An Economic Order Quantity (EOQ) Model for Chemotherapy Drugs Using New Patients' Arrival Rates

Victor Suhandi
Ph.D. Candidate, Department of Industrial and Systems Engineering
Chung Yuan Christian University
Chungli, Taoyuan City, Taiwan
g10702408@cycu.edu.tw

Ping-Shun Chen
Professor, Department of Industrial and Systems Engineering
Chung Yuan Christian University
Chungli, Taoyuan City, Taiwan
pingshun@cycu.edu.tw

Abstract

The Covid-19 pandemic situation and cancer burden trend lead the changes in the chemotherapy drugs demand. Chemotherapy can have several cycles of administration that take months. Moreover, delays can occur if the patient's physical condition is not ready to undergo the process of administration, and the data will be complete after several months. The availability of new patients' arrival data is faster than the demand data. The approach to integrating this arrival data into the economic order quantity (EOQ) model is the focus of this study. The demand rate is estimated using new patient arrivals data and the constant transition probabilities. Model development using infinite geometric series and validated by simulation using a spreadsheet. The results show the effectiveness of new patients' arrivals data replacing the demand data with the resulting sensitivity equivalence. Inventory decisions are sensitive when new patients' arrival rates are close to zero.

Keywords

Chemotherapy drugs, inventory management, economic order quantity (EOQ), arrival rate, demand rate

1. Introduction

This study discusses the inventory policy for chemotherapy (CT) drugs using new patients' arrival rates to estimate the demand rate. Where the availability of arrival rate data for new patients is much faster than demand data for the entire administration cycle so that the inventory model can be more responsive to changes in demand in the future. The demand changes may occur in the long and short terms. Sung et al. (2021) estimates that the cancer burden will increase by 47% in 2040 compared to 2020 and be influenced by the growth and aging of the population, and it leads to long-term changes. The Covid-19 pandemic is one example of causing the cancer treatment demand changes in the short term (Drescher et al. 2022). During the pandemic, people are encouraged to stay at home, and the health care capacity is reduced for safety reasons. Czeisler et al. (2020) estimates that 41% of US adults delayed or avoided medical treatment during the onset of the COVID-19 pandemic.

The EOQ model is used in this study to provide a basic concept of inventory policy. The simplicity and ease of implementation offered by the EOQ model keep this model prevalent, also in the pharmaceutical industry (Dewi et al. 2020; Gnanasekaran and Karthikeyan 2016; Lamson et al. 1982). This study uses Doxorubicin as a CT drug for female breast cancer. In 2020 this cancer had the highest number of new cases reaching 2.3 million (11.7%) beat lung cancer cases (Sung et al. 2021).

This study uses a different approach when using the arrival rates in the inventory model. Previous studies used arrival rates directly as demand in the inventory model (Ghosh et al. 2022; Hill and Dominey 2001; Khedlekar et al. 2014;

Lyu et al. 2010; Marand et al. 2019), whereas the current study uses new patients' arrival rates to estimate demand in all CT cycles in the future.

This study focuses on the characteristics of the demand for CT drugs in the hospital pharmacy inventory system. These characteristics are affected by the administration cycle that exists in CT. Sevinc et al. (2013) provided an example of a regimen for breast cancer using Doxorubicin as one of the drugs and requiring four cycles of administration with an interval of three weeks between administrations. Thus the CT can take 12 weeks. Moreover, delays can occur if the patient's physical condition is not ready for administration. Figure 1 shows the rate of new patient arrivals (λ) and the two patient states. The first condition is the patient who will do the administration in cycle 1 (S1), and the second condition is the patient who will do the administration in cycle 2 (S2). The patient's physical readiness test conducts before the administration process in each cycle. If the results of laboratory checks do not meet the requirements, then a one-week delay and re-checks are carried out. After the administration process, the patient rest for three weeks to proceed to the next cycle.

