was, $N = 252$. Figure 1 represents the smoothed curve of human cases infected by ZIKV, during the first epidemiological outbreaks registered in the province of Salta, Argentina, during the epidemiological weeks between EW 4 - EW 23 and EW 45 - EW 52, year 2017, also EW 1- EW 6, year 2018. The curve was obtained using the 4 EW moving average window technique.

The estimate of the λ parameter obtained for the data corresponding to the first Zika virus outbreak obtained was

$$\widehat{\lambda} = 13.092 \; \frac{cases}{week} \tag{3.1}$$

with $95\% \; CI \; [11.889 - 15.110]$. The maximum probability of occurrence of ZIKV infections per epidemiological week was 0.1089 during that period. To verify the goodness of fit, the Pearson test χ^2 was used. At the level of significance of $\alpha = 0.05$, there is no evidence to reject, at this level, the proposed Poisson model for these data, the probability of error was $p = 0.9\%$ (p=0.0093, chi2stat= 27.92).

Figure 2 shows the mass function of Poisson Model for the number cases of this first historical outbreak of Zika, year 2017, in localities of the Departments of the Northern and Northeastern of the Province of Salta, specifically in the Departments of Orán, General San Martín and Rivadavia.

Table 1 shows the probabilities provided by the estimated Poisson model and the cumulative values obtained determined by the first historical outbreak of Zika, this allows us to estimate a probabilistic model for the situation presented in the North-Northeast region of the Salta Province, in northwestern of Argentina.
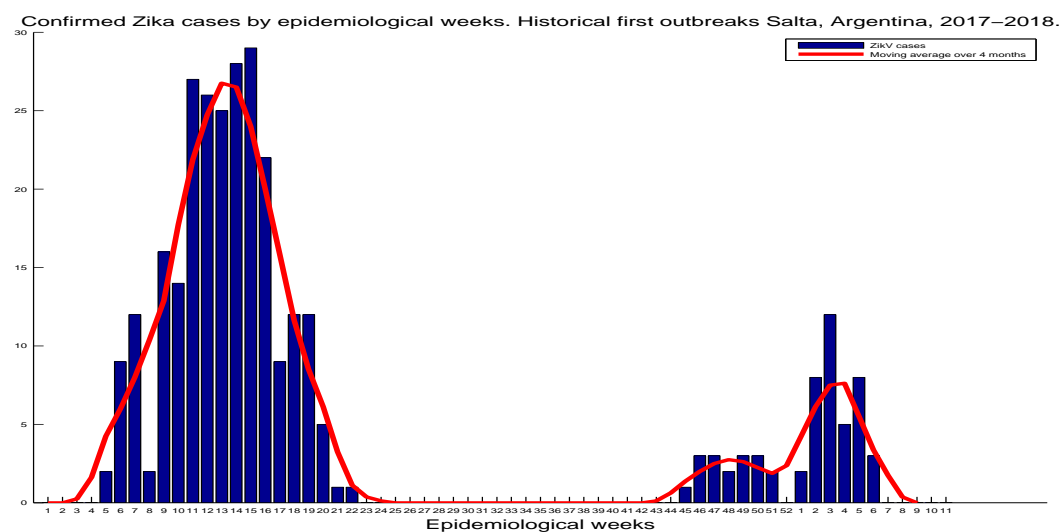
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Figure 1: The first historical outbreaks of ZIKV in the departments of Orán, General San Martín and Rivadavia, Salta Argentina, 2017 and 2018.
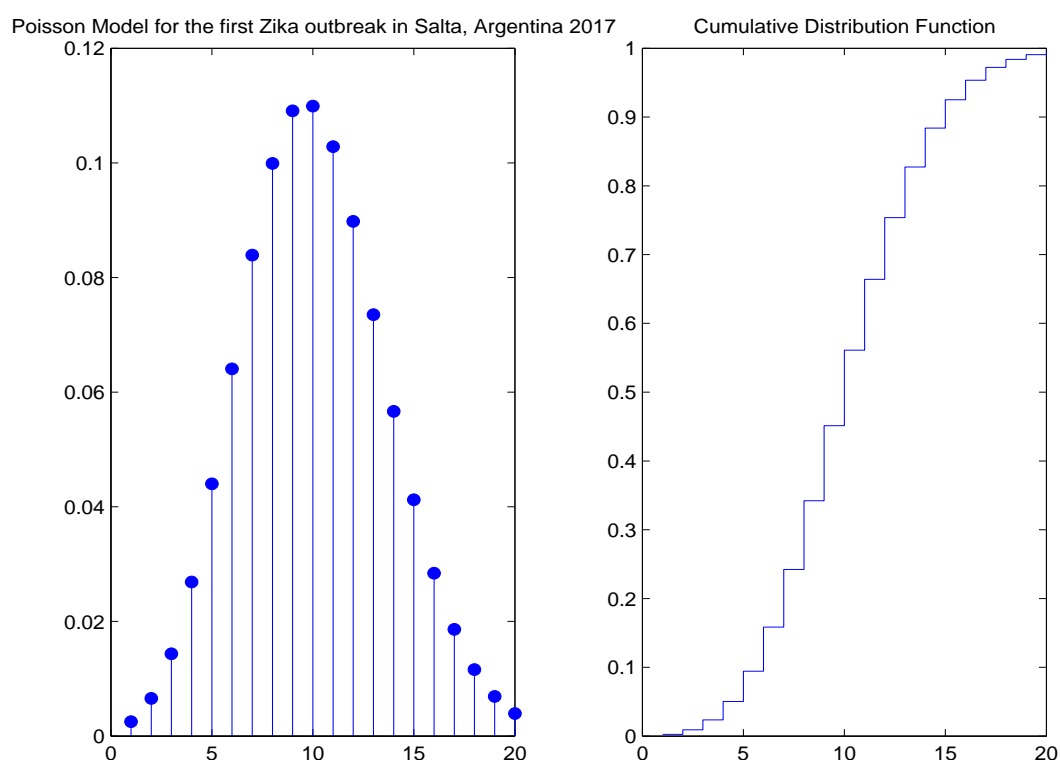

