A simulation model to evaluate pharmaceutical supply chain costs in hospitals: the case of a Colombian hospital

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RESEARCH ARTICLE

A simulation model to evaluate pharmaceutical supply chain costs in hospitals: the case of a Colombian hospital

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Abstract

Background Healthcare costs is one of the most studied issue in our days because of increasing demand and the aging of population. Final costs of medicines is one of the most important issue in patient treatment and determine its real value is an important task within hospitals. Simulation models and in this case system dynamics allows to build representations of reality considering the interaction of the whole variables that affect the system where first a causal loop diagram allows to represent and identify the interaction between variables for develop a stock flow diagram to determine the final results.

Objective Develop a simulation model that allows decision makers in Hospitals and Governments to identify the variables that affect the final cost of medicines and to determine the legal reimbursement allowed by national agencies.

Methods This paper presents a conceptual modeling framework using a causal loop diagram and a dynamic simulation model in the real case of a hospital in Colombia to explore how different internal charges for medicines affect the behavior of the final unit-dose cost of medicines, considering the complexity of the pharmaceutical system. We developed a simulation model to represent and characterize the pharmaceutical supply chain in a hospital and by using real data we validate the results of the model and conclude about the supply chain of medicines in Colombia using the legal regulations as a main factor of analysis.

Results and conclusions We found that in some cases the maximum reimbursement value is less than the final cost of medicines within the hospital, which means that hospitals lose money on the administration of medicines to patients. The benefit of this model is that with the result the hospital can determine the real final monetary value of medicines, including the different processes starting from the reception of the medicines, ending with the administration to patients.

Keywords Medicine costs · System dynamics · Health care systems · Pharmaceutical supply chain · Simulation

Introduction

In recent years, the medical cost per capita for medical outpatients and inpatients has increased due to variables that are not easily manipulated by decision makers, such as the increase of life expectancy, the growing population, and the emergence of new diseases, among others. According to official statistics from the World Bank, the global population is growing at a rate of 200,000 per day, and it is higher in countries with medium and low incomes [1]. Another factor that increases the demand for health services is the substantial increase in life expectancy; currently, according to the World Health Organization (WHO), the life expectancy is 73 years for a woman and 68 years for a man [2].

The health system is composed of different actors as shown in Fig. 1 [3]. The main actors are patients who require health services. The biological environment generates the pathologies that increase the demand for services and treatments. On the other hand, the government creates policies for medical services, where public and private entities such as pharmacies and hospitals are responsible for managing the health care service, all framed within an economic environment. There are also the producers that can be divided into: research and development, generic manufacturers, local manufacturers, contract manufacturers and biotechnology companies [4].

The pharmaceuticals industry, like many other industries, is a complex system [4], principally due to the processes,

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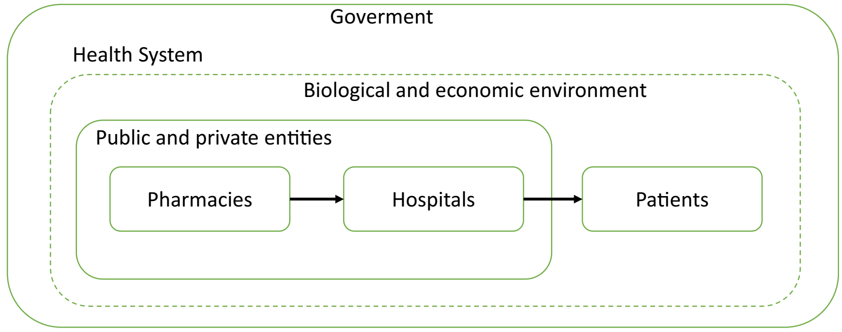
Fig. 1 Health care system



operations and organizations involved in the discovery, development and manufacture of medicines.

