JoCASS
Çukurova Anestezi ve Cerrahi Bilimler Dergisi
2018 Adana

WHEN TO IMPLEMENT PHARMACEUTICS POLICIES: DEDUCTIONS FROM THE PERIODICALLY INTEGRATED AVERAGE COST PER PRESCRIPTION DATA

İLAÇ POLİTİKALARI NE ZAMAN UYGULANMALI: PERİYODİK BÜTÜNLEŞİK REÇETE BAŞINA ORTALAMA MALİYET VERİSİNDEN ÇIKARIMLAR

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Geliş Tarihi/Received: 05.07.2021 Kabul Tarihi-Accepted: 23.07.2021 Available Online Date/Çevrimiçi Yayın Tarihi: 31.08.2021
Cite this article as: Turgay Yıldırım Ö, Yılmaz T, Yıldırım S. When to Implement Pharmaceutics Policies: Deductions from the Periodically Integrated Average Cost per Prescription Data J Cukurova Anesth Surg. 2021;4(2):102-12.
Doi: 10.36516/jocass.2021.78

Abstract

Introduction: Pharmaceutics are integral to the healthcare; therefore, dynamics of their prices affects not only firms but the wellbeing of the public as well. Consequently, this study aims to investigate the dynamics of the pharmaceutical prices as well as the effect of shocks on the series for the purpose of policy implementation, exploiting the periodic structure of the series.

Materials and Methods: The study focuses on the end user prices hence the price data is taken as average price of prescriptions. The data is a time series obtained from Social Security Institution's Monthly Statistical Bulletins and includes the period 2008m12 - 2020m02. The series is investigated using periodic models.

Results: The series depicts strong periodicity, moreover it is found out to be periodically integrated. Consequently, the monthly average price of prescriptions is modeled using periodically integrated autoregressive models. The time varying accumulations of shocks of the models indicate the shocks on spring and summer months have the most severe effect such that it may change the stochastic trend of the series. Additionally shocks on winter have large, long-run impacts.

Conclusion: The shocks can occur intentionally as government policies on pharmaceutics or unintentionally such as pandemics, unexpected fluctuations in exchange rates. On one hand intentional shocks in winter have larger long run effects, but such shocks are less likely to change the dynamics of the series. On the other hand, unintentional shocks at winter should be dealt carefully since their effect is going to be long lasting. Finally the models agree that policy shocks in spring and summer seasons are more likely to be successful whereas policy makers must take swift action when an unintentional shock occurs in these seasons.

Keywords: Pharmaceutics pricing policies, average cost of prescriptions, periodic autoregression

Öz
Giriş: İlaçlar, sağlık hizmetlerinin ayrılmaz bir parçasıdır, bu nedenle fiyatlarının dinamikleri sadece firmaları değil, halkın refahını da etkiler. Bu çalışma, serinin periyodik yapısından yararlanarak, politika uygulaması amacıyla ilaç fiyatlarının dinamiklerini ve şokların seriler üzerindeki etkisini araştırmayı amaçlamaktadır.
Gereç ve Yöntem: Çalışma, son kullanıcı fiyatlarına odaklandığından, fiyat verileri ortalama reçete maliyeti olarak alınmıştır. Veriler, Sosyal Güvenlik Kurumu Aylık İstatistik Bültenlerinden alınan bir zaman serisi olup 2008m12- 2020m02 dönemini içermektedir. Seri, periyodik modeller kullanılarak incelenmiştir.
Bulgular: Serinin güçlü bir periyodiklik gösterdiği, ayrıca periyodik entegre olduğu tespit edilmiştir. Sonuç olarak, reçetelerin aylık ortalama fiyatı, periyodik olarak entegre edilen otoregresif modeller kullanılarak modellenmiştir. Modellerin zamana göre değişen şok birikimleri, ilkbahar ve yaz aylarındaki şokların serinin stokastik eğilimini değiştirebilecek şekilde en şiddetli etkiye sahip olduğunu göstermektedir. Ek olarak, kış şoklarının uzun vadede büyük etkileri vardır.
Sonuç: Şoklar, devletin eczacılık politikalarına yönelik politikaları olarak kasıtlı veya pandemi, döviz kurlarında beklenmeyen dalgalanmalar gibi kasıtsız olarak ortaya çıkabilir. Bir yandan, kışın kasıtlı şokların daha uzun vadeli etkileri vardır, ancak bu tür şokların serinin dinamiklerini değiştirmesi daha az olasıdır. Öte yandan, kışın istenmeyen şoklar, etkileri uzun süreli olacağından dikkatli davranılmalıdır. Son olarak modeller, ilkbahar ve yaz mevsimlerindeki politika şoklarının başarılı olma olasılığının daha yüksek olduğu, ancak bu mevsimlerde kasıtsız bir şok meydana geldiğinde politika yapıcıların hızlı hareket etmesi gerektiği konusunda hemfikirdir.