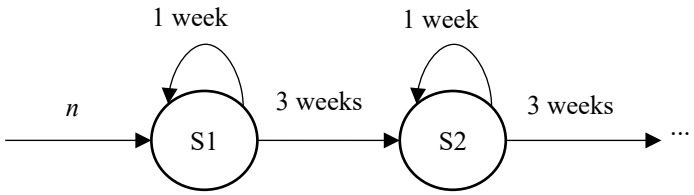

Figure 1. Chemotherapy administration cycles.

Demand rates are usually estimated using historical data from previous months. This estimation method has disadvantages for CT drugs. The completion of historical data on patient demand can occur after several months due to several administration cycles. Another alternative to estimate the value of the demand rate is needed to increase responsiveness to face the changes in demand parameters in the future. This study focuses on increasing the responsiveness of the inventory model by estimating demand based on the arrival rate of new patients. New patient arrival rate data is available relatively quickly compared to historical demand data for the entire CT cycle. The arrival rate data for new patients can estimate the demand for all CT cycles. The expected demand value for all CT cycles is the input for the EOQ model.

The structure of this paper is as follows. Section 2 shows the previous studies related to the EOQ model as a basic model with various development and applications in the pharmaceutical industry, and the studies considered the arrival rates in the inventory model. Section 3 shows the development of an EOQ model for CT drugs with new patients' arrival rate as inputs instead of demand rate. Section 4 discusses the model application for a CT drug that has multiple administration cycles and takes months. Section 5 describes the validation process using a spreadsheet for estimating the CT drugs demand rate using the new patients' arrival rate. Finally, section 6 concludes the results and future research development.

2. Literature Review

Harris (1990) formulated the first economic lot size for production planning and inventory control and published it in 1913. He explained that the optimal order size occurs when total ordering costs are equal to total holding costs mathematically and graphically. He also stated the robustness of the EOQ to changes in some parameters. The development of EOQ is still ongoing in recent years involving various innovations related to situations and conditions that continue to develop.

The integration of various other factors in the EOQ model makes EOQ more applicable to various situations. Alamri et al. (2022) associated EOQ with carbon emissions, inflation, deterioration, and learning effects. Choudhury et al. (2022) determined the economic lot size by considering the factors of product deterioration, expiration date, pollution,

and fuzziness. Zadjafar and Gholamian (2018) added health, environmental, and income factors from waste into the EOQ model.

The development of the EOQ model can also be related to the characteristics of the existing parameters. Nestorenko et al. (2020) were concerned with price fluctuations and variable reorder time into the EOQ model. Khan et al. (2022) were concerned about the effect of the amount of stock on the demand rate for products that are experiencing deterioration. Taleizadeh et al. (2022) modeled the demand rate affected by price and carbon emission. Cardenas-Barron et al. (2022) modeled the EOQ inventory model with non-linear demand and also depending on price.

The EOQ model has been applied to pharmaceutical industries for a long time. Previous studies showed the advantages of using the EOQ model. Ouellet et al. (1982) reported the successful implementation of the EOQ model at a drug manufacturing plant in Montreal. Dobson et al. (2015) optimized the inventory policy for compound sterile products by considering time-varying holding and ordering costs. Dewi et al. (2020) applied the EOQ model to the pharmacy inventory of a hospital and succeeded in reducing costs.

Inventory models considering customer arrival rate had been carried out by previous studies. The studies showed arrival rate directly substitutes the demand rate for the inventory model. Hill and Dominey (2001) used the Poisson customer arrival rate for a continuous review model, with the probabilistic demand quantity from each customer must be fulfilled in full or not at all. Lyu et al. (2010) used the customer arrival rate for a replenishment simulation model in collaborative supplier and retailer conditions, Marand et al. (2019) used the customer arrival rate for a continuous review inventory model integrated with the queuing model, and Ghosh et al. (2022) used customer arrival in the retail inventory model by considering customer preferences.

