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Article

Influence of vaccination on COVID-19 reproduction rate: Time trends and persistence analysis

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Abstract: This paper aims to study how the increase in vaccination rate in Israel affect to the behavior of COVID-19 reproduction rate, from 19 December 2020, to 25 April 2021. Multiple advanced econometrics methodologies are used to analyze the degree of persistence, to understand the relationship between these two times series and the long-term behavior. The results of our study indicate that the vaccinations cause long-run effects to COVID-19 reproduction rate and the vaccination provides useful information to predict the COVID-19 reproduction rate. Also, we determine whatever exogenous shocks related with the virus reproduction will have a very short impact over time. The first change in trend occurs on 13 January 2021, with 24.37% of the population vaccinated and when it can be seen that the increased rate of vaccinations causes the infection rate to decrease.

Keywords: COVID-19 reproduction rate; vaccination rate; fractional integration; FCVAR model; wavelet analysis

1. Introduction

Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) is a member of the Coronaviridae (COVID) family and caused a public health emergency of international concern [1]. It became the most serious public health crisis in recent times, with significant impact on geopolitics and the global economy [2]. This virus is transmitted from person to person and is extremely infectious [2]. It has spread rapidly due to aerosol exposure [1]. In addition, the virus can cause multi-organ failure [3], which can be fatal for a large number of infected persons [4].

Globally, this virus spread rapidly [5]. Because of this, COVID-19 was considered a pandemic by the World Health Organization (WHO) on 11 March 2020 [6]. Following the onset of this pandemic and its global spread, disastrous impacts took place in a variety of domains, mainly those related to health and lifestyles. Although COVID-19 can affect populations of all ages, it is noteworthy that older people are more sensitive to the virus and are more likely to suffer a higher mortality rate [1,7,8].

In an unprecedented attempt to find viable vaccines in time to limit the COVID-19 pandemic, the scientific community worked incredibly hard [9].

It usually takes five to ten years to develop a vaccine [10], but since lives and health were at risk, the world's population could not afford to wait that long. Unfortunately, many people contracted the disease and died day after day. As a result, according to a recently proposed paradigm for vaccine development, the development period was shortened from ten to fifteen years to one to two years [11]. However, in this particular case, the vaccine was developed in a matter of months rather than years. Thus, pharmaceutical companies have been able to offer several COVID-19 vaccines in as little as 12 months since the first cases were discovered, thanks to the extraordinary efforts of the scientific community [12].

The FDA authorized the COVID-19 vaccine manufactured by Pfizer and BioNTech on 11 December 2020. This kind of vaccination is a messenger ribonucleic acid (mRNA) vaccine that has been changed by nucleotides and is made with lipid nanoparticles (BNT162-2 mRNA). For this vaccination, there will be two intramuscular doses (30 µg, 0.3 mL each), spaced 21 days apart from one another [13].

The first country to carry out mass vaccination against COVID-19 was Israel. On Sunday, 20 December 2020, the Israeli population received the first dosage of the vaccine [14–16], resulting in a vaccination rate of 60% of adults and those in at-risk categories.

Kulhánek [17] claimed that a great deal of research has been done on the COVID-19 pandemic; many of these studies have concentrated on the impact the virus has had on society rather than vaccination [18–20].

