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EXTENDED ABSTRACT

Impact of the Covid-19 pandemic on dispensing of anticoagulant therapy

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Introduction:

On the 11th of March 2020, the World Health Organization (WHO) declared a pandemic due to the disease caused by the novel coronavirus, Sars-Cov-2 [1]. Governments implemented many measures to decrease the incidence of COVID-19 cases and control the spread of this disease like social distancing, periods of lockdown, etc. Such measures affected people's lives and may have reduced access to health care and services. In this regard, we want to understand whether the pandemic had an immediate and or long-term impact on dispensing of novel oral anticoagulants (NOAC) drugs, which are drugs used to help prevent blood clots. To answer this research question, we used interrupted time series analysis (ITS) [2], a method proposed to evaluate the effectiveness of population-level interventions or health events that have been implemented at a defined point in time.

Methods:

Data collection was carried out at the level of consumption of NOACs (WHO ATC class: B01AA03, B01AA07, B01AE07, B01AF01, B01AF02 and B01AF03) on an outpatient basis in Portugal, it was collected from the hmR Information System, which is a national database that provides national and regional estimates representative of drug dispensing data for all medicines, from about 84% of all Portuguese community pharmacies. The data used was from January 2017 to December 2021.

For the analysis, the measure of interest was the DHD (DDD per 1000 inhabitants per day). The DDD is the assumed the average maintenance dose per day for a drug used for its main indication in adults [3]. To obtain an estimate of the resident population in Portugal, the INE Portal was used. The DHD was calculated using the formula: total DDD / (number of days in the period under analysis * population) *1000. For the analysis of the interrupted time series, four variables of interest were used. The dependent variable was the total DHD per month and the independent variables were time; the intervention as a dummy variable (0-pre-intervention; 1-post-intervention); and the trend – time since the start of the intervention. Results will be stratified by substance. A segmented linear regression model was built, adjusted with ARIMA (Autoregressive Integrated Moving average) errors. $Y = \beta 0 + \beta 1 * \text{Time} + \beta 2 * \text{Intervention} + \beta 3 * \text{Trend} + \epsilon t$, with $\epsilon t \sim \text{ARIMA}(p, d, q)$ [4]. In this model, β0 estimates the baseline level of the outcome, mean number of DHD per month, at time zero;, β1 estimates the change in the average number of DHD per month before the intervention; β2 estimates the level variation in the mean number of DHD immediately after the intervention (immediate effect), and β3 estimates the change in the trend of the average monthly number of DHD per month after the threshold compared to the monthly trend before the threshold (long-term effect). Statistical analysis was performed in R. Significance level adopted was 0.05.

Results:

According to the results of the exploratory analysis, the data appear to have an increasing linear trend over the years and do not show seasonality. In addition, in the series graph, there is a peak in March 2020 that can be explained due to the implementation of the quarantine in which there was a considerable increase in demand for treatment stocking. The data of March was considered an outlier, so it was excluded from the modeling analysis of the models in order not to bias the analysis results. Figure 1 represents the graph of the trend before and after the intervention. To select the orders of ARIMA (p and q), we inspected the graphs of the sample autocorrelation and partial autocorrelation functions and for order d, we use the first difference. Through the result, some models were proposed that fit the data, the best model found was ARIMA (2,1,1) with an AIC of 109.44 and the coefficients were all statistically significant. The values of the time, intervention, and trend coefficients were 0.164, -1.128, and 0.051 respectively. Figure 2 shows the graph of the distribution of residuals, autocorrelation, and partial autocorrelation respectively of the

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Conflict of interest:
The authors declare no conflict of interests.