Several previous studies used a demand quantity of one unit per customer so that the demand rate equals the arrival rate and can replace the demand rate directly in the inventory model (Ghosh et al. 2022; Lyu et al. 2010; Marand et al. 2019). Then for the arrival of customers with more than one unit demand (Hill and Dominey 2001), the total demand is estimated by multiplying the expected value of the customer arrival rate and the quantity per customer. In the current study, the estimation of demand rate using the new patients' arrival rate combined with the transition probabilities between administration cycles. And the steady-state condition is estimated using an infinite geometric series. This study deals with the EOQ model using patient arrivals for chemotherapy drugs inventory management to increase responsiveness. Thus it can use a more agile EOQ model to deal with changes in the arrival rate of new patients.

3. Methodology and Model Development

This study integrates the new patients' arrival rate and constant transition probabilities into the CT EOQ model. The new patients' arrival rate estimates the arrival rate in the following cycles, using the constants transition probabilities. The infinite geometric series estimate the overall demand rate in steady-state. This overall demand rate becomes an input in the EOQ model.

A numerical analysis uses Doxorubicin as a breast cancer CT drug. The regimen follows the example of Sevinc et al. (2013), and the dose is estimated within the range recommended by MHRA (2020). The sensitivity analysis examines the equivalence to the change of demand rate and the robustness of the order quantity decision and total costs performance. And the validation process to see if the overall demand rate calculated by the model is correct. It is conducted by simulation using a spreadsheet.

This section consists of four subsections. First, subsection 3.1 contains the notation used in the model. Subsection 3.2 describes the assumptions used in this study. Subsection 3.3 is a mathematical modeling process to produce the desired formula. And lastly, Subsection 3.4 represents previous studies that have the potential to collaborate with this study as future research.

3.1 Notation

The notations are introduced as follows.

- λ: new patients' arrival rate per period.
- S_i: state of patients who will perform the i-th cycle of administration.
- S_e: state of patients who exit the CT.

- S_f: state of patients who finish all CT cycles.
- k: dose per patient.
- d_{it}: demand at cycle i and period t.
- D_i: total demand at cycle i.
- D: total demand for all cycles is the total demand for every period in a steady-state condition.
- c: number of cycles.
- α_i: transition probabilities that patients take CT at cycle i.
- β_i: transition probabilities that the patients shift one week at cycle i.
- TOC: total ordering costs.
- THC: total holding costs.
- TC: total costs.
- Q: order quantity.
- EOQ: economic order quantity.
- A: ordering costs.
- h: holding costs.

3.2 Assumptions

The four assumptions are introduced as follows.

- The transition probabilities are constant.
- The arrival rate is constant.
- CT has four cycles.
- All the basic EOQ assumptions are applied.

3.3 Model Formulation

This study differentiates the actual demand from the potential demand rate. The oncologist gives a regimen and makes a schedule of CT for a patient. This regimen is the potential demand. The actual demand rate will occur when the patient can attend the CT administration. The patients may decline the CT or not pass the physical evaluation by laboratory check (LC). S1 is the state of a patient scheduled to take the CT at the 1st cycle (potential demand). The actual demand rate (the patient who takes the CT) will be less than or equal to the number of patients in state S1. The actual demand rate in the 1st cycle becomes a potential demand in the 2nd cycle (S2). For the patients who do not pass the LC, their states are the same in the next period. If patients decline, it becomes an end or exit state (S_e). The actual demand estimations are in every state until the last cycle administration (S_f). The arrival rate for new patients is λ per period (week).

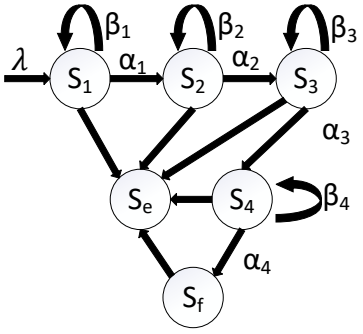

Figure 2. The state transition of the chemotherapy patients.

In steady-state conditions, all cycles may have demand with various experiences of patients (figure 2). Patients may experience delays whenever they want to take the administration. For example, in a period, some new patients will do the first cycle, and together with some previous patients who experience delays and also will do the first cycle. Thus the demand in a period is the sum of various patients who have different experiences. This situation also can be applied to the next administration cycle. In this case, the demand rate under steady-state conditions is the expected value of demand from all patient experiences in each cycle. The demand related to the patients' experiences is calculated using the transition probabilities.