Anahtar Kelimeler: İlaç fiyatlandırma politikaları, ortalama reçete maliyeti, periyodik otoregresyon

Introduction

Healthcare system in Turkey has undergone a total overhaul in 2003 with the launch of the Health Transformation Program (HTP). The private sector's share began to increase with the inauguration of HTP. Adopting various models of public-private partnership projects, which were applied in 1990's around the world, as the main tool of financing, especially the construction and administration of city hospitals since 2013, distanced the provision of health services from the dominance of the state in the sector[1]. Additionally HTP is suggested to be proceeding in a positive direction regarding patients[2].
The effects of state losing its dominance in the sector, and suggestions regarding the patients are investigated in the literature. The overall change in health outcomes, variables and scope of the HTP or health reforms implemented in Turkey has been well researched[3,4,5]. However the specific effects of these changes on the pharmaceutical market have been largely overlooked[6].
Turkey experienced a significant increase in total pharmaceutical sales from US$ 2.5 billion in 2002 to US$ 8.0 billion in 2012 as a consequence of the improved access to healthcare services following the implementation of the HTP initiated in 2003[7]. The expenditure on pharmaceuticals would have been even greater, unless the pricing mechanism had been changed during the implementation of HTP[7]. In 2006, the pharmaceutical positive list was integrated into health insurance plans and reference pricing was established[8]. In order to reduce pharmaceutical spending a global budget, which will be in effect for three years between 2010 until the end of 2010 is negotiated where SSI holds rights to further public rebates of drugs on the aforementioned positive list unless the budget is met[8]. A further measure to reduce pharmaceutical expenditure has been the encouragement of generic medicine utilization [9,10].
Pharmaceutical expenditure provides only one facet of the impact of HTP on

pharmaceutical market as well as the perspective of pharmaceuticals' overall utilization: the economic one. Pharmaceutical expenditure is essentially influenced by both prices and volumes of the drugs[11]. Hence, this study aims to investigate the dynamics of the price of medicines per prescription. Furthermore this study this study examines the impact of (policy) shocks on the series, in order to establish the optimal timing for implementation of policies regarding the price of pharmaceutics.

Materials and Methods

The data on average cost per prescription is obtained from Social Security Institution's (SSI) Monthly Statistical Bulletins (SGK, Aylık İstatistik Bültenleri) which are publicly available. The data is a time series which calculates the average price in Turkish Liras and consists of the period 2008m12 - 2020m02. In other words, the average price per prescription series starts on December 2008 and ends in February 2020, has monthly frequency and has 135 observation points. A time series plot of the data is available at figure 1.