From the point of view of the analysis of the effects of vaccination on the virus, Toharudin et al. [21] examined the influence of vaccination on the spread of the pandemic and examined if stringent public restrictions had a mitigating effect on the COVID-19 outbreak in Jakarta. The authors' findings regarding vaccination were ambiguous and inconsistent. They claimed that immunization had caused the COVID-19 trend to decline, but they later clarified that limits were the reason for the decline in new cases. Furthermore, the claim that 0.7% of vaccinated individuals may stop the pandemic is wildly speculative, thus there is insufficient vaccination data to draw firm conclusions regarding the effectiveness of vaccinations. The analysis conducted by Rustagi et al. [22] focuses on the impact of immunization in Asian nations. They used support vector machines, polynomial regression, and linear regression techniques. They say that after the initial vaccination dosage, there is a drop in overall fatalities and cases; however, the reduction increases to 75% with a second dose. Chen et al. [23] endeavored to quantify the impact of immunization on the progression of COVID-19 in the United States. Hospitalizations and the total number of cases were the dependent variables in their OLS regressions. They concluded that vaccination slowed the expansion of the two dependent variables. The number of illnesses and fatalities that the immunization campaign avoided was modeled by Kayano et al. [24]. They assert that their study resulted in an almost 30% decrease in overall cases and a nearly 70% decrease in mortality. In addition, they note that a significant impact of the vaccination variable is the number of cases and fatalities averted. Watson et al. [25] estimated the number of cases and fatalities saved using the Metropolis-Hastings Markov Chain technique. Jain et al. [26] examined the effectiveness of the COVID-19 vaccine in 32 European nations against the Omicron strain of the virus. The Poisson regression model with fixed effects was selected by the authors. They discovered a really significant finding: a percentage increase in complete immunization corresponds to an almost 17% drop in overall cases. Some other studies suggested vaccine efficacy against COVID-19 [14,27,28].

Israel has been among the top nations in the world during the SARS-CoV-2 pandemic for its ability to develop organizational planning for emergency response and its capacity for calm reaction. This has led to an incredibly successful vaccination program, largely because of effective deployment at the health services level and a sizable financial investment in the purchase of vaccines, specifically those developed by Pfizer-Biotech laboratories (BNT162b2). This allowed for the population to attain a state of partial immunity and a greater percentage of vaccinated individuals [29].

His vaccination distribution organization aimed to stop or at least mitigate the severe effects of COVID-19 on public health by immunizing as many people as possible with a single dose.

The BNT162b2 vaccine was administered to 86,601 participants in a research conducted recently in Israel [30], and it was shown that the immunizations were effective 14–20 days after the first dosage. Hassan-Smith et al. [31] conducted additional studies of BNT162b2 vaccination data and assessed vaccine effectiveness to be between 89% and 91% in the 15–28 days period following the first dose. Levine-Tiefenbrun et al. [32] achieved very similar results.

After examining 4081 Israeli healthcare professionals, Amit et al. [33] found that, in the first ten days following vaccination, only 22 of them contracted the virus, and only 13 of them experienced COVID-19 symptoms.

In the literature, several studies such as Broutin et al. [34], Xiao et al. [35], Althouse and Scarpino [36], Shioda et al. [37] used wavelet analysis to observe the behavior of vaccines against different infections that have caused a serious public health problem.

Other researchers such as Biswas et al. [38], Wang et al. [39], Bohdanovet al. [40], among others used models such as SARIMA, ARIMA or ARISA to understand and forecast the behavior of various infectious diseases.

But in none of the cases, to analyze the COVID-19 virus.

To our knowledge, this research work is the first to use time series techniques as fractional integration and fractional cointegration models to measure the degree of persistence and the long-term relationship of total vaccination and infection rate for the case of Israel. It also uses methodologies based on Bai and Perron's [41] analysis and the continuous wavelet transform (CWT) to identify the structural break in which vaccination changes the trend of virus infection, being able to identify the effective percentage of vaccinated persons needed to change the trend of infection.

The paper is organized as follows. Section 2 and 3 data source and methodology applied in the paper are shown. Section 4 presents the main empirical results, while the final section shows the main conclusions of this research work.

2. Data

The data used to carry out this study have been obtained from Ritchie et al. [42] which is published and managed by researchers at the Blavatnik School of Government at the University of Oxford. The data used in this research paper have a daily frequency and the sample period is from 19 December 2020 to 25 April 2021.

The time series we have used refer to: 1) COVID-19 reproduction number to see the pattern or trajectory of the average number of people to whom a single infected person will transmit the virus; and 2) total (accumulated) vaccinations in the case of Israel. The data used in this study is represented in **Figure 1** to show the behavior of both.

