



## USE OF DYNAMIC REGRESSION MODEL FOR REDUCTION OF SHORTAGES IN DRUG SUPPLY

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**Abstract.** The study is given to the use of dynamic regression model for reduction of shortages in drug supply:

*Purpose* – the use of a dynamic regression model to identify the influence of lead-time on the reduction of time delays in drugs supply. To reach the goal, the author focuses on the improvement of drugs availability and the minimisation of time delays in drugs supply.

*Research methodology* – the application of dynamic regression method to minimise shortage. The author suggests a dynamic regression model and accompanies it with autocorrelation and heteroskedasticity tests: Breush-Godfrey Serial Correlation LM Test for autocorrelation and ARCH test for heteroskedasticity.

*Findings* – during analysis author identifies the relationship between lead-time and time delays in drugs supply. The author delivers a specific regression model to estimate the effect of deterministic lead-time on shortage. Probability F and Probability Chi-Square of this testing show that there is no significant autocorrelation and heteroskedasticity.

*Research limitations* – the research is delivered for a one-month time frame. For the future, the study could review other periods. The author has incorporated the lead-time component in shortage reduction study by leaving capacity uncertainty component unresearched. The future studies could incorporate both elements into shortage reduction case analysis.

*Practical implications* – presented framework could be useful for practitioners, which analyse drug shortage reduction cases. The revision of supply time table is recommended for pharmacies aiming to minimise the shortage level.

*Originality/Value* – the analysis of deterministic lead-time and identification that the periodicity of shortage is evident each eight days. The study contributes to lead-time uncertainty studies where most of the authors analyse the stochastic lead-time impact on shortages.

**Keywords:** supply, shortage, drugs, delays, regression, causes.

**JEL Classification:** C20, L65.

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## **Introduction**

Shortages of medicines put patients at risk to get the most efficient health improvement. It is crucial to ensure the rights of patients and patients' accessibility to health care, the right of access to preventive health care and the right to benefit from medical treatment. Each of the national health systems of the EU countries manifests quite different realities concerning patients' rights.

However, there are political, economic, historical, environmental and other reasons causing shortage. The disruption of supply has negative impact for all supply chain actors. Many pharmaceutical manufacturers import raw components from India, China and Europe. If some of these foreign suppliers have supply disruption (Newman, 2016) due to political, economic, historical (Coomber, Moyle, & South, 2016), environmental issues, this could cause shortage. Delays in the supply of raw materials lead to overcrowding on the production when raw materials are received. For economic reasons, manufacturers may reduce their production volumes or cease the production. There are more cases where some manufacturers withdraw drugs from the market because they are less than profitable, or demand is higher than the available capabilities of manufacturer. By stating above mentioned reasons in studies, authors usually face the problem that it is not easy to provide solution which could help to minimize the impact on patients.

Author selects single component for the study and proposes solution for shortage reduction in paper below, which could result into better drug's accessibility for patients.

The study consists of three parts. The first part is dedicated to the literature review and criticality of lead-time as supply parameter. The second part of the paper presents the methodology. It constructs a dynamic regression model. Finally, the author applied the proposed regression model. A case study is presented here and options for shortage reduction.

The results showed the tendencies of shortage cases appearance and bring a solution for their minimization.

### **1. Literature review**

There are many inventory policies, but these do not consider supply constraints. In the literature, shortage causes are analyzed under the models dedicated to various activities: collection, production, inventory and delivery. A review of contemporary literature in the area of Operations research and Management Science was presented by Snyder et al. (2016). Their study focuses on supply chain disruptions and models present in the literature.

Authors Snyder et al. (2016) review 180 papers on the topic and identify five categories affecting supply disruptions: inventory, flexibility, sourcing, facility location, and interaction with partners. Some of these causes are presented below (see Table 1). Most of them are linked with distribution factors or human work aspects.

The models presented in the literature seek to plan an inventory considering internal supply parameters such as capacity and lead-time. Several forms of supply uncertainty are discussed by researchers. There are models with supply uncertainty, which include different period versions: single-period and multi-period.