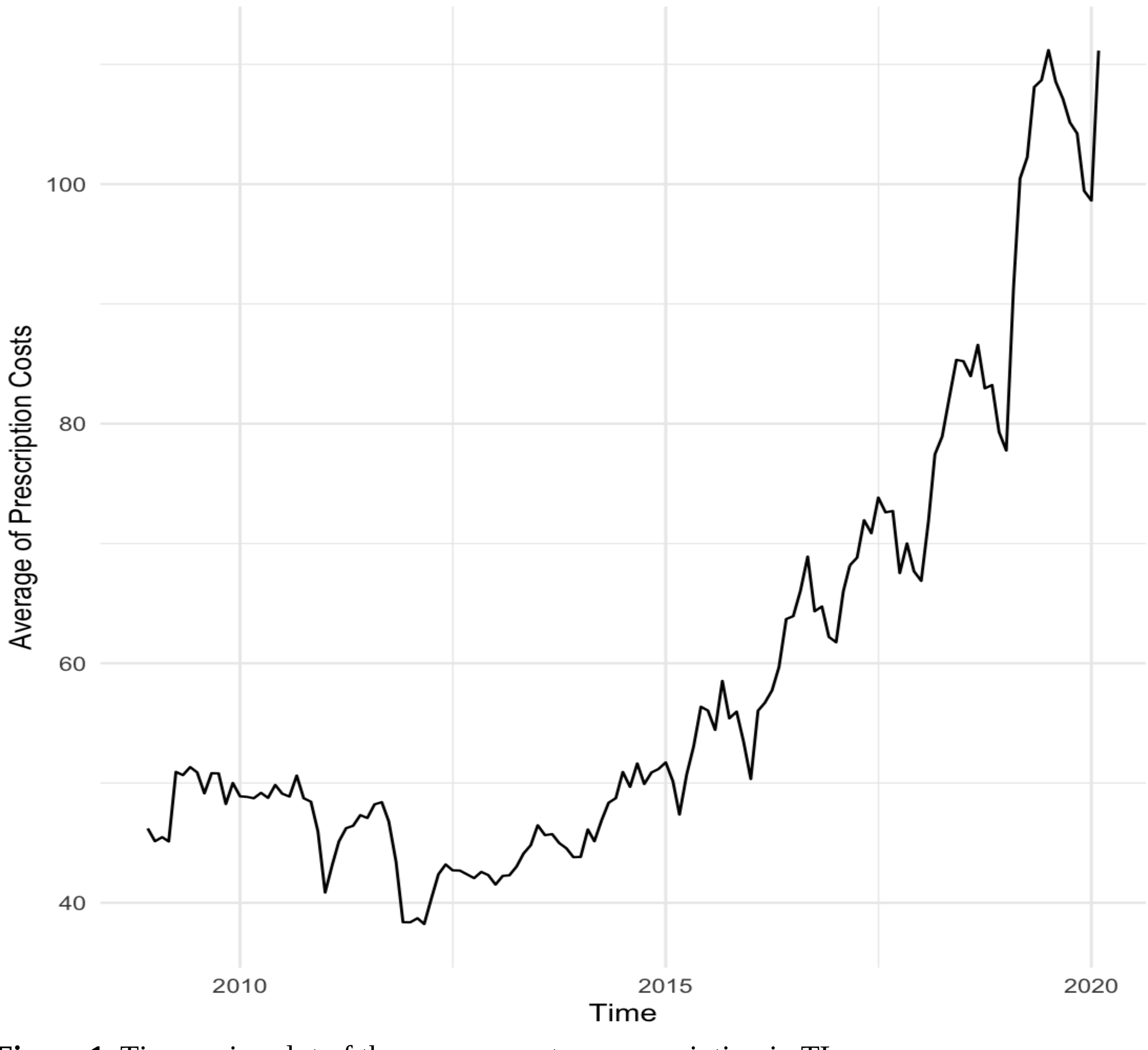

Figure 1. Time series plot of the average cost per prescription in TL

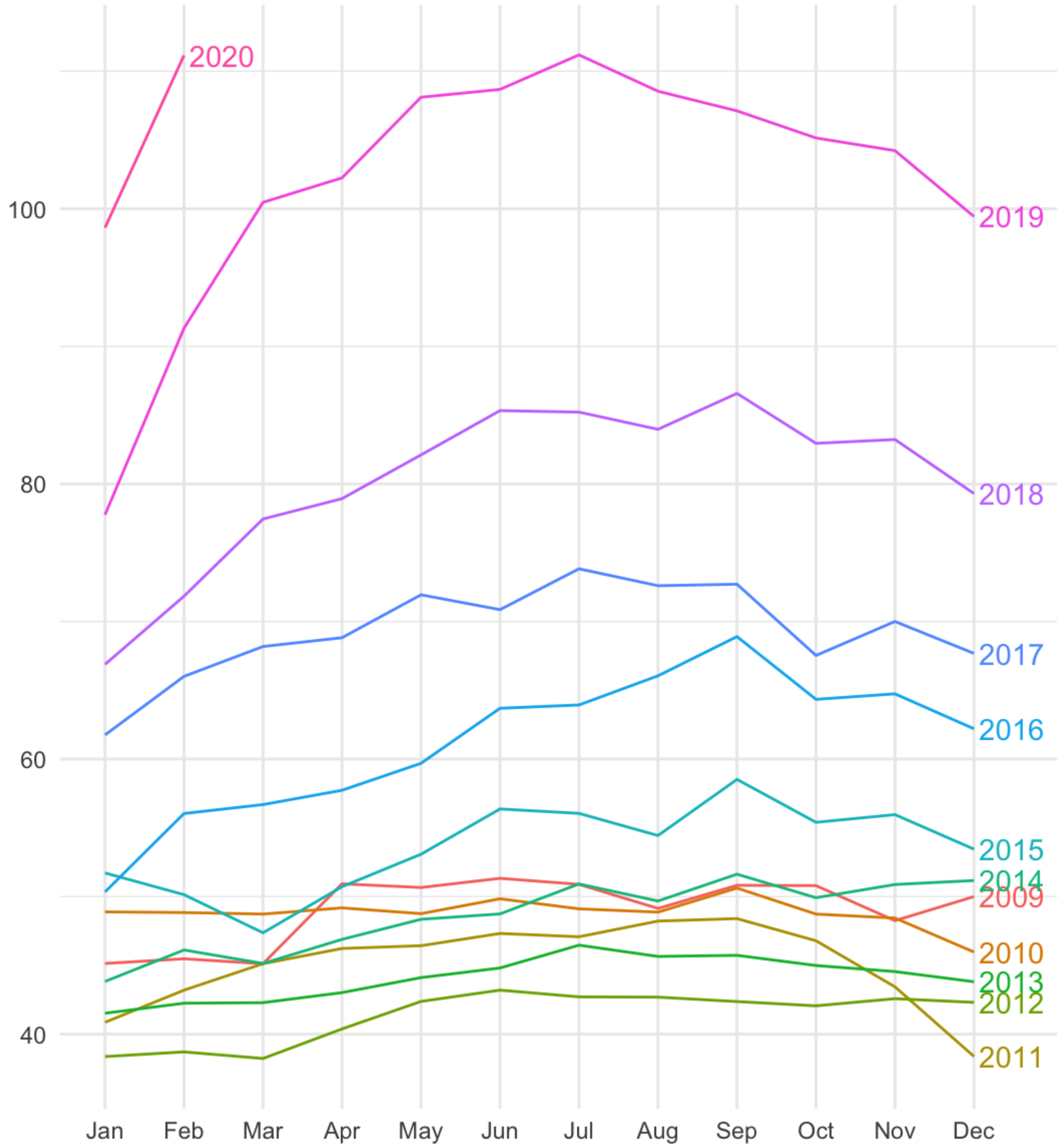

Figure 2. Seasonal plot of the the average cost per prescription

The figure shows that average cost per prescription has characteristic trait which are the upward trend and the oscillations in the series. The seasonal plot of the series in figure 2 cements this observation. In figure 2 instead of a continuous plot form start to end, each year's observations are laid out against the months for each year separately. The 2nd figure clearly indicate that there is an increasing trend, since the observations for each month is higher that observations at the same month in previous years. Furthermore the periodic movement in the series becomes more apparent in figure 2, especially in recent years the average prices in summer months and at beginning of fall have higher values than.

Many studies filter out such periodic motions in a time series due to the problems it creates in empirical analysis. However periodicity is an important feature of a series and investigation of it may unravel characteristics of the series which may not be notices otherwise. Consequently the dynamics of average cost of prescriptions investigated using periodic autoregressive models (PAR) in this study. PAR models by construction take periodic fluctuations, which arise due to seasonality in this case, into account. Due to inclusion of separate AR models such models can handle both cyclic and seasonal patterns better than seasonal ARMA models[12].