Pharmacies, clinics and hospitals operate in a very regulated market. Governments and regulatory entities fix the prices for producers, distributors and hospitals, imposing the margins for each of the players in the supply chain. While producers can establish their own times for producing and distribution, wholesalers and pharmacies must guarantee a service level according to the demand. The economic crisis and monetary limitations are forcing pharmacies to change the way they made decisions related to purchasing, ordering more frequently and in lower volumes, so the warehouses must work with these requirements in order to synchronize the supply chain [5]. Besides the regulations and the economic crisis, the pharmaceutical supply chain is affected by medicines' perishability and shortages [6].

The system studied in this paper consists of a market heavily regulated by governmental policies. Medicines given to patients by hospitals are paid for by the government but a maximum refund value that hospitals can access has been established. So, it is possible for hospitals to lose money in the process of buying medicines from companies or providers, and the whole process is related to the administration to patients. With this specific system, we want to answer the following questions: What is the behavior of the internal cost of medicines? What actors are involved in the process and how is their interaction with the system studied? What is the variation of the real cost of administering medicines to patients?

As the system studied involves several actors and is complex, the main purpose of this paper is to provide an approximation to understand the system's behavior using a system dynamics approximation that allows hospitals to determine the real internal costs of medicines and to determine if the system is generating losses or gains. Also, the simulation model can be used as a framework to determine the real maximum of prices that the regulation agencies can pay to hospitals (reimbursements) considering the real issues that affects the final prices.

This paper proceeds as follows: first we will describe some papers from the literature that have worked on similar problems; next we will describe our approximation using causal loop diagrams and the simulation model. Finally, we will present and discuss the results.

Related literature

Different approaches are used to determine the cost of medicines from the medicine manufacturers to the administration to patients. Some models provide a statistical function to estimate the price of a brand-name medicine and a generic substitute [7]. The model considers the quantity of firms that produce the medicine and constructs a utility function of a representative consumer with market and product segmentation by using a sensitivity analysis in which the boundaries of medicine consumption with ranges of prices are obtained.

Kaiser et al. [8] propose a pricing regression model to infer the change of prices due to a legal reform in Denmark, where medicine prices are regulated by a set of reference prices. The regulation of prices has been used in other countries and it has been evaluated in the literature [9–12]. A similar work was developed by Lauenroth and Stargardt, who studied pharmaceutical pricing in Germany [13] and in Egypt [14]. The model evaluates the effect of changing the medicine prices. With this change, they show that consumers tend to substitute branded medicines.

In [15] is developed a fuzzy logic model to estimate the medicine pricing for a new medicine using fuzzy logic**.** Fuzzy logic is used for the representation and acquisition of knowledge and data uncertainty. The model uses the product life cycle to estimate different factors that affect the medicine pricing during different stages of the life cycle [16].

In [17] is developed a model to study the behavior of pharmaceutical costs in China using system dynamics. The model addresses problems related with the high prices of medicines and pharmaceutical fees and takes into account a problem related to the unnecessary use of expensive medicines by medical staff.

The model is based on articles that approximate a hospital's problems with system dynamics [18] [19] [18–20] [21, 22]. Kunc et al. [23] developed a system dynamics simulation model to represent the pharmaceuticals market for chronic cardiac disease in Bulgaria. The main idea of the simulation model is to test different policies related with drug regulation, like providing timely access to the market, influencing the prescribing of generic medicines and implementing programs for increasing the percentage of diagnosed patients, based on the dynamics of the pharmaceuticals market for one chronic disease.

In [24] a system dynamics simulation model is developed. In the study authors propose a simulation model studying the different variables that are associated with the drug policies in India. Authors first identify the different variables associated and create a causal loop diagram and then a Forrester model is proposed. This article presents a big contribution in the decision making in drug policies, nevertheless some results and experimentations are missing to check the results of the model proposed.

Most of the articles in the literature try to study methods to determine the prices of medicines. Nevertheless, the main contribution of this research is to study the behavior of the change of internal costs of medicines in hospitals considering the several processes and actors involved. Therefore, with this study and the model developed decision makers in both sides (hospitals and government) can support the process of decision making by deeply studying the interaction between the uncertainty factors and variables that affect the final costs of medicines.