Table 1. A literature review on shortage causes

Shortage causes	Models	Authors
Production lead-time	The stochastic aggregate production planning model	Mirzapour Al-e-Hashem, Baboli, and Sazvar (2013)
Nonconforming items	Stochastic integrated manufacturing and remanufacturing model with a shortage	Moshtagh and Taleizadeh (2017)
Supplier fault	A deteriorating item inventory model with a shortage	Rau, Wu, and Wee (2004)
Lack of integration in planning	Integrated production and maintenance planning model with time windows and shortage	Najid, Alaoui-Selsouli, and Mohafid (2011)
A decision was taken by a single supply chain partner	An integrated inventory model for deteriorating items under a multi-echelon supply chain	Rau, Wu, and Wee (2003)
Incoordination	Three-echelon supply chain model	Heydari, Mahmoodi, and Taleizadeh (2016)
Inventory management	Vendor managed inventory of multi-item economic order quantity model under shortage	Nia, Far, and Niaki (2014)
Bullwhip effect	Information hub model	Lee and Whang (2000)
Expiration of products	An inventory model for deteriorating items with expiration dates	Tiwari, Cárdenas-Barrón, Goh, and Shaikh (2018)
Complexity in perishable supply chain	Quantitative models in the blood supply chain	Osorio, Brailsford, and Smith (2015)
Limited warehouse space	Optimal lot-sizing model of integrated multi-level multi-wholesaler supply chain	Hoseini Shekarabi, Gharaei, and Karimi (2019)

There are models considering uncertainty, where demand is stochastic but is having continuous distribution. Other models assume probability that a supplier delivers the order with the highest reliability. When a supplier is unreliable, the disruption affects the lead-time – if disruption occurs with a fixed probability, the standard lead-time is increased by a stochastic delay. When likelihood is random, i.e. the quantity delivered or produced is a random variable, i.e. the supply quantity depends on order quantity. Researchers focus on probability, and they identify that the current period is influenced by supplier performance in the previous period.

Models with capacity uncertainty are treating capacity as a random variable, which is independent of order quantity.

For supply uncertainty analysis, authors, which are identified in Table 1, use linear regression, simulation techniques, Markov process, Bayesian model and other methods (Azghandi, Griffin, & Jalali, 2018). In these models, regression results are often transmitted directly into causal analysis or causal implications (e.g., searching for improvement of overall outcome). The authors point the attention that some studies with multiple regression analysis, had

multicollinearity which appeared due to high correlations among independent variables and led to unreliable results (Schmitt, Kumar, Stecke, Glover, & Ehlen, 2017).

Among supply uncertainty topic, researchers investigate lead-time uncertainty and capacity uncertainty due to the modelling and managerial differences between them, as first one focus on period aspects and the second one – the lack of resources.

Below author is presenting the analysis of lead-time component for drug shortage reduction. Author has selected single component for empirical research as very important component to be studied.

### 1.1. A lead-time component in shortage studies

Lead-time plays a vital role in many areas, including the drug supply chain. The time component is investigated by authors Lacerda, Xambre, and Alvelos (2015), Rivera and

Chen (2007), Dinis-Carvalho et al. (2015), Cuatrecasas-Arbos, Fortuny-Santos, and Vintro-Sanchez (2011) as a critical operational profile.

Lead-time uncertainty represents stochasticity in order processing. These authors analyse lead-time (or time from order-to-delivery) component of different nature: as stochastic, flexible, random, and randomly interruptible lead-time. Paul and Venkateswaran (2017) analysis lead-time component in drug production. There are studies, which focus on lead-time fluctuations, for example, those, which pay attention to Ripple effect (Sawik, 2017).

The lead-time component could be classified into two types:

1. Stochastic lead-time means that lead-time is a random variable;
2. Deterministic lead-time means that lead-time is fixed.

Many authors study the drug inventory problem with stochastic lead-time. The authors incorporating deterministic lead-time into their studies, assuming the lead-time is short-lasting. In the study below, the author focusses on the deterministic lead-time case, as the one to which was not given enough attention in previous studies.

Let's assume that order is placed at the beginning of the planning horizon ( $t$ ), and under normal conditions, the supply from the supplier is expected on  $(t+1)$ , where  $(t+1)$  represents lead-time required for production and transportation. This lead-time is the minimum delivery time from the supplier. In unnormal conditions, the maximum delivery lead-time is given for supply. This case of supply is disbalancing products' demand and leads to a shortage. When a product runs out of stock shortage appears.

It is evident that lead-time is strong component in inventory management and ordering. It is vital for ordering cycle time  $T$ , which is a period from one ordering point to another ordering point (i.e. time from order-to order). And in case ordering and delivering points are fixed and specified by concrete weekdays, it consists time table.