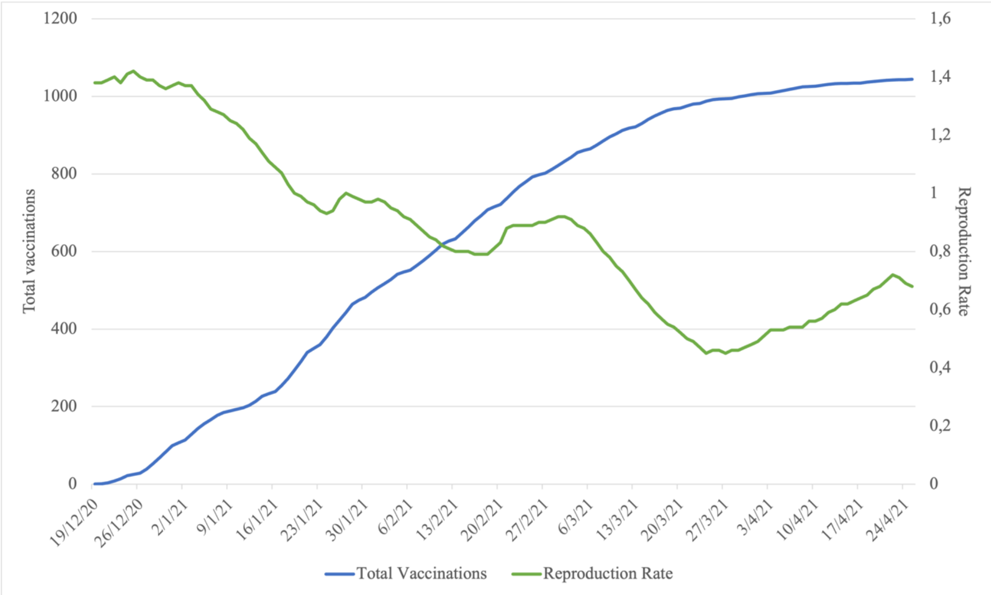

Figure 1. Daily data for total vaccinations and COVID-19 reproduction rate in Israel.

3. Methodology

3.1. Unit roots

Unit roots can be tested in many different ways. To this research we use ADF test based on Dickey and Fuller [43]. There are many other tests available to calculate unit roots that have a greater power such as Phillips and Perron [44] in which a non-parametric estimate of the spectral density of u_t at the zero frequency is used. Also, considering deterministic trends, we use the methodology based on Kwiatkowski et al. [45] and Elliot et al. [46], producing all essentially the same results.

3.2. ARFIMA (*p*, *d*, *q*) model

Following authors such as Diebold and Rudebusch [47], Hassler and Wolters [48], Lee and Schmidt [49] and others, it is now a well stylized fact that all unit root methods have very low power if the true data generating process displays long memory or if it is fractionally integrated. Thus, in what follows, fractional orders of differentiation are allowed.

For this reason, we use the ARFIMA (p, d, q) model where the mathematical notation is:

$$(1-L)^d x_t = u_t, t = 1, 2, \tag{1}$$

In Equation (1), x_t refers to the time series that has an integrated process of order d ($x_t \approx I(d)$), d refers to any real value, L is the lag-operator ($Lx_t = x_{t-1}$) and u_t refers to I(0). The Akaike information criterion [50] and Bayesian information criterion [51] were used to select the appropriate AR and MA orders in the models.

The d parameter has been estimated considering all combinations of AR and MA terms ($p; q \leq 2$) for the time-series and for the subsamples taking into account their confidence bands at 95%.

3.3. Breitung-candelon test

The causality test proposed by Breitung and Candelon [52] contributes to providing an idea about whether the relationship between both time series is temporary or permanent [53–55]. Because it interprets Granger causality across several frequency domains, this test has an advantage over other frequently used causality tests. To this end, two-time series—one based on coherence and the other on the bivariate spectral-density matrix—are categorized according to their spectral associations. An overall count of immediate forward and backward causality mechanisms is then obtained from the categorization.