Methods

The pharmaceuticals supply chain process is a complex and dynamic system with multiple non-linear relationships. For this reason, this study uses a simulation continuous-time modeling approach [25]. System dynamics was selected to develop this study because of its ability to evaluate different strategic policies and integrate the system feedback and delays, as well as to evaluate the relationship between the main variables and their impact on the behavior of the final price of medicines. The main interest of our contribution is twofold: (i) build a conceptual causal-loop diagram that represent the whole situation of interest based on some previous studies that support the idea of the building of the causal loop and (ii) generate a simulation model that enable to study the behavior of the final costs of medicines within hospitals. Nevertheless, with this study we have some limitations as: transduction of causal-loop to Forrester model generates the configuration of some variables with the information available in hospitals, therefore some variables cannot been modeled, other limitation is that our main interest is to study the behavior of the final costs of medicines and contrast with the reimbursement policies, we don't build the simulation model to generate policies to reduce the prices of medicines because some variables can't be affected directly by hospitals, they're only affected by legal regulation or government policies.

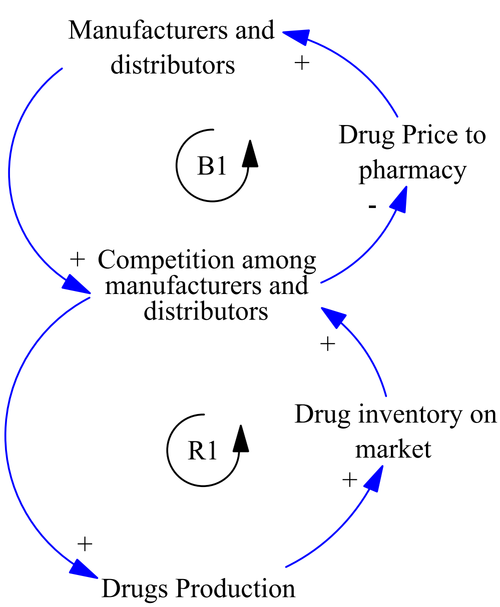


Fig. 2 Manufacturers and distributors causal loop diagram

Process description

The clinic selected for this study is Universitary Colombian Hospital which is divided into operational areas. The areas analyzed in this study are: (i) the pharmaceuticals area and (ii) logistics and supply chain area. The main objective of the pharmaceuticals area is to provide the clinic with the medicines required for patients. The pharmacy oversees receiving medicines, making records in the databases and updating inventory records for medicines, packaging medicines as individual items (a legal requirement to guarantee a medicine's traceability), keeping the inventory in good order, receiving the requirements from the clinic and dispatching in the right quantities and conditions. The pharmacy sends the requirements for medicines to the logistics area. The logistics area negotiates with suppliers to get discounts on the amount of medicines needed. Once a patient is healthy, the hospital makes a request to the local government to receive payment for the medical treatment. In Colombia, there is a regulation that establishes the range of prices for medicines and