Demand for 1st cycle:

$D_1 = \sum_{t=1}^{\infty} d_{it}$ for $i = 1$, where $d_{11} = \alpha_1.\lambda$
$d_{it} = \beta_i^{t-1} \times d_{11}$ for $i = 1,\ t > 1$
D_1 becomes geometric series with *t* going to infinity. Equation (1) shows the formula of D_1.

$$D_1 = \frac{d_{11}}{1-\beta_1} \quad (1)$$

Demand for 2nd cycle:
Total demand for every cycle is a summation until infinity. Whenever it starts is not affected. It assumes the second cycle start at period two. Equation (2) shows the formula of D_2.

$d_{22} = \alpha_2 \times d_{11}$
$d_{23} = \alpha_2 \times d_{12} + \beta_2 \times d_{22} = \alpha_2 \times d_{12} + \beta_2 \times \alpha_2 \times d_{11}$
$d_{24} = \alpha_2 \times d_{13} + \beta_2 \times (\alpha_2 \times d_{12} + \beta_2 \times \alpha_2 \times d_{11})$
to continue until $d_{2\infty}$
$D_i = \sum_{t=(i-1).l+1}^{\infty} d_{it}$ for $i > 1$

$$D_2 = \frac{\alpha_2 \times d_{11}}{1-\beta_1}\left(1 + \frac{\beta_2}{1-\beta_2}\right) \quad (2)$$

Demand for 3rd cycle:
The demand for the third cycle uses the same D_i formula as the second cycle and is assumed to start in the third period. Equation (3) shows the formula of D_3.

$d_{33} = \alpha_3 \times d_{22} = \alpha_3 \times \alpha_2 \times d_{11}$
$d_{34} = \alpha_3 \times d_{23} + \beta_3 \times d_{33} = \alpha_3 \times d_{23} + \beta_3 \times \alpha_3 \times d_{22}$
$d_{35} = \alpha_3 \times d_{24} + \beta_3 \times (\alpha_3 \times d_{23} + \beta_3 \times \alpha_3 \times d_{22})$
to continue until $d_{3\infty}$

$$D_3 = \alpha_3 \frac{\alpha_2 \times d_{11}}{1-\beta_1}\left(1 + \frac{\beta_2}{1-\beta_2}\right)\left(1 + \frac{\beta_3}{1-\beta_3}\right) \quad (3)$$

Total demand:
The total demand until c cycles we get from the summation of Equations (1), (2), and (3).

$D = D_1 + D_2 + D_3 + \cdots + D_c$
$D = \frac{d_{11}}{1-\beta_1} + \frac{\alpha_2 \times d_{11}}{1-\beta_1}\left(1 + \frac{\beta_2}{1-\beta_2}\right) + \alpha_3 \frac{\alpha_2 \times d_{11}}{1-\beta_1}\left(1 + \frac{\beta_2}{1-\beta_2}\right)\left(1 + \frac{\beta_3}{1-\beta_3}\right) + \cdots + D_c$

Equation (4) shows the formula of the expected value of the demand rate.

$E(D) = \frac{\alpha_1 \times k \times \lambda}{1-\beta_1} + \frac{\alpha_2 \times \alpha_1 \times k \times \lambda}{1-\beta_1}\left(1 + \frac{\beta_2}{1-\beta_2}\right) + \alpha_3 \frac{\alpha_2 \times \alpha_1 \times k \times \lambda}{1-\beta_1}\left(1 + \frac{\beta_2}{1-\beta_2}\right)\left(1 + \frac{\beta_3}{1-\beta_3}\right) + \cdots + D_c$

$$E(D) = k \times \lambda \times \sum_{i=1}^{c} \frac{\prod_{j=1}^{i} \alpha_j}{\prod_{j=1}^{i}(1-\beta_j)} \quad (4)$$

The total cost (*TC*) is adopted from Hopp and Spearman (2011) without the acquisition costs. Substituting the demand with Equation (4) to get Equation (5). The EOQ model with patient arrivals is Equation (6).