According to Breitung and Candelon [52], the VAR(p) model below can be used to specify the interdependence between two variables, x and y:

$$x_t = \alpha_1 x_{t-1} + \alpha_p x_{t-p} + \beta_1 y_{t-1} + \cdots + \beta_p y_{t-p} + \beta_{1t} \tag{2}$$

The null hypothesis, $H_0: M_{y \to x}(w) = 0$, as tested by Geweke [56], matches the null hypothesis of linear restriction given as:

$$R(w)\beta = 0 \tag{3}$$

where β denotes the coefficient vector of y. $R(w)$ is defined as:

$$R(w) = \left[\frac{\cos(w)\cos(2w) \ldots \cos(pw)}{\sin(w)\ \sin(2w) \ldots \sin(pw)}\right] \tag{4}$$

The F-statistics for the null hypothesis in Equation (3) has an approximated distribution of $F(2, T-2P)$ for $Fw \in (0, \pi)$. Furthermore, co-integration is frequently used as a framework for examining the frequency-based Granger causality test. Therefore, Breitung and Candelon [52] substitute x_t in Equation (2) for Δx_t. As a result, the existence of cointegration between the series suggests that the primary long-term causation and zero-frequency causality share conceptual similarities. However, if there is no long-term link in the stationary case, the evidence of a causal association at a low frequency implies that the variable under consideration's frequency element can be predicted by a different variable.

3.4. FCVAR model

Following Johansen and Nielsen [57], we use their multivariate Fractional Cointegration Vector Autoregressive (FCVAR) model to check the relationship of the variables in the long term. The FCVAR model is notated in the next equation:

$$\Delta^d X_t = \alpha\beta' L_b \Delta^{d-b} X_t + \sum_{i=1}^{k} \Gamma_i \Delta^b L_b^i Y_t + \varepsilon_t \tag{5}$$

where ε_t is a term with mean zero and variance-covariance matrix Ω that is p-dimensional independent and identically distributed; α and β are $p \times r$ matrices where $0 \leq r \leq p$. The relationship in the long-term equilibria in terms of cointegration in the system is due to the matrix β. Controlling the short-term behavior of the variables is due to parameter Γ_i. Finally, the deviations from the equilibria and their speed in the adjustment is due to parameter α.

3.5. Continuous Wavelet Transform (CWT)

Time series are an aggregation of components operating on different frequencies. So, the most outstanding information is hidden in the frequency content of the signal.

For this reason, this methodology makes a lot of sense.

Wavelet coherence and wavelet phase difference have been used to deepen this research in the time-frequency domain. This study allows to analyze the interaction of the time series in the time domain and revealing structural changes without the need for it to comply with the stationarity characteristic [58,59].

To identify hidden patterns and/or information, we use the wavelet coherency plot that measure the correlation between the time series in the time-frequency domain. To get this result, we calculate the $WT_x(a,\tau)$ that is the wavelet transform of a time series $x(t)$, projecting the mother wavelet ψ to map the original time series onto a function of τ and a:

$$WT_x(a,\tau) = \int_{-\infty}^{+\infty} x(t)\frac{1}{\sqrt{a}}\psi^*\left(\frac{t-\tau}{a}\right)dt \tag{6}$$

We choose Morlet wavelet as the mother wavelet because it is a complex sine wave within a Gaussian envelope, so we will be able to measure the synchronism between time series (see [59]).

Taking into account the results that we get using Wavelet Transform, Wavelet COherence helps us understand how one time series interacts with respect to the other. We can define this term as:

$$WCO_{xy} = \frac{SO\left(WT_x(a,\tau)WT_y(a,\tau)^*\right)}{\sqrt{SO(|WT_x(a,\tau)|^2)SO\left(\left|WT_y(a,\tau)\right|^2\right)}} \tag{7}$$

The SO parameter represents the smoothing operator in time, being relevant since if it were dispensed with, the wavelet coherence for all scales and times would be one (see [60]). It is possible to find the codes developed with MATLAB for the CWT solution on the Aguiar-Conraria website.

4. Empirical results

4.1. Unit roots

We start with the use of Unit Root tests (ADF, PP and KPSS) to determine whether a series is stationary I(0) or non-stationary I(1). In data analysis this is very important as it allows a more consistent interpretation of the model parameters. A trend or seasonal variation can distort the results and lead to erroneous conclusions about the underlying relationships in the data. The results are displayed in **Table 1**.

We have obtained the results using the Augmented Dickey-Fuller (ADF) test, the Phillips Perron (PP) test and the Kwiatkowski-Phillips-Schmidt-Shin (KPSS) test displayed in **Table 1**, which suggest that the total vaccination rate is stationary I(0). In the case of the COVID-19 spread rate we conclude that the time series are non-stationary I(1). Thus, we have to calculate the first differences to make this time series stationary I(0) (see **Table 1**).