The author in the study is giving attention to existing ordering and delivering time table and its effect on drug shortages.

## 2. Methodology

Aiming to identify if order and the delivering point is selected correctly, the author investigates the occurrence of shortage. The author performs systematic shortage analysis aiming to

identify shortage causes. The shortage of trendline for various products is analyzed, aiming to identify a shortage of days.

The author uses period analysis, where each period has  $n$  number of order days,  $m$  number of delivery days, and  $z$  number of drugs availability days.

Aiming to investigate if supply time table is directly linked with shortage, a dynamic regression method is used.

Shortly about the method. Let's say that we need to predict  $X(t+1)$  given  $X(t)$ . Then the source and target variables will look like as follows (see Table 2):

Table 2. Dynamic regression database for  $t+1$  period

X(t)	X(t+1)
1	2
2	3
3	4
4	5

Dataset would look like rolling windows of variables that follow a precedent one in succession (see Table 3).

Table 3. Dynamic regression database for periods interval between  $t-2$  and  $t+1$

X(t-2)	X(t-1)	X(t)	X(t+1)
1	2	3	4
2	3	4	5
3	4	5	

Then, the author uses the transformed dataset to figure out the autocorrelation coefficients from  $X(t-2)$  to  $X(t)$ .

The author delivers a regression model, which general formulation is as follows:

$$sh_t = \beta_0 + \theta_{sh} L_{sh} + \beta_3 dot_t + \theta_{dot} L_{dot} + \varepsilon_t. \quad (1)$$

Variables:

$sh_t$  – a shortage of period  $t$ ;

$L_{sh}$  – lags operator for shortages;

$dot_t$  – delivery on time of period  $t$ ;

$L_{dot}$  – lags operator for delivery on time;

$\theta_{sh}$  – a matrix of coefficients for the lag operator of shortages;

$\theta_{dot}$  – a matrix of coefficients for the lag operator of shortages;

$\varepsilon_t$  – an error term (iid).

The dynamic regression has testing statistics: Breush-Godfrey Serial Correlation LM Test for autocorrelation and ARCH test for heteroskedasticity.

The application of constructed regression model is revised in the case study analysis, where the ordering cycle time is of 7 days.

For the analyse non-prescription drugs are selected. In study case the data is collected from pharma enterprise database and is analysed by calendar days and weekdays. The main data about 235 non-prescription drugs and 10 pharmacies is identified in the study, in such presentation: product ID, pharmacy ID, supplier ID, order day, order quantity, delivery day stated in order, actual delivery day, delivery quantity and quantity in stock at the end of particular day. For the statistical analysis eViews software is applied.

### 3. Results of the research

According time table, most of the deliveries are on Thursday and Friday, and most of the shortage is on Monday and Wednesday. This inforces the revision of suppliers time table and slight reschedule of delivery days. The average lead-time for products is 4.1 day (see Table 4). The number of generated orders per week is 1444 orders (or 6.1 orders per product), and the reliability of suppliers is 97 percentage, i.e. the supply performance of these orders. This shows that the orders are generated continuously, and that the reliability of suppliers is quite high.

Table 4. Lead-time parameters (4 weeks' time period)

Number of products	Generated orders a week	Average-lead time (from order day to delivery day)	Reliability of suppliers (quantity delivered vs quantity ordered)
235	6.14	4.1	97 percentage

Statistical analysis shows that the number of pharmacies facing drug shortage is almost constant. In part of pharmacies which do not receive delivery from a supplier and has no buffer stock, the shortage is evident, and in another part of pharmacies, which have the buffer stock the shortage is not be present. Moller's Junior 45 pieces, Neuromed 15 tablets (e.g. Figure 1), Carbon 300 mg 20 tablets (e.g. Figure 2), A+E 30 tablets and Super Validol 60 mg 10 tablets have the same shortage trend at the beginning of the month, and it is evident at the 2nd part of the month, such is not common only for Magnis+B6 complex and Humer 150 ml cases.

There is also systematic shortage, which appears at 2<sup>nd</sup> and 3<sup>rd</sup> day of the month for sample products.

There is also systematic shortage which increases at 10th day of the month for some products (following are evident in Figure 1 and Figure 2). Moreover, the supplier could revise delivery schedules from the producer as at the same time; various pharmacies struggle with a high level of shortage if they do not have a buffer for problematic products.