Figure 2: Left Poisson Model for the first outbreak in the departments of Orán, General San Martín and Rivadavia, Salta Argentina. Right Cumulative Distribution Function

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Table 1 Probabilities provided by the estimated Poisson model and the cumulative values obtained for the historical peak first of Zika ocurred from EW 4 to EW 20, Salta, Argentina, 2017.*

height$Z$	Probabilities	Cumulative Probabilities
1	0.0025	0.0025
2	0.0066	0.0091
3	0.0144	0.0235
4	0.0269	0.0504
5	0.0440	0.0944
6	0.0641	0.1585
7	0.0839	0.2424
8	0.0999	0.3423
9	0.1091	0.4514
10	0.1099	0.5613
11	0.1028	0.6641
12	0.0898	0.7539
13	0.0735	0.8274
14	0.0566	0.8840
15	0.0412	0.9252
16	0.0284	0.9536
17	0.0186	0.9722
18	0.0116	0.9838
19	0.0069	0.9907
20	0.0039	0.9946

*: Total number of Zika cases in the first historical outbreak in Salta, $N = 252$.

The values in Table 1, based on the data from the first Zika outbreak in Salta, allow us to propose a probabilistic model, as specified in the following Proposition 3.1.

Proposition 3.1. *The estimation for the c.d.f., $F_X(x)$ based on the data corresponding to the historical outbreak first of ZIKV occurred in Salta, Argentina, 2017, in the Departments of San Martín, Orán and Rivadavia, provide the following probabilistic model, $F_X : \mathbf{R} \to [0,1]$, defined with the assignment*

$$x \mapsto F_X(x) = \begin{cases} 0.0000 & x \in (-\infty, 1] \\ 0.0025 & x \in (1, \quad 2] \\ 0.0091 & x \in (2, \quad 3] \\ 0.0235 & x \in (3, \quad 4] \\ 0.0504 & x \in (4, \quad 5] \\ 0.0944 & x \in (5, \quad 6] \\ 0.1585 & x \in (6, \quad 7] \\ 0.2424 & x \in (7, \quad 8] \\ 0.3423 & x \in (8, \quad 9] \\ 0.4514 & x \in (9, \quad 10] \\ 0.5613 & x \in (10, 11] \\ 0.6641 & x \in (11, 12] \\ 0.7539 & x \in (12, 13] \\ 0.8274 & x \in (13, 14] \\ 0.8840 & x \in (14, 15] \\ 0.9252 & x \in (15, 16] \\ 0.9536 & x \in (16, 17] \\ 0.9722 & x \in (17, 18] \\ 0.9838 & x \in (18, 19] \\ 0.9907 & x \in (19, 20] \\ 0.9946 & x \in (20, 21] \\ 0.9953 & x \in (21, 22] \\ 0.9956 & x \in (22, 23] \\ 1.0000 & x \in (23, +\infty) \end{cases} \tag{3.2}$$

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With the probabilistic model obtained, we carried out computational experiments in order to describe qualitatively and quantitatively the first historical outbreak of the Zika virus that occurred in the province of Salta in 2017. The first historical outbreak that marked the arrival of Zika in Salta, in 2017, registered 252 human cases.

Several runs were performed each with 252 stochastically obtained Zika cases. Some examples of these results are presented in the Figure 3. Figure 3 shows four examples of these runs, to the left, simulations of 10 runs (- blue lines) and the actual outbreak of Zika in Salta, 2017 (-red line). To the right, the corresponding average values of number cases of Zika stochastically obtained (*- blue lines) and the actual outbreak Zika in Salta, 2017 (-red line)
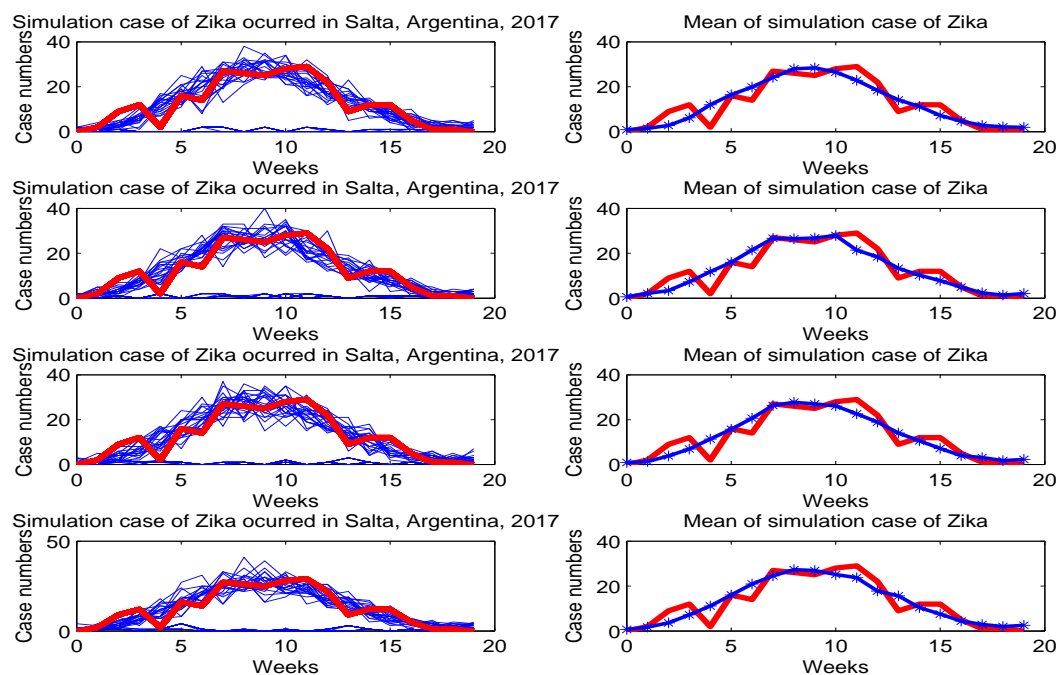

Figure 3: Left, an example showing four simulations of 10 runs (- blue lines) and the actual outbreak of Zika in Salta, 2017 (-red line). Right, the corresponding average values of number cases of Zika stochastically obtained (*- blue lines) and the actual outbreak Zika in Salta, 2017 (-red line).