Table 1. Unit root tests.

	ADF			PP			KPSS	
	(i)	(ii)	(iii)	(i)	(ii)	(iii)	(ii)	(iii)
Original Data and First Differences in total vaccinations rate								
Total Vaccination Rate	−3.1534*	−3.7529*	−5.3104*	−382.2684*	−414.7715*	−490.6638*	0.3670*	0.1432*
d Total Vaccination	-	-	-	-	-	-	-	-
Original Data and First Differences in COVID−19 reproduction rate								
Reproduction Rate	−2.1438*	−1.7209	−1.0642	−2.1852*	−1.6399	−0.8765	1.1968	0.1631
d Reproduction Rate	−4.8185*	−5.1280*	−5.3382*	−4.7607*	−5.1275*	−5.2919*	0.2456*	0.0799*

(i) No deterministic components; (ii) intercept, (iii) linear time trend. * Statistic significant at the 5% level.

The results suggest that the total vaccination rate is stationary I(0). In the case of the COVID-19 reproduction rate we conclude that the time series are non-stationary I(1). Therefore, for the case of reproduction rate time series presents a trend that is not deterministic but stochastic. This means that deviations from the mean are not automatically corrected over time. Each future value depends on the previous value plus an error term, thus accumulating the impact of all past errors. Once we apply to this latter time series the first differences, we get a stationary behavior I(0).

4.2. Fractional integration

Following the results obtained in **Table 1** and due to the lower power of the unit root methods under fractional alternatives, we also employed ARFIMA (p, d, q) models to study the persistence of the time series related to total vaccination and COVID-19 spread rate in Israel.

The advantages of using the ARFIMA (p, d, q) model over any Unit Root tests are several; 1) They allow fractional values for d providing greater flexibility in how the series is modeled; 2) They capture long-term dependence; 3) They offer a complete framework for modeling and predicting time series.

Table 2 displays the fractional parameter d and the AR and MA terms obtained using Sowell's [61] maximum likelihood estimator of various ARFIMA (p, d, q) specifications with all combinations of p, $q \leq 2$, for each time series.

Table 2. Results of long memory tests.

Long memory test						
Data analyzed	**Sample size (weeks)**	**Model Selected**	***d***	**Std. Error**	**Interval**	**I(*d*)**
Total Vaccination Rate	128	ARFIMA (2, d, 1)	0.32	0.0691	[0.21, 0.43]	I(d)
Reproduction Rate	128	ARFIMA (1, d, 0)	0.59	0.0982	[0.43, 0.75]	I(d)

We observe from **Table 2** that the estimates of d that we get focusing on the total vaccination rate and the COVID-19 reproduction rate is lower than 1 in both cases ($d < 1$). Also, we conclude that the results obtained are fractional $I(d)$ because are in the range (0, 1), that implies fractional integration. Therefore, these results suggest that both time series are expected to be mean reverting and the exogenous shocks will have a very short impact over time and the trends of the series analyzed will recover in a short period of time.

4.3. Frequency causality test based on Breitung and Candelon

Once we have studied the statistical properties of each time series, we use the frequency causality test to examine the interactions between both time series in the short, mid and long-term.

Performing a bivariate causality analysis allows us to identify the influences that one variable or time series exerts on the other. Also, past values of the causal variable provide useful information that can be exploited to predict future values of the dependent variable.

Using the full-time series to estimate the causality in frequency domain, we find different results. Focusing on the results of the Wald test statistics and the p-value (in parentheses) shown in **Table 3**, we find the vaccinations (Vacc) causes long-run effects to COVID-19 reproduction rate (Repr) and the result is statistically significant at 10% in the long-run. These results indicate that vaccination provides useful information to predict the COVID-19 reproduction rate.

Table 3. Breitung and Candelon frequency domain causality test results.