The author has investigated that ordering cycle time is directly linked with shortages. From Table 4 parameters analysis, we could see that minimisation of lead-time, especially at the beginning of the month, is the priority. The highest shortage occurs on weekend days when there are no deliveries from suppliers. In case the supplier is delivering less than ordered, a new order is processed only after one day.

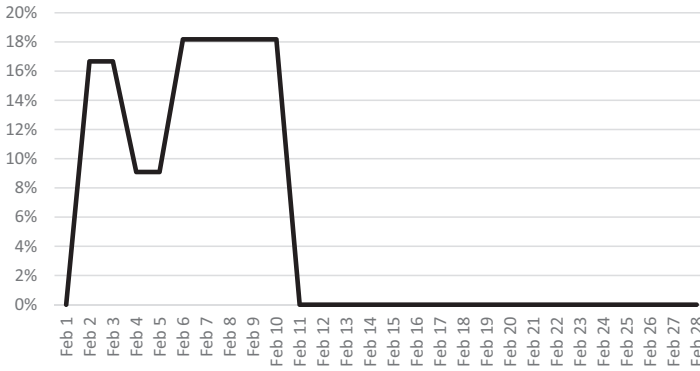


Figure 1. Shortage Trendline for Neuromed 15 tablets

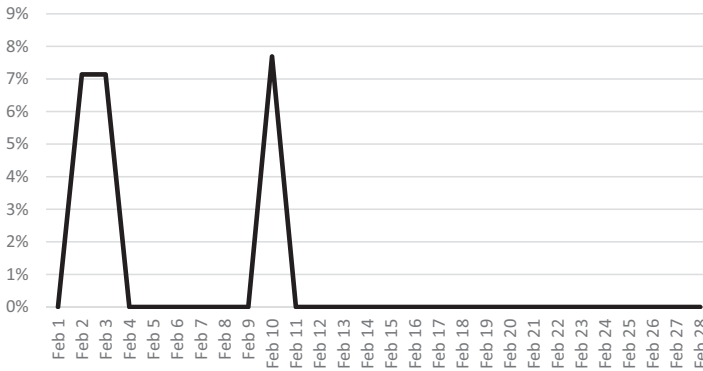


Figure 2. Shortage Trendline for Carbon 300 mg 20 tablets

The author finds out the probabilities of events: the likelihood that shortage lasts two days is 38.7 percentage. The possibility of delivery is 82 percent on the day of shortage. The probability of facing shortage next day after delivery is 23.4 percentage. Below the application of dynamic regression model is provided.

The application of dynamic regression techniques gives interesting results. Below is the chart presenting values of normalised variables (e.g. Figure 3) and main statistics attributes.

The correlation coefficient is equal to 0.65, and the R squared of the regression is 0.6.

The author delivered a specific regression model, which formulation is:

$$sh_t = \beta_0 + \beta_1 sh_{t-1} + \beta_2 sh_{t-8} + \beta_3 dot_t + \beta_3 dot_{t-1} + \varepsilon_t. \tag{2}$$

This dynamic regression delivered results as follows:

$$sh_t = 0,095 + 0,583 sh_{t-1} + 0,056 sh_{t-8} + 0,148 dot_t - 0,07 dot_{t-1}.$$

(5.69)    (19.72)            (2.54)            (15.61)            (-6.7)

The equation is presenting t-statistic. The equation shows that if the shortage appears, it lasts for one period more ( $t+1$ ). The periodicity of shortage is each eight days. Having the data starting from Monday, the statistical significance of 8<sup>th</sup> lagged value, which means that shortages occur after each weekend. This is the evidence of not enough supplies that occur periodically. Such a period cycle is very closely linked with a delivery time table.

The dynamic regression model is presented graphically in Figure 4.