$TC = THC + TOC$
$TC = \frac{h \times Q}{2} + \frac{A \times D}{Q}$

$$TC = \frac{h \times Q}{2} + \frac{A \times k \times \lambda \times \sum_{i=1}^{c} \frac{\prod_{j=1}^{i} \alpha_j}{\prod_{j=1}^{i}(1-\beta_j)}}{Q} \quad (5)$$

$$EOQ = \sqrt{\frac{2 \times A \times D}{h}}$$

$$EOQ = \sqrt{\frac{2 \times A \times k \times \lambda \times \sum_{i=1}^{c} \frac{\prod_{j=1}^{i} \alpha_j}{\prod_{j=1}^{i} (1-\beta_j)}}{h}} \quad (6)$$

3.4 Future Development

The use of arrival rates and transition probabilities can also be collaborated with previous studies by considering demand with cycles. Model development does not only use the EOQ model but can be related to other inventory models. Several studies can be a reference for further development. The economic production quantity (EPQ) is the closest model to the EOQ (Askari et al. 2021; Gharaei, Hoseini Shekarabi, et al. 2020; Gharaei, Hoseini Shekarabi, and Karimi 2021; Gharaei, Hoseini Shekarabi, Karimi, et al. 2021). Several studies related to vendor managed inventory (VMI) (Gharaei, Karimi, et al. 2021), multi-echelon supply chains (Amjadian and Gharaei 2021; Gharaei, Amjadian, et al. 2021; Gharaei et al. 2019; Gharaei, Karimi, et al. 2020; Giri and Bardhan 2014; Giri and Masanta 2020; Hoseini Shekarabi et al. 2019; Rabbani et al. 2020; Sarkar and Giri 2020; Shah et al. 2020; Tsao 2015), maintenance scheduling (Duan et al. 2018), and EOQ with special conditions (Kazemi et al. 2018).

4. Numerical Analysis

The parameters used in this study were the rate of new patient arrivals, doxorubicin administration dose, ordering cost, and holding cost. The arrival of new patients (λ) is six patients/week. The dose given for each administration (k) is 60 mg (MHRA, 2020), which is equivalent to 37.5 mg/m2 for women and 31.6 mg/m2 for men. These meet the 30 – 40 mg/m2 limit for CT with doxorubicin in combination with other drugs. The ordering cost (A) is 65 USD, estimated using the activities needed by staff and managers to place an order. Holding cost (h) is estimated at 1%/week of the drug price, equal to 0.0844 USD/mg/week, where the drug price is 844 USD/100mg. Stationary transition probabilities are assumed as follows: $\alpha_1 = 0.85$, $\beta_1 = 0.05$, $\alpha_2 = 0.70$, $\beta_2 = 0.10$, $\alpha_3 = 0.55$, $\beta_3 = 0.15$, $\alpha_4 = 0.40$, $\beta_4 = 0.20$.

The calculation results show the D of 816 mg, the EOQ of 1121 mg, and the TC of 94.61 USD/week. Under these conditions, TOC and THC are equal to 47.30 USD/week. Figure 3 shows the effects of change in order size (Q) on costs.