Hypothesis	**Lag**	**Long Term** ($\boldsymbol{\omega = 0.05}$)	**Medium Term** ($\boldsymbol{\omega = 1.5}$)	**Short Term** ($\boldsymbol{\omega = 2.5}$)
Original Time Series				
Repr → Vacc	4	1.21 (0.56)	0.58 (0.75)	1.09 (0.58)
Vacc → Repr		5.60^{*} (0.06)	1.52 (0.47)	1.79 (0.41)

4.4. Results of FCVAR

Once we have determined that the relationship exists between vaccination and reproduction rate and is not spurious (the relationship between both is significant), we want to determine the long-run equilibrium relationship of the two variables jointly and their co-movements. To do so, we use Fractional Cointegration VAR model (see [57]). The results are summarized in **Table 4**.

Table 4. Results FCVAR model.

	$\boldsymbol{d \neq b}$	**Cointegrating equation beta**	
		Total Vaccination Rate	**Reproduction Rate**
Panel I: Total Vaccination Rate and COVID-19 Reproduction Rate	$d = 0.864\ (0.081)$ $b = 0.864\ (0.072)$	1.000	−61.818
	$\Delta^d\left(\begin{bmatrix}\text{Total Vaccination Rate}\\ \text{COVID}-19\ \text{Reproduction Rate}\end{bmatrix}-\begin{bmatrix}0.000\\0.000\end{bmatrix}\right) = L_d\begin{bmatrix}-0.878\\-0.000\end{bmatrix}\nu_t+\sum_{i=1}^{2}\hat{\Gamma}_i\Delta^d L_d^i(X_t-\mu)+\varepsilon_t$		

According to the results that we get using FCVAR model, we are going to focus in two terms. In the integrating and cointegrating part ($d \neq b$) and the beta term to analyze the behavior of the time series.

From Panel I, where we analyze the long-term relationship between both time series, we observe that the order of integration of the individual series is 0.864 ($d =$

0.864) getting the same magnitude in the reduction in the degree of integration ($b = 0.864$) in the cointegration regression. This result implies I(0) cointegration errors. So, we cannot reject the hypothesis where the shock duration is short-lived due to the error correction term shows short-run stationary behavior.

On the other hand, we observe from the cointegrating equation beta that a one-point increase in the total vaccination rate in Israel imply a decrease in the COVID-19 reproduction rate (around 62 points).

4.5. Structural breaks and continuous wavelet transform

In order to verify whether the total number of people vaccinated in Israel has brought about a change in the trend of the COVID-19 spread rate and when this change in trend has occurred, we use Perron and Vogelsan [62] and Bai and Perron [41] approaches. The break dates, for the daily case are reported in **Table 5**.

Table 5. Structural breaks.

Time Series	Structural break dates at significance level 5%
	13 January 2021
COVID-19 Reproduction Rate	5 February 2021
	12 March 2021

To see if this is verified, we use multivariate analysis based on time-frequency domain to understand the correlation that exists between both variables during the structural break dates identified previously.

From **Figure 2**, we can get several results. Wavelet Coherency is represented in section (a) of **Figure 2** and tell us when and at which frequencies the interrelations between time series occur and when they are the strongest, identifying the main regions with statistically significant coherency (5% of significance level). To identify the regions we used Monte Carlo simulations (n = 1000). We observed that the main regions with statistically significant consistency coincide with the structural changes cited above, finding that the impact of vaccines on the rate of COVID-19 spread is significant.