Regarding the comparisons of the simulations provided by the two models, we find results as presented, e.g.

Table 2 Anova table for comparison of simulations obtained by the Poisson model and the model found in [8][JCR2021].

Source	Sum of Squares	Df	Mean Square	F-Ratio	P-Value
Between groups	0,17952	19	0,00944843	0,00	1,0000
Within groups	39155,7	380	103,041		
Total (Corr.)	39155,9	399			

The ANOVA table, see Table 2, decomposes the variance of the data into two components: a between-group component and a within-group component. The F-ratio, which in this case equals

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0,0000916955, is a ratio of the between-group estimate to the within-group estimate. Since the P-value of the F-test is greater than or equal to 0,05, there is not a statistically significant difference between the means of the variables at the 5% significance level.

According the multiple comparison procedure to determine which means are significantly different from which others, in this case, there are no statistically significant differences between any pair of means at the 95,0% confidence level. Also, one homogenous group is identified by letter A's. The same letter form a group of means within which there are no statistically significant differences. On the other hand, the method currently being used to discriminate among the means is Fisher's least significant difference (LSD) procedure. With this method, there is a 5,0% risk of calling each pair of means significantly different when the actual difference equals 0. Figure 4 show the intervals based on Fisher's least significant difference (LSD) procedure. They are constructed in such a way that if two means are the same, their intervals will overlap 95,0% of the time. These intervals are used to determine which means are significantly different from which others.
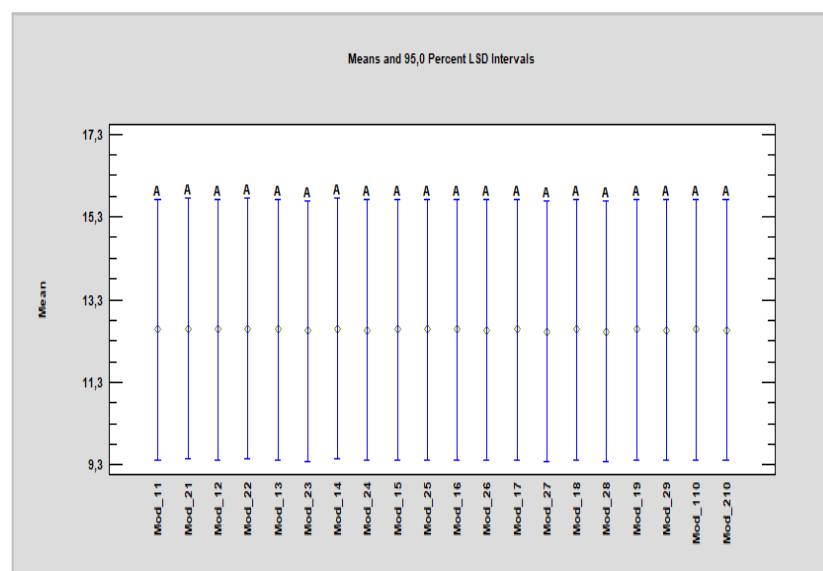

Figure 4: Means and 95% LSD Intervals.