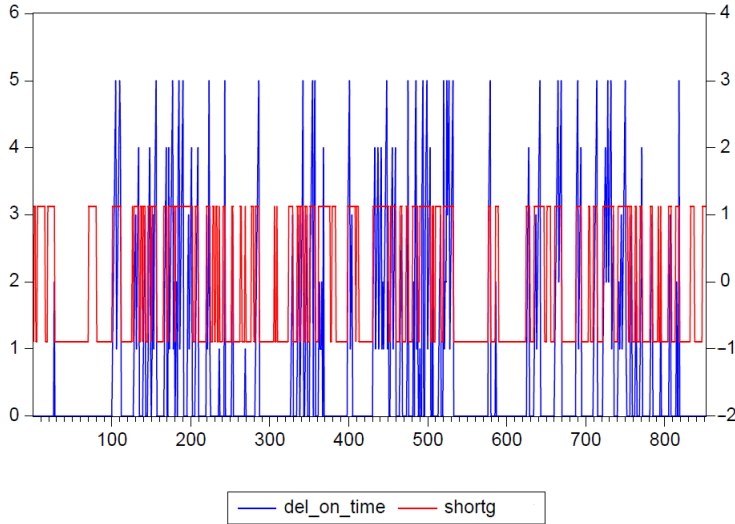


Figure 3. Dynamic regression results

where: on the x-axis – number of time series, on the primary y-axis (on the left) – delivery in calendar days, on the secondary y-axis (on the right) – the appearance of normalised shortage event

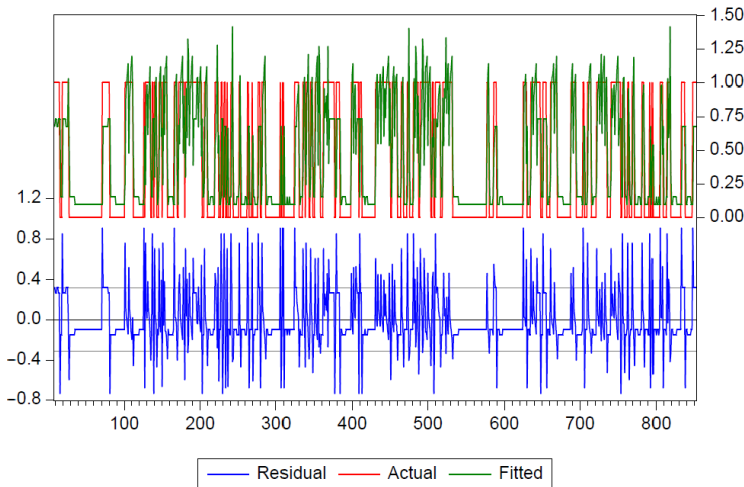


Figure 4. Dynamic regression results

where: on the x-axis – number of time series, on the primary y-axis (on the left) – output of regression model, on the secondary y-axis (on the right) – the appearance of shortage event



In Figure 4, the red line represents the original shortage, while the green line demonstrates the modelled shortage according to the estimated equation; the blue line shows residuals of the dynamic regression model.

The author provides also testing statistics for autocorrelation and heteroskedasticity. Main tests are provided for autocorrelation analysis – Breusch-Godfrey, for heteroskedasticity analysis – ARCH test and ML ARCH – Normal distribution (BFGS / Marquardt steps) test. Probability F and Probability Chi-Square of these testing statistics show that there is no significant autocorrelation and heteroskedasticity. The more detailed results of the dynamic regression analyses are presented in the Annex of this paper.

The author obtains the evidence that ordering cycle time is directly linked with the number of shortage cases. According to the research results, it is possible to shorten ordering cycle time by one day aiming to reduce the number of shortage cases. Author suggests the reduction of ordering cycle time to 6 days, instead of the existing one with 7 days.

The provided solution formulation could be treated as shortage research framework evaluating shortage cases.

## Conclusions

The case study shows that lead-time component must be revised in drug supply. Also, the drug supply chain must be tightened up, as in most of the cases. According to the literature time constrain is main attribute for shortage avoidance.

The author researches the lead-time component for shortage reduction purposes. To respond to studies with unsuccessful multi-regression analysis, the author selects dynamic regression technique and constructed the model. The model is applied for pharmaceutical supply chain case study.

The case study shows that if shortage appears a day before, then is the probability of 38.7% that it will occur on the next day. The equation shows that on the day of shortage the likelihood of delivery is 82%. Which means that those deliveries come at the end of a day not at the beginning thereof and the lead-time between ordering and delivering is too long. If delivery occurs, it diminishes probability on shortage next day by 23.4%. The empirical part of the study confirms a dynamic regression model and proves that time table improvement could help to minimize drug shortages. The performed practical assessment shows that the suggested framework is applicable for the delivery of drug shortage reduction.

The findings suggest future research directions. The study results also give insights on the necessity to have more frequent deliveries for products. The action to be taken for supplier time table revision aiming to increase the number of deliveries and minimize shortage at the beginning of the month. Also, future studies may include capacity attribute as playing important role for shortage minimization, into these studies.