A simple PAR model of order p or PAR (p) in short, can be written as follows

$$y_t = \phi_{1s} y_{t-1} + \ldots + \phi_{ps} y_{t-p} + \varepsilon_t \; ; \; s = 1,2,\ldots,12 \; , \; t = 1,2,\ldots,n \; , \; \varepsilon_t \sim iid(0,1) \qquad (1)$$

where n is the number of observations which is 135 in this case. The PAR(p) model includes 12 different autoregressive model of order p, or AR(p) models, one for each month of the year. Therefore, for a monthly series, equation (1) can be rewritten with the more convenient multivariate notation or monthly vector notation.

$$\Phi_0 Y_{s,T} = \Phi_1 Y_{s,T-1} + \ldots + \Phi_p Y_{s,T-P} + \varepsilon_T \; , \; \varepsilon_T \sim iid(0,1) \qquad (2)$$

where Φ_0, Φ_1, … , Φ_P, are the (12×12) matrices which contain the parameters in equation (1). The parameters in the matrices defined as follows

$$\Phi_0(i,j) = \begin{cases} 1, i = j \\ 0, j > i \\ -\phi_{i-j,i}, j < y \end{cases}$$

$$\Phi_k(i,j) = -\phi_{i+4k-j,i}$$

for $i, j = 1,2,\ldots,12$ and $k = 1,2,\ldots,\mathrm{P}$.

This notation is especially useful since it is used to calculate the time varing impact of shocks, which is also a (12×12) matrix. The time varing impact of shocks reaval an crutial feature of the series; it is used to determine the relationship between stochastic trend and seasonal fluctuation[13]. The cumulative effect of the shocks becomes more severe in the month corresponding to the row with the highest values in the impact matrix. Therefore, fluctuation in the stochastic trend of the series is more likely to occur. Similarly, the month corresponding to the column with the highest values has the largest long-run effect[14].

Modeling the series with PAR model if the series is perodically integrated, creates severe problems. Periodic integration is a form of nonsitationarity that arises for existance of unit root in the series which is periodic. Non-stationarity is a characteristic of a time series which, simply put, indicates the distiributional properites of the time series does not remain the same throughout the series[15]. It indicates that any shock on the series have lasting effect, the impact of the shock does not fade away. In other word the impact of the shock jumps one month to the next. In case of periodic integration the shock jumps from same month to the same month in consequetive years, skipping the observations in between[16].

Periodic integration is tested in two steps. First the null hypothesis of the existance of unit root in the series is tested. If this null hypothesis cannot be rejected, either the series has a long run unit root or a seasonal unit root. If the series has long run unit root the series must be estimated an periodic autoregressive with integration (PARI) model or periodically integrated autoregressive (PIAR) model. The second step is to establish whether the series is guided by PARI process or PIAR process. In order to distinguish among PARI and PIAR processes the following null hypothesis is tested; H_0:α_s=1 and H_0:α_s=−1 where α_s are seasonally varying parameters in the periodically differenced representation of equations (1) and (2). If both null hypothesis are rejected the PIAR model is chosen. The time varying impact of shocks can be calculated for PIAR model as well. It works the same way mentioned previously; the rows give information on severity of the shocks, whereas columns give information on long-run effect.

Finally, for modeling purposes two different deterministic components are considered throughout the study. The first deterministic component SI+GT indicates seasonal intercept (SI) and global trend (GT) is added to the model. The second deterministic component SI+ST indicates seasonal intercept (SI) and seasonal trend (ST) is added to the model. SI, which is present in both deterministic components, simply tells us that the series moves around a non-zero value that depends on the month. Moreover the trend, which is discernible in figures 1 and 2, in the series must be controlled for in the models. The trend might be either due to seasonal factors, which can be controlled for with the incorporation of ST into the model, or due to a long-run factor that is globally present in the series, which can be controlled for with the incorporation of GT into the model. The deterministic components prevent any wrong conclusion that might arise due to omission of these cases.