Figure 5 shows twelve simulations, six of the Poisson model found and six of the model obtained in the work of Rosales *et. al.*, 2021 [8]. In them you can see the qualitative description provided by the models of the first historical outbreak of the arrival of Zika to regions of Salta, Argentina for the first time in 2017.
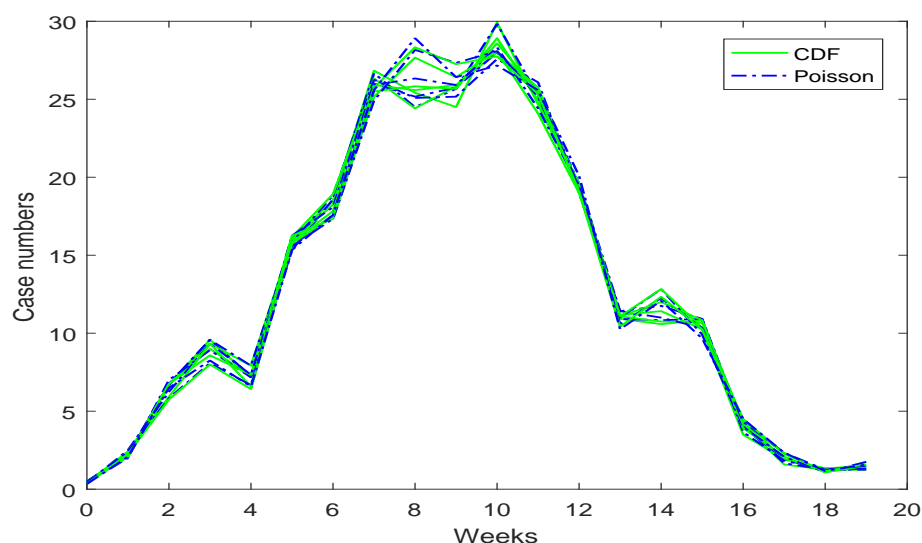
Figure 5: Comparisons between Poisson simulations and a model with an empirical cumulative distribution function. First historical ZIKV Outbreak in Salta, Argentina in 2017, simulated with CDF (- green) and simulated with Poisson Model (-. blue).

4   Discussion

Figure 1 shows the time series of Zika cases in the years 2017-2018, a seasonal behavior is observed, with a first peak greater than the second. The historical entry of ZIKV for the first time to the province of Salta had a rather low impact in terms of intensity according to the intrinsic growth rate [8] [JCR2021], perhaps this allowed the epidemic to not be sustained at an endemic level, in the years 2022 and 2023 despite the fact that cases of dengue and chikingunya have occurred, no new cases of Zika have been reported in the region under survey.

The Table 1 shows the probabilities of Zika cases number and its cumulative probabilities for the historical peak first of Zika ocurred from EW 4 to EW 20, Salta, Argentina, 2017, according to the Poisson model obtained. On the other hand, the function given by (3.2) provides, the estimation for the c.d.f., $F_X(x)$ based on the data corresponding to the historical outbreak first of ZIKV occurred in Salta, Argentina, 2017, in the Departments of San Martín, Orán and Rivadavia, resulting like this theoretical probabilistic model obtained.

Pearson's goodness-of-fit test, at a significance level of 0.05, shows that the data could be described with a Poisson model with parameter $\widehat{\lambda} = 13.092 \frac{cases}{week}$. However, the variance of the data is much greater than the mean. The data present the phenomenon of overdispersion, nevertheless this does not prevent the hypotheses of the model from being fulfilled, as Pascual points out [15][Pascual2022]. This situation could be improved by performing some transformation on the dependent variable. On the other hand, as Kay points out [16][Kay2022] the estimated intensity could allow simulating the times between cases occurrences. It relies on the property that the interarrival times are IID $exp(\widehat{\lambda})$ random variables.

Figures 3 shows four simulated epidemic runs respectively from the model built based on the real data of the first historical outbreak of Zika in Salta, Argentina. On the left, it is observed that, the greater the number of runs, a certain convergence region is generated by the simulations. However, it is observed that some simulations remain outside the convergence region, an effect that could be caused by the overdispersion that the data presents. Perhaps this could be improved by applying some transformation to them to mitigate this phenomenon or by applying pseudo-Poisson and negative Binomial models.