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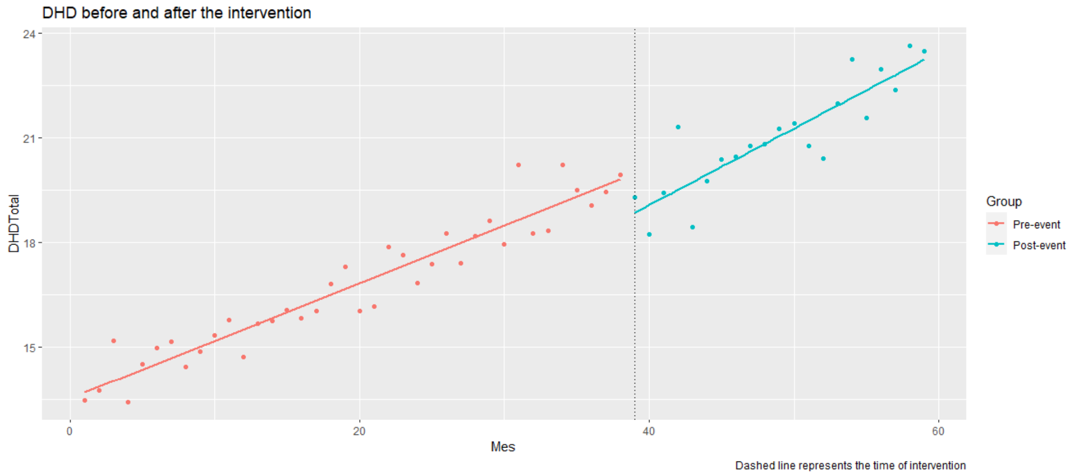

Figure 1 - Distribution of the Interrupted Time Serie

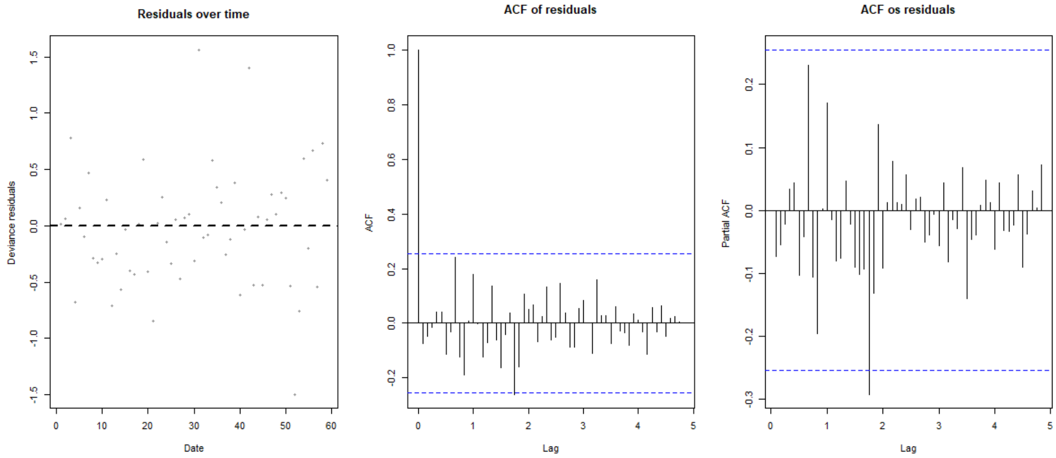

Figure 2 - Distribution of residuals, autocorrelation, and partial autocorrelation of residuals from ARIMA

ARIMA model. The residuals appear to be randomly distributed and the Ljung-Box test does not reject the hypothesis that the residuals are random (p-value =0.07). The autocorrelation graph does not show significant autocorrelation however, we have a lag that reaches the marginal of the interval.

Conclusion:

The analysis suggested that the COVID 19 pandemic had an immediate and significant impact on NOAC consumption (a decrease of 1,128 DHD), with the absolute effect of the intervention being 11,7 patients and the relative change in DHD associated with the intervention was of -5.8%). Also, a long-term impact seen by a positive and significant change in trend after the start of the pandemic period (+0.051 DHD per month) compared to the pre-pandemic period.

References:

1. Organização Mundial da Saúde OPA da S. Histórico da pandemia de COVID-19. Histórico da pandemia de COVID-19. Avalaible from : https://www.paho.org/pt/covid19/historico-da-pandemia-covid-19
2. Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. J Clin Pharm Ther. 2002;27(4):299-309. https://doi.org/10.1046/j.1365-2710.2002.00430.x
3. WHO Collaborating Center for Drug Statistics Methodology. Difinition and introduction of DDD. Difinition and introduction of DDD. Avalaible from : https://www.whocc.no/lists_of__temporary_atc_ddds_and_alterations/
4. Fattah J, Ezzine L, Aman Z, El Moussami H, Lachhab A. Forecasting of demand using ARIMA model. Int J Eng Bus Manag. 2018;10:1-9. https://doi.org/10.1177/1847979018808673