Results

The time series plot is in figure 1 and 2 indicate periodicity in the average cost of prescriptions, this can be formally tested with an F-test. The existence of periodicity at any lag (order of the model) can be tested with the null hypothesis $f_{is} = f_i$ which states the series is not periodic for s=1,2,...,12 and i=1,2,...,p; against the alternative hypothesis of periodicity. The null hypothesis implies no periodicity, so AR (p) model is a good approximation. The alternative hypothesis, on the other hand, implies the periodic fluctuations exist in the series and PAR(p) model should be chosen. The results of this test for the average cost of prescriptions are reported in table 1. For the sake of robustness of findings models of order 1,2 and 3 is considered under both of the aforementioned deterministic components. The result of the test indicates the null hypothesis is rejected, thus the series are periodic in all cases addressed in table 1.

Table 1. Test for periodicity in the autoregressive parameters

deterministic component	order of the model	test statistics	degrees of freedom	p-value
SI+GT	1	9.70	(11,120)	<0.001
SI+ST	1	3.36	(11,109)	<0.001
SI+GT	2	6.13	(22,118)	<0.001
SI+ST	2	3.13	(22,107)	<0.001
SI+GT	3	4.52	(33,116)	<0.001
SI+ST	3	2.68	(33,105)	<0.001

Table 2 reports the findings on model selection criteria. Although working with more models provides more robust findings, the main disadvantage is the confusion due to the large number of results derived from tests and estimation of the models. Reducing the number of models one works with using statistical criteria helps clear the confusion.

Table 2. Model Selection

Deterministic Component	Criteria	Order of the Model		
		p=1	p=2	p=3
SI+GT	BIC	616.3774	645.5174	678.4377
	F-next	1.5745295	1.1380867	0.7423004
	p-value	0.1118186	0.3414765	0.7056932
SI+ST	BIC	651.0958	669.9589	694.0901
	F-next	1.9799833	1.3873362	0.8843325
	p-value	0.0357786	0.1916612	0.5669620

For each alternative model mentioned in table 1, F-next test and Bayesian Information Criterion (BIC) is employed to select appropriate models. F-next tests whether model of order one higher that estimated is more appropriate. For example, F-next test on PAR(p) models checks whether PAR(p+1) should be chosen. The p-value reported below F-next in the table is the one calculate for this test. F-next test helps to select only among various orders of a model; the other criteria, BIC, can help one to choose The BIC can identify optimal model among various functional forms. In other words BIC can be used to choose the model that deterministic component that fits the data. The smaller the BIC is the better the model characterized the series. In table BIC clearly favors PAR(1) regardless of deterministic component. Furthermore BIC prefers the model with SI+GT instead of the PAR model with SI+ST. In short, BIC advocates PAR(1) with SI+GT deterministic terms. The F-next test is considered separately for each form of the deterministic term. For the case of SI+GT, the p-values of the tests for each order are greater than 5%, which suggest that PAR(1) is the best choice. However for the case of SI+ST p-value of the test for the PAR(1) model is less that 5%, this indicates that the null hypothesis of PAR(1) is rejected in favor of PAR(2) model with the same set of deterministic models. Consequently these findings indicate PAR(1) with SI+GT to be the optimal model. Furthermore for the sake of robustness of the findings PAR(2) with SI+ST is also considered in the study, since the F-next test supports order 2 for the case of SI+ST.

Table 3 reports results of the seasonal heteroskedasticity test which is a diagnostic of the selected models. Heteroskedasticity arises when the variance of residuals on the model is not constant. Consequently any test on a model with heteroskedasticity problem is unreliable. The test checks the null hypothesis of no heteroskedasticity against the alternative of the problem existing in the model. Therefore a p-value greater that 5% means that there is no heteroskedasticity in the model. Fortunately any of the selected PAR models are devoid of heteroskedasticity problem, since the p-values are greater than 5%.

Table 3. Periodic Heteroskedasticity Test

deterministic component	order of the model	test statistics	degrees of freedom	p-value
SI+GT	1	1.09	(11,133)	0.3759
SI+ST	2	1.46	(11,132)	0.1559

The next step in the modeling of the average cost per prescriptions is the investigation of unit root in the series. For this purpose two separate tests are conducted; first tests whether there is unit root in the series, and the second test whether it is a long run unit root are a periodic unit root. Unit root in a series states that the series is nonstationary; any shock on the series does not die down.