On the right, are the averages of the simulations generated with the proposed Poisson model,

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compared with the true values of reported Zika cases. It could be said that the model describes the Zika outbreak qualitatively, however, from the quantitative point of view, better descriptions were obtained with the empirical model of accumulated frequencies obtained in the work of Rosales *et. al.* [8][JCR2021]. Although the intensity of the Poisson process could be estimated, we prefer the empirical probabilistic model determined by the cumulative distribution function determined by the number of ZIKV cases per week.

The estimated probabilities could be used to estimate the basic reproductive number R_0 for the outbreaks of ZIKV in this region, as was done by Rocklöv *et. al.* [17][Roclovketal2016] for the initial phase of the epidemic in America assuming a Poisson distribution using weekly count data. They found average R_0 estimates in a range of 2.2-4.8, although we, found much lower R_0 ($R_0 \approx 1.105$ 95% CI [1.104-1.106] and $R_0 \approx 1.111$ 95% CI [1.110-1.112]) estimates using other methods, but which are consistent with the low intensity of these outbreaks that occurred for the first time in this province of Argentina [JCR2021].

With respect to the comparisons of the stochastic simulations provided by the Poisson Model found in this work and the model obtained in a previous work [8], we see that, from the statistical point of view, there are no significant differences according to the analysis carried out for different runs experienced. In the example of the analysis presented here, for ten simulations provided by the Poisson model and ten respectively using the CDF model found in [8], the aforementioned can be observed. Both by the multiple comparison procedure to determine which of the simulated stochastic outbreaks are significantly different in means, as well as by the Fisher's least significant difference (LSD) procedure Figure 4, we did not find statistically significant differences between the means at a 5% level of significance. On the other hand, we observed that, from a qualitative point of view, the descriptions obtained with the CDF model would seem better. These observations could be deduced from the different simulations, such as those presented, for example, in Figure 3 and 5.

Deterministic models were favored over stochastic approaches [Kobreetal2019], this paper presents a theoretical probabilistic model whose estimated intensity of the described epidemic process could be used in deterministic models, making the descriptions they could provide more realistic.

It is necessary to deepen research with stochastic models applied to neglected diseases, this would improve the discussions, especially for situations in this region of Argentina, which is characterized by a subtropical climate whose maximum temperatures continue to increase year after year, aggravating the situation in regions that are postponed due to shortages of infrastructures for drinking water, electricity and a health system with multiple deficiencies.

5   CONCLUSIONS

In this work we have qualitatively described the first historical outbreaks of Zika that occurred in Salta, in 2017 and 2018, using moving average whit 4-week window. At present, after the outbreaks of 2017 and 2018, Zika has remained in a phase of silence in this region of Argentina.

The model found to describe the probabilistic behavior for the first historical outbreak of Zika in Salta in its expansion through South America has been presented in Proposition 3.1. We found an intensity for the Poisson epidemic process of 13.092 cases per week presented in the expansion of Zika to this region of South America in northwestern Argentina.

We have paid more attention to the most significant outbreak of the historical entry of Zika for the first time to this region of Salta located in the northwest of Argentina. The estimated intensity and 95% CI, were $\widehat{\lambda} = 13.092$, $95\% \, CI \, [11.889 - 15.110]$ respectively and the maximum probability of occurrence of ZIKV infections per epidemiological week was 0.1089 during that period. The descriptions simulated by the Poisson model do not present differences statistically speaking with respect to a model using the empirical CDF obtained in a previous work. However, the descriptions from a qualitative point of view, according to our criteria, are not better than those provided by the model with the CDF.

In the case analyzed, the Poisson model found describes the first historical outbreak from the qualitative and quantitative point of view when the number of cases provided is analyzed, however

the descriptions of each simulation are not better than those provided by the model of cumulative frequency, made in a previous study.

Perhaps more realistic descriptions of the scenarios could be obtained for the situation presented for the first time by the entry of ZIKV in Salta, Argentina, considering Pseudo-Poisson or negative binomial models. The possibility remains open for the development of future work in this sense.

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