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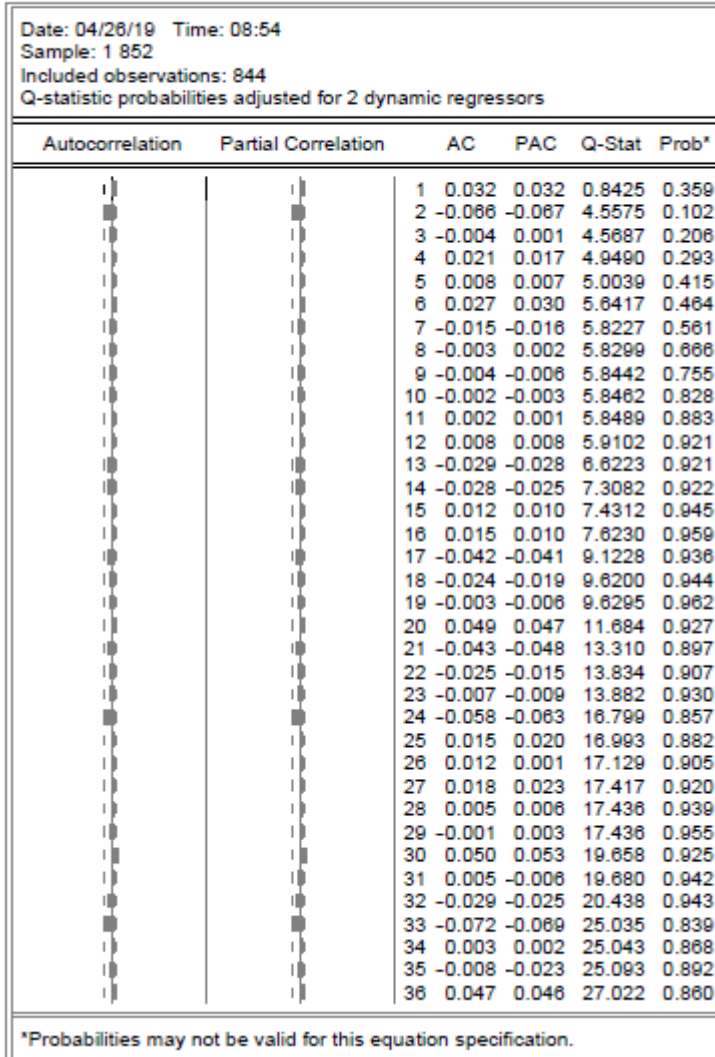
## Appendix

### Formation of Equation (1)

Dependent Variable: SHORTG_YES				
Method: Least Squares				
Date: 04/26/19 Time: 08:53				
Sample (adjusted): 9 852				
Included observations: 844 after adjustments				
Variable	Coefficient	Std. Error	t-Statistic	Prob.
C	0.095433	0.016744	5.699641	0.0000
SHORTG_YES(-1)	0.582895	0.029529	19.73968	0.0000
SHORTG_YES(-8)	0.056079	0.022067	2.541297	0.0112
DEL_ON_TIME	0.147911	0.009473	15.61323	0.0000
DEL_ON_TIME(-1)	-0.069225	0.010333	-6.699287	0.0000
R-squared	0.599322	Mean dependent var		0.438389
Adjusted R-squared	0.597412	S.D. dependent var		0.496484
S.E. of regression	0.315018	Akaike info criterion		0.533534
Sum squared resid	83.25938	Schwarz criterion		0.561603
Log likelihood	-220.1512	Hannan-Quinn criter.		0.544289
F-statistic	313.7376	Durbin-Watson stat		1.934439
Prob(F-statistic)	0.000000			

Analysis of autocorrelation (AC and PAC values are lower than 0,1)