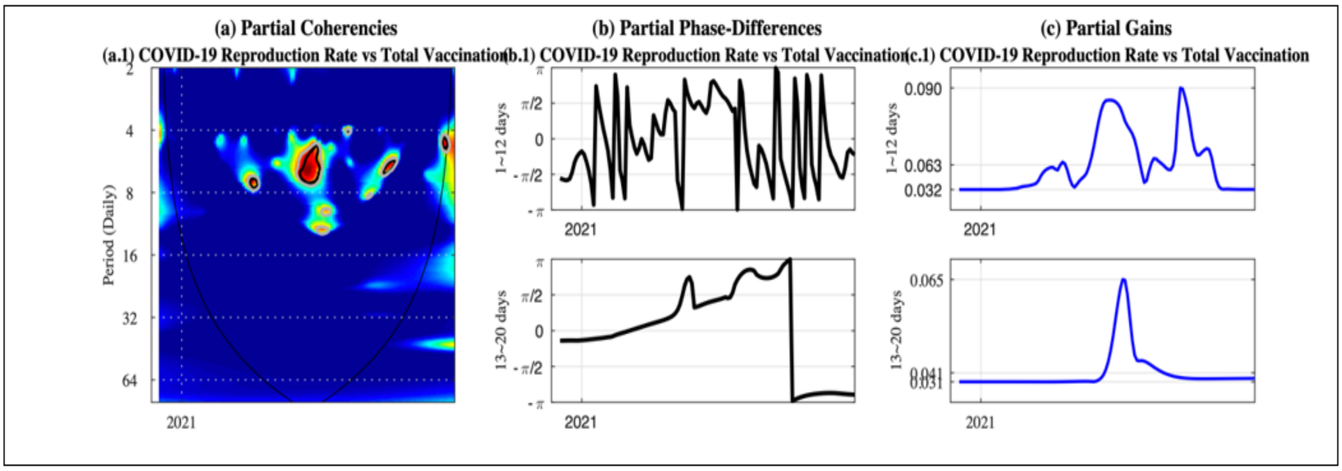

Figure 2. Wavelet coherency and phase difference between total vaccination and reproduction rate.

Once we have identified the regions that corresponds to the high coherency, we have to look the results obtained in section (b), that is the partial difference in the 1–12 frequency band. This result allows us to determine the impact and importance of the shock of one variable in relation to the other. On the results previously obtained, the phase difference is between [$\pi/2$, π]. This means that an increase in vaccination causes the infection rate to decrease. According with these results, we conclude that the contraction of the virus is confirmed 26 days after the start of the vaccination rollout in Israel, with 24.37% of people vaccinated.

5. Concluding comments

The first country to carry out mass vaccination against COVID-19 was Israel. Starting in December 2020, Israel implemented a rapid and efficient vaccination campaign, managing to vaccinate a large proportion of its population in a short period of time. This effort included procuring a sufficient quantity of vaccines and mobilizing its health system to ensure rapid and effective distribution of doses. Israel's strategy served as a model for other countries in terms of speed and vaccination coverage. His vaccination distribution organization aimed to stop or at least mitigate the severe effects of COVID-19 on public health by immunizing as many people as possible with a single dose.

In order to understand the behavior of the COVID-19 reproduction rate depending on total vaccine distributed per day in Israel, we conduct this research paper using the database provides by Ritchie et al. [42] which is published and managed by researchers at the Blavatnik School of Government at the University of Oxford. The period analyzed is 19 December 2020, to 25 April 2021.

Our first focus has been to analyze the statistical properties of these time series using several unit root methods, including ADF [43], PP [44], and KPSS [45]. The results suggest that the total vaccination rate is stationary I(0). In the case of the COVID-19 spread rate we conclude that the time series are non-stationary I(1). Thus, we have to calculate the first differences to make this time series stationary I(0). We also used techniques based on fractional integration, and the results indicated that the values of d in the ARFIMA model are below 1, where an exogenous shock in the vaccination or in the infection trend rate of the virus is not going to be significant and does not cause a change in the trend in the future.

Once we have studied the statistical properties of each time series, and in order to understand the interactions between both time series in the short, mid and long-term, we perform a bivariate frequency causality test. The results indicate that vaccination provides useful information to predict the COVID-19 reproduction rate.

With the analysis we performed with the FCVAR model, we observed that the combination of both variables in the long term presents a degree of cointegration I(0), that is, a stable and long term relationship. On the other hand, we observe from the cointegrating equation beta that a one-point increase in the total vaccination rate in Israel imply a decrease in the COVID-19 reproduction rate (around 62 points).

Finally, using Bai and Perron [41] we found three structural changes that we also observed using wavelet analysis. In addition, with this last methodology we demonstrate that vaccination begins to affect the transmission of the virus between 4 and 16 days from the administration of the doses and the first change in trend occurs on 13 January 2021 with 24.37% of the population vaccinated and when it is apparent that the increased vaccination has caused the infection rate to decrease.

Conflict of interest: The author declares no conflict of interest.

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