Table 4. Single Unit Root in PAR(p) model

deterministic component	order of the model	test statistics		Critical values 5%	Critical values 10%
SI+GT	1	LR	0.41	9.24	7.52
		LR_τ	0.64	-2.41	-2.57
SI+ST	2	LR	1.46	12.96	10.50
		LR_τ	-1.21	-3.41	-3.12

The test of single unit root in PAR(p) model in table 4 is the aforementioned test, which establishes the existence of the unit root in the series. LR and LR_τ test statistics reported in the table both indicate that the series has unit root. The next step is therefore to establish whether this unit root is a long-run unit root or periodic unit root. This test is reported in table 5. The test in table 5 tests null of long run unit root against periodic unit root. The test results reject the null hypothesis in favor of periodic unit root.

The unit root tests clearly indicate periodic unit root, therefore the series are called periodically integrated. Therefore such series have to be modeled with methods that can take periodic integration into account, which PIAR is one of them. As a result the series are modeled with PIAR(1) with SI+GT and PIAR(2) with SI+ST. The matrix of time varying accumulation of shocks of the PIAR(1) and PIAR(2) are reported in table 6 and 7 respectively. As mentioned previously the rows of time varying accumulation of shocks matrix has information on the intensity of a shock while the columns have information on the long-run impact of the shock.

Table 5. Test of Periodic Unit root

deterministic component	order of the model	the null hypothesis	test statistics	degrees of freedom	p-value
SI+GT	1	$\alpha_s = 1$	9.74	(11,121)	<0.001
		$\alpha_s = -1$	1938.35	(11,121)	<0.001
SI+ST	2	$\alpha_s = 1$	2.1	(11,97)	0.0268
		$\alpha_s = -1$	10.55	(11,97)	<0.001

Table 6. Time varying accumulation of shocks for PIAR(1)

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Jan	1.000	0.833	0.723	0.755	0.716	0.733	0.731	0.773	0.810	0.871	0.885	0.971
Feb	1.200	1.000	0.867	0.906	0.859	0.880	0.877	0.928	0.972	1.045	1.062	1.166
Mar	1.384	1.153	1.000	1.044	0.990	1.014	1.011	1.070	1.121	1.205	1.225	1.344
Apr	1.325	1.104	0.958	1.000	0.949	0.972	0.968	1.025	1.073	1.154	1.173	1.287
May	1.397	1.164	1.010	1.054	1.000	1.024	1.021	1.080	1.131	1.216	1.237	1.357
Jun	1.364	1.136	0.986	1.029	0.976	1.000	0.997	1.055	1.105	1.188	1.207	1.325
Jul	1.369	1.140	0.989	1.033	0.980	1.003	1.000	1.058	1.108	1.192	1.211	1.329
Aug	1.293	1.078	0.935	0.976	0.926	0.948	0.945	1.000	1.047	1.126	1.145	1.256
Sep	1.235	1.029	0.892	0.932	0.884	0.905	0.902	0.955	1.000	1.075	1.093	1.199
Oct	1.148	0.957	0.830	0.867	0.822	0.842	0.839	0.888	0.930	1.000	1.017	1.116
Nov	1.130	0.941	0.816	0.852	0.809	0.828	0.825	0.874	0.915	0.984	1.000	1.097
Dec	1.029	0.858	0.744	0.777	0.737	0.755	0.752	0.796	0.834	0.896	0.911	1.000

Table 7. Time varying accumulation of shocks for PIAR(2)