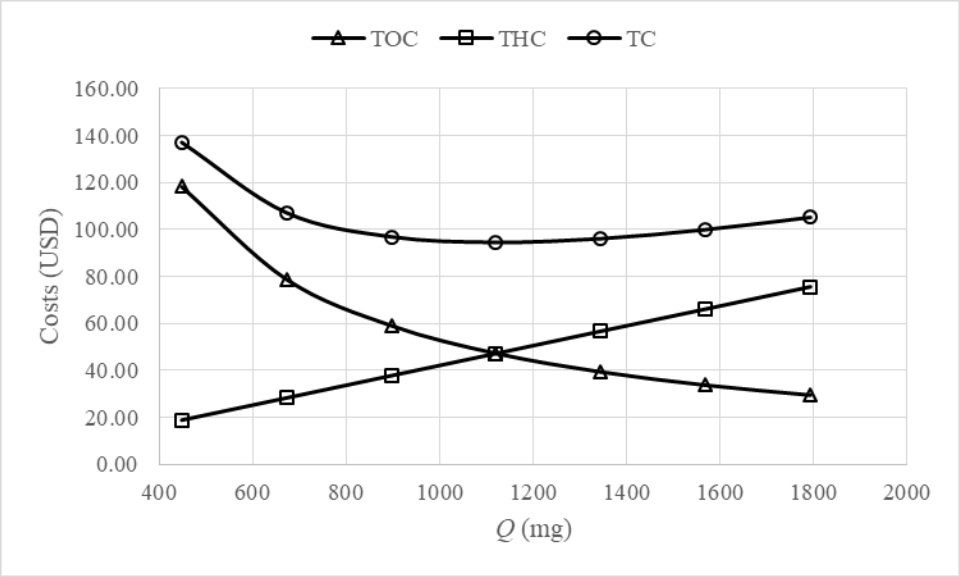

Figure 3. The inventory costs graphics.

Figure 4 shows that the changes in the patient arrival rate will change the drug demand rate linearly, and Table 1 shows the percentage of changes in demand rate is equal to the changes in patient arrival. Thus the effect of the arrival rate on inventory policies is equivalent to the usual demand rate. Besides, the arrival data provides an advantage for it can be collected earlier than the demand for CT drugs. One week of arrival data can estimate demand for more than 12 weeks. Thus better responsiveness can help make more precise inventory decisions when changes occur.

Table 1. The new patients' arrival rate changes.

λ	D	Q	TOC	THC	TC	$\Delta\lambda$ (%)	ΔTC (%)	ΔD (%)	ΔQ (%)
2.40	326	709	29.92	29.92	59.84	-60%	-37%	-60%	-37%
3.60	489	868	36.64	36.64	73.28	-40%	-23%	-40%	-23%
4.80	653	1003	42.31	42.31	84.62	-20%	-11%	-20%	-11%
6.00	816	1121	47.30	47.30	94.61	0%	0%	0%	0%
7.20	979	1228	51.82	51.82	103.64	20%	10%	20%	10%
8.40	1142	1326	55.97	55.97	111.94	40%	18%	40%	18%
9.60	1305	1418	59.84	59.84	119.67	60%	26%	60%	26%

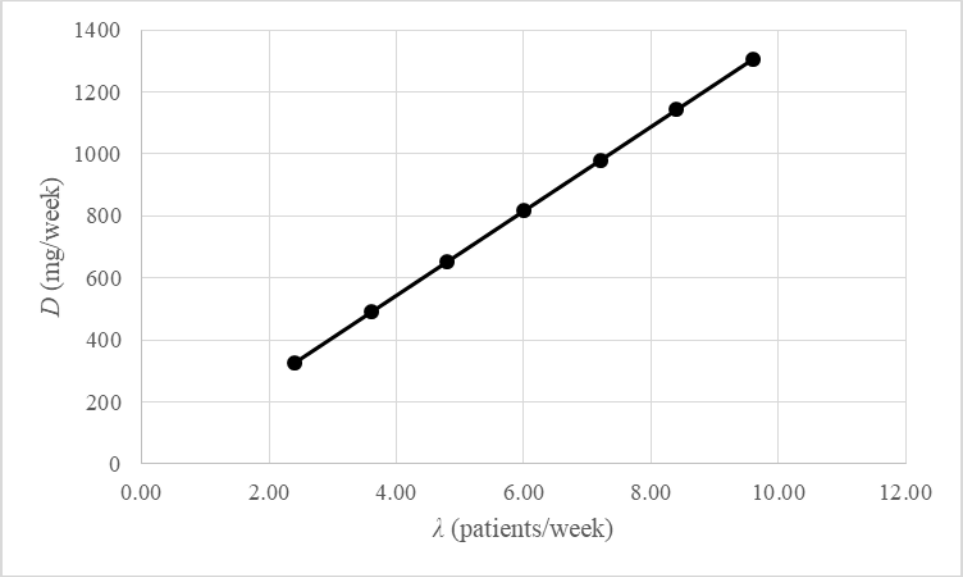

Figure 4. Demand rate graphic with various new patients' arrival rates.