Correlogram of Residuals



## Autocorrelation analysis: Breusch-Godfrey test

Breusch-Godfrey Serial Correlation LM Test:				
Null hypothesis: No serial correlation at up to 9 lags				
F-statistic	0.668200	Prob. F(9,830)	0.7382	
Obs*R-squared	6.071249	Prob. Chi-Square(9)	0.7328	
Test Equation:				
Dependent Variable: RESID				
Method: Least Squares				
Date: 04/26/19 Time: 08:54				
Sample: 9 852				
Included observations: 844				
Presample missing value lagged residuals set to zero.				
Variable	Coefficient	Std. Error	t-Statistic	Prob.
C	0.001735	0.053303	0.032547	0.9740
SHORTG YES(-1)	-0.028065	0.202753	-0.138418	0.8899
SHORTG YES(-8)	0.010785	0.046505	0.231917	0.8167
DEL ON TIME	0.000802	0.009574	0.083791	0.9332
DEL_ON_TIME(-1)	0.006575	0.033778	0.194643	0.8457
RESID(-1)	0.061209	0.205976	0.297164	0.7664
RESID(-2)	-0.053546	0.120934	-0.442772	0.6580
RESID(-3)	0.007973	0.078716	0.101290	0.9193
RESID(-4)	0.023031	0.056944	0.404450	0.6860
RESID(-5)	0.007827	0.045765	0.171029	0.8642
RESID(-6)	0.033034	0.040147	0.822829	0.4108
RESID(-7)	-0.015132	0.036560	-0.413891	0.6791
RESID(-8)	-0.008265	0.054564	-0.151479	0.8796
RESID(-9)	-0.012116	0.043559	-0.278158	0.7810
R-squared	0.007193	Mean dependent var	5.20E-17	
Adjusted R-squared	-0.008357	S.D. dependent var	0.314270	
S.E. of regression	0.315580	Akaike info criterion	0.547641	
Sum squared resid	82.66046	Schwarz criterion	0.626236	
Log likelihood	-217.1046	Hannan-Quinn criter.	0.577757	
F-statistic	0.462600	Durbin-Watson stat	1.996361	
Prob(F-statistic)	0.944990			

## Heteroskedasticity analysis: ARCH test

Heteroskedasticity Test: ARCH				
F-statistic	0.003210	Prob. F(1,841)	0.9548	
Obs*R-squared	0.003218	Prob. Chi-Square(1)	0.9548	
Test Equation:				
Dependent Variable: RESID^2				
Method: Least Squares				
Date: 04/26/19 Time: 08:55				
Sample (adjusted): 10 852				
Included observations: 843 after adjustments				
Variable	Coefficient	Std. Error	t-Statistic	Prob.
C	0.098450	0.007079	13.90700	0.0000
RESID^2(-1)	0.001954	0.034483	0.056660	0.9548
R-squared	0.000004	Mean dependent var	0.098643	
Adjusted R-squared	-0.001185	S.D. dependent var	0.180152	
S.E. of regression	0.180259	Akaike info criterion	-0.586478	
Sum squared resid	27.32679	Schwarz criterion	-0.575239	
Log likelihood	249.2003	Hannan-Quinn criter.	-0.582171	
F-statistic	0.003210	Durbin-Watson stat	2.000224	
Prob(F-statistic)	0.954829			

Heteroskedasticity analysis: ML ARCH – Normal distribution test

Dependent Variable: SHORTG YES				
Method: ML ARCH - Normal distribution (BFGS / Marquardt steps)				
Date: 04/26/19 Time: 08:56				
Sample (adjusted): 9 852				
Included observations: 844 after adjustments				
Convergence achieved after 48 iterations				
Coefficient covariance computed using outer product of gradients				
Presample variance: backcast (parameter = 0.7)				
GARCH = C(6) + C(7)*RESID(-1)^2 + C(8)*RESID(-2)^2 + C(9)*GARCH(-1) + C(10)*GARCH(-2)				
Variable	Coefficient	Std. Error	z-Statistic	Prob.
C	0.091819	0.037765	2.431324	0.0150
SHORTG_YES(-1)	0.583175	0.051614	11.29875	0.0000
SHORTG_YES(-8)	0.051871	0.022804	2.274666	0.0229
DEL_ON_TIME	0.150258	0.011621	12.92983	0.0000
DEL_ON_TIME(-1)	-0.069213	0.009375	-7.382485	0.0000
Variance Equation				
C	0.032383	0.006430	5.036148	0.0000
RESID(-1)^2	-0.011394	0.018790	-0.606379	0.5443
RESID(-2)^2	0.075015	0.024421	3.071751	0.0021
GARCH(-1)	1.209086	0.134534	8.987239	0.0000
GARCH(-2)	-0.601848	0.116540	-5.164293	0.0000
R-squared	0.599212	Mean dependent var	0.438389	
Adjusted R-squared	0.597301	S.D. dependent var	0.496484	
S.E. of regression	0.315061	Akaike info criterion	0.520295	
Sum squared resid	83.28228	Schwarz criterion	0.576434	
Log likelihood	-209.5645	Hannan-Quinn criter.	0.541807	
Durbin-Watson stat	1.938894			