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Jan	1.000	0.821	0.685	0.669	0.654	0.676	0.680	0.723	0.775	0.754	0.844	0.935
Feb	1.219	1.000	0.834	0.815	0.797	0.824	0.829	0.881	0.944	0.918	1.029	1.140
Mar	1.460	1.198	1.000	0.977	0.955	0.987	0.993	1.056	1.131	1.101	1.233	1.366
Apr	1.495	1.227	1.024	1.000	0.978	1.011	1.017	1.081	1.158	1.127	1.262	1.399
May	1.529	1.254	1.047	1.022	1.000	1.033	1.040	1.105	1.184	1.152	1.290	1.430
Jun	1.479	1.214	1.013	0.989	0.968	1.000	1.006	1.069	1.146	1.115	1.249	1.384
Jul	1.471	1.207	1.007	0.983	0.962	0.994	1.000	1.063	1.139	1.108	1.241	1.375
Aug	1.383	1.135	0.947	0.925	0.905	0.935	0.941	1.000	1.072	1.043	1.168	1.294
Sep	1.291	1.059	0.884	0.863	0.844	0.873	0.878	0.933	1.000	0.973	1.090	1.207
Oct	1.327	1.089	0.908	0.887	0.868	0.897	0.902	0.959	1.028	1.000	1.120	1.241
Nov	1.185	0.972	0.811	0.792	0.775	0.801	0.806	0.856	0.918	0.893	1.000	1.108
Dec	1.069	0.877	0.732	0.715	0.699	0.723	0.727	0.773	0.828	0.806	0.903	1.000

In table 6, the PIAR(1) model indicates that any shocks on March, May, June and July have a stronger effect on the series. Therefore any intentional shocks such as policy shocks on the series are more likely to be effective. Then the column of the table 6 are checked, the shocks on winter months (November, December and January) have the largest long-run impact. The findings on shocks regarding PIAR(2) in table 7 are in consensus with the aforementioned results with a slight difference. PIAR(2) model indicates impact to shocks becomes more severe any shocks on March, April, May, June and July, Addition to March, May, June and July mentioned for the PIAR(1) model, PIAR(2) model includes April into the list of months when impact of shocks are most severe. The findings on the columns of the model are in total agreement with the PIAR(1) model, attesting the shocks on winter months have larger long-run effects.

The impact of policy shocks are investigated in this study using PIAR model. This model is constructed through a tedious modeling process which can be summarized as follows;

i. periodicity of the series is tested,
ii. optimal functional form of the model is selected,
iii. existence of heteroskedasticity in the selected models are tested,
iv. the series is tested for unit root, where the series are found out to be periodically integrated, and
v. The series are modeled as PIAR.

The model selection process indicated PIAR(1) with the deterministic terms SI+GT to be the optimal model, we further continued to use PIAR(2) with SI+ST the check the robustness of the results. After the modeling process the impact of shocks are investigated via the time varying accumulation of shocks matrix. The findings indicate any shocks on spring and summer has a more severe impact that shocks on any other months. Furthermore the long-run impact of the shock on winter months is found to be higher.

Discussion

The shocks mentioned in this study stem form policy interventions, exogenous foreign factors such as increasing the cost of transportation of pharmaceuticals or exchange rate fluctuations. In other words shocks might be intentional such as policy interventions, as well as unintentional. The findings in this study imply that any policy implemented on spring and summer seasons are more likely to be effective whereas policies implemented in winter season have longer lasting effect. Furthermore any undeliberate shocks on these seasons should be considered carefully. We especially recommend swift action against exogenous (unintentional) and detrimental shocks on the price of prescriptions which occur on spring and summer seasons. Additionally policies against the (unintentional) shocks on winter must be deliberated and implemented carefully since the shocks on these months have larger and longer effect.

Conclusion

PIAR(1) and PIAR(2) models are employed to model average cost per prescription, which is good indicator of pharmaceutical prices. These models are further employed to examine the impact of shocks on the average cost per prescription series. The shocks can occur intentionally as government policies on pharmaceutics or unintentionally such as pandemics, unexpected fluctuations in exchange rates. The models indicate that spring and summer are the most likely seasons when policy implementations which reduce the price of drugs are most likely to succeed; since during period fluctuation in the stochastic trend of the series is more likely to occur. However any unintentional shocks in these months must be dealt swiftly, before the shocks effect the prices.

Conflict of Interest

Opinions expressed are solely authors' and do not express the views or opinions of the institutions the authors are affiliated with. The authors declared they do not have anything else to disclose regarding conflict of interest with respect to this manuscript.

Funding

None

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