Figure 5 shows an increase in patient arrivals affects the *EOQ* decision variable that also increases. In addition, this change also affects *TC*. Table 1 shows the percentage of change in *EOQ* and *TC* has the same value when there is a change in the rate of new patient arrivals (λ). Figures 5 and 6 show *EOQ* and *TC* get steeper changes as the arrival rate approaches zero. It shows the robustness of the inventory decision. The *EOQ* is less robust when the arrival rate is near zero.

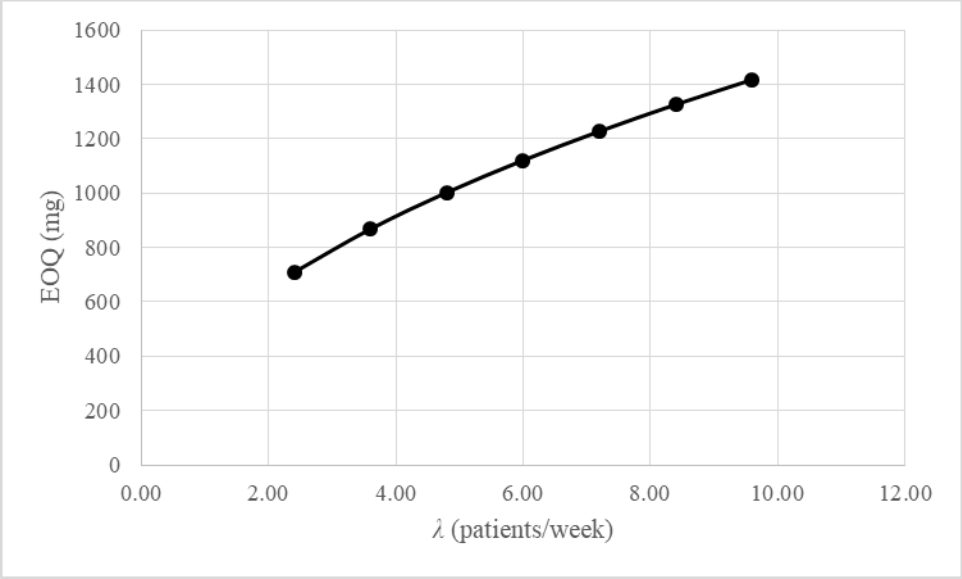

Figure 5. *EOQ* graphic with various new patients' arrival rates.

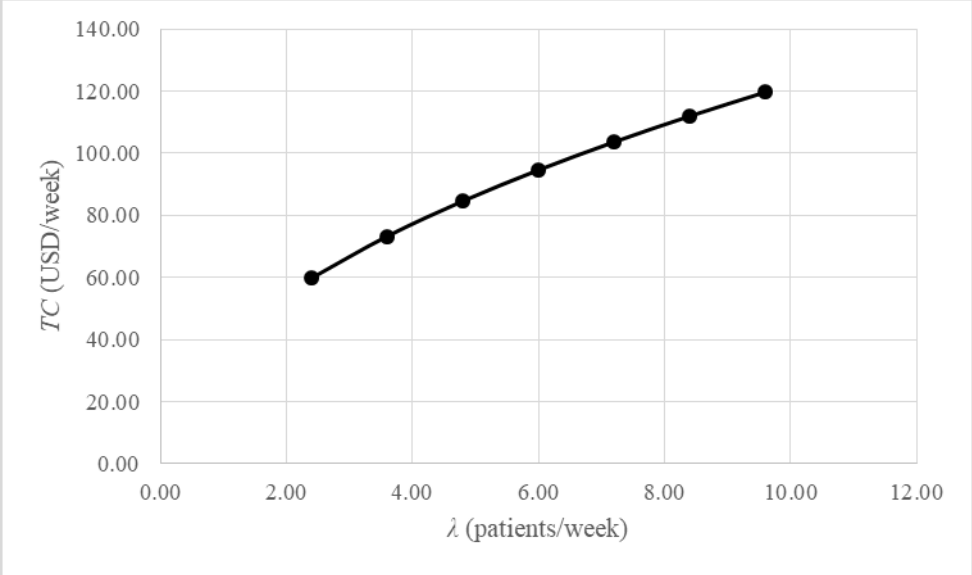

Figure 6. *TC* graphic with various new patients' arrival rates.

5. Validation

Validation is using a simulation with the help of a spreadsheet. It starts with new patients presenting in the first week and follows the transition probabilities. It starts from the first cycle to the fourth cycle. The transitions occur until the demand value is close to zero and can be neglected. Then it is continued with new patients who come in the second week, the third week until the 13th week who have reached a steady-state following the pattern of patients who come in the first week there is only a period shift. When it reaches a steady state, the total demand that appears at that time is the drugs demand rate that will be used in the inventory model. Figure 7 shows that for new patients who come in the first week (p1), the expected demand for the first (s1), second (s2), and third (s3) cycles is close to zero, while the s4 is 2 mg at week 13. Demand from new patients who come in the 13th week (p13) of 306 mg for s1, whereas s2 to

s4 still do not exist at week 13. The expected value of demand at week 13 is 815 mg. The following week has the same total although with a different composition. This result is the same as the formula used in Equation (4).

week	p1				p2				p3				p4			
	s1	s2	s3	s4	s1	s2	s3	s4	s1	s2	s3	s4	s1	s2	s3	s4
13	0	0	0.006	2.062	0	0	0.036	7.658	0	0	0.222	23.56	0	4E-04	1.325	47.12

week	p5				p6				p7				p8			
	s1	s2	s3	s4	s1	s2	s3	s4	s1	s2	s3	s4	s1	s2	s3	s4
13	0	0.004	7.363		0	0.042	35.34		0	0.402	117.8		1E-04	3.749		

week	p9				p10				p11				p12			
	s1	s2	s3	s4	s1	s2	s3	s4	s1	s2	s3	s4	s1	s2	s3	s4
13	0.002	32.13			0.038	214.2			0.765				15.3			

week	p13				Total
	s1	s2	s3	s4	
13	306				815.1

Figure 7. The demand composition at the 13th week.

6. Conclusion

This study proposes the EOQ model for CT drugs using new patients' arrival rates. The CT drug demand rate in the EOQ model is substituted by new patients' arrival rate and the transition probabilities between administration cycles using infinite geometric series. The results show arrival rate is equivalent to the demand rate, and the data on the arrival of new patients is faster to collect than the demand data. The demand data for complete CT cycles takes more than 12 weeks. Thus the proposed model can produce an inventory policy that is more responsive to changes in the future. A near-zero arrival rate will make inventory decisions more sensitive. The changes in arrival rate have the same effect on the economic lot size decisions (*EOQ*) changes and the total costs (*TC*) changes. The variability of chemotherapy drugs can be a consideration for further research. This variability can be a mixture of CT drugs for a regimen. The EOQ model is a basic model to provide basic concepts, so it needs further development to be more applicable in some areas, e.g., economic production quantity (EPQ) and multi-echelon supply chain.

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Biographies

Victor Suhandi is a Ph.D. candidate in the Department of Industrial and Systems Engineering, Chung Yuan Christian University, Taiwan. He obtained a Master's degree in the Department of Industrial Engineering and Management, Bandung Institute of Technology, Indonesia. And Bachelor's degree from the Department of Industrial Engineering, Maranatha Christian University, Indonesia. His research interests are production and inventory management, supply chain, and simulation modeling.

Ping-Shun Chen is a professor in the Department of Industrial and Systems Engineering, Chung Yuan Christian University, Taiwan. He obtained a Ph.D. degree in the Department of Industrial and Systems Engineering, Texas A&M University, USA. His research interests are supply chain management, system simulation, and healthcare simulation applications.