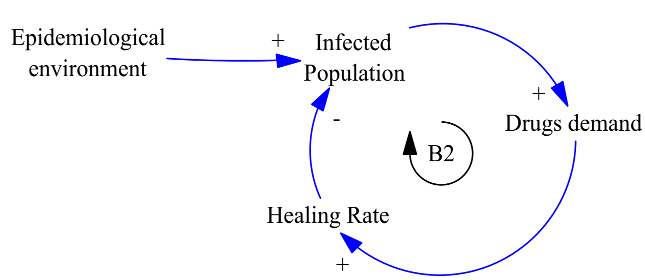


Fig. 3 Demand for medicines causal loop diagram

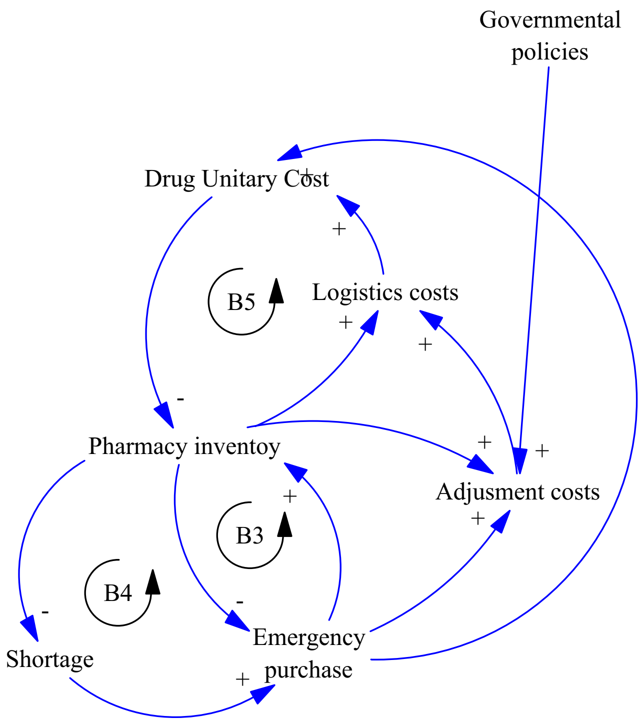


Fig. 4 Pharmacy causal loop diagram

treatments, so hospitals are not able to receive payments over the maximum legal price allowed.

Causal loop diagram and dynamic hypothesis

The system dynamics model was created with the main objective of capture the behavior of the final cost of medicines within hospitals, describing the interaction between the main variables and parameters that are involved in the determination of the final cost of medicines. The main idea was to map the variation of the costs including the interaction and variation of the variables to contrast its value with the maximum reimbursement value defined by governmental agencies for define if the final cost of medicines can exceed or not the maximum amount of money that the hospital will be receive by the process of reimbursement. The objective of the model was not to replicate the exact pattern followed by the costs including all the variables, since there are some variables and conditions that cannot been modeled with the information available in hospitals.

The initial working hypothesis was mainly designed for testing the effect on the change of prices for suppliers, internal processes and varying also the reimbursement values to contrast this value. Gaining an understanding of the pharmaceuticals supply chain in the hospital is the first crucial step of the simulation model. System dynamics modeling requires the development of a causal loop diagram which captures the interactions between the key components [26]. Based on the factors involved in the pharmaceuticals process of the clinic, general and specific causal loop diagrams are developed.

For building the causal-loop diagram, we have used some previous studies which identify and characterize some main variables that affect the costs of medicines, also we have include some studies which also made simulation based on system dynamics for a very similar research situation (see [8, 9, 17, 23, 24, 27]). We have developed a conceptual structure divided into three main sectors. Figure 2 shows the first causal loop diagram that contains manufacturers and distributors of medicines. The variables used are:

- Manufacturers and distributors: refer to the number of companies selling medicines to pharmacies
- Competition among manufacturers and distributors: refers to the pricing strategy for selling to pharmacies
- Drugs production: refers to the quantity of drugs produce and distributed by the manufacturers and distributors
- Drug inventory on market: refers to the quantity available for selling to pharmacies
- Drug price to pharmacy: refers to the selling price of medicines to hospitals and/or pharmacies

A market with producers and distributors with competition is driven by a balance feedback loop (B1). Higher number of medicine companies (manufacturers and distributors), imply the increasing of competition for getting a portion of the market, because companies are interested in reaching a major proportion of the market, meaning that there is major competition between producers and distributors. Hence, as the competition increase, it generates a reduction of the selling price to hospitals and pharmacies. On the other hand, as the selling price of medicines increase, the market becomes attractive and the number of manufacturers and distributors will increase. When increasing production on the market a reinforcement process is presented (R1). Higher competition generates an increasing production of medicines, thus the market will have a high number of medicines on the market that generates more competition between manufacturers and distributors.

Figure 3 shows the causal loop diagram of the demand for medicines, this causal loop is based on the very known illness causal loop, also developed in [28]. The variables used are:

- Infected population: refers to the quantity of population infected in a period
- Healing rate: refers to the rate that population is healing
- Drugs demand: refers to the consumption of medicines in hospitals
- Medicines demand: refers to the consumption of medicines in hospitals
- Epidemiological environment: refers to the quantity of diseases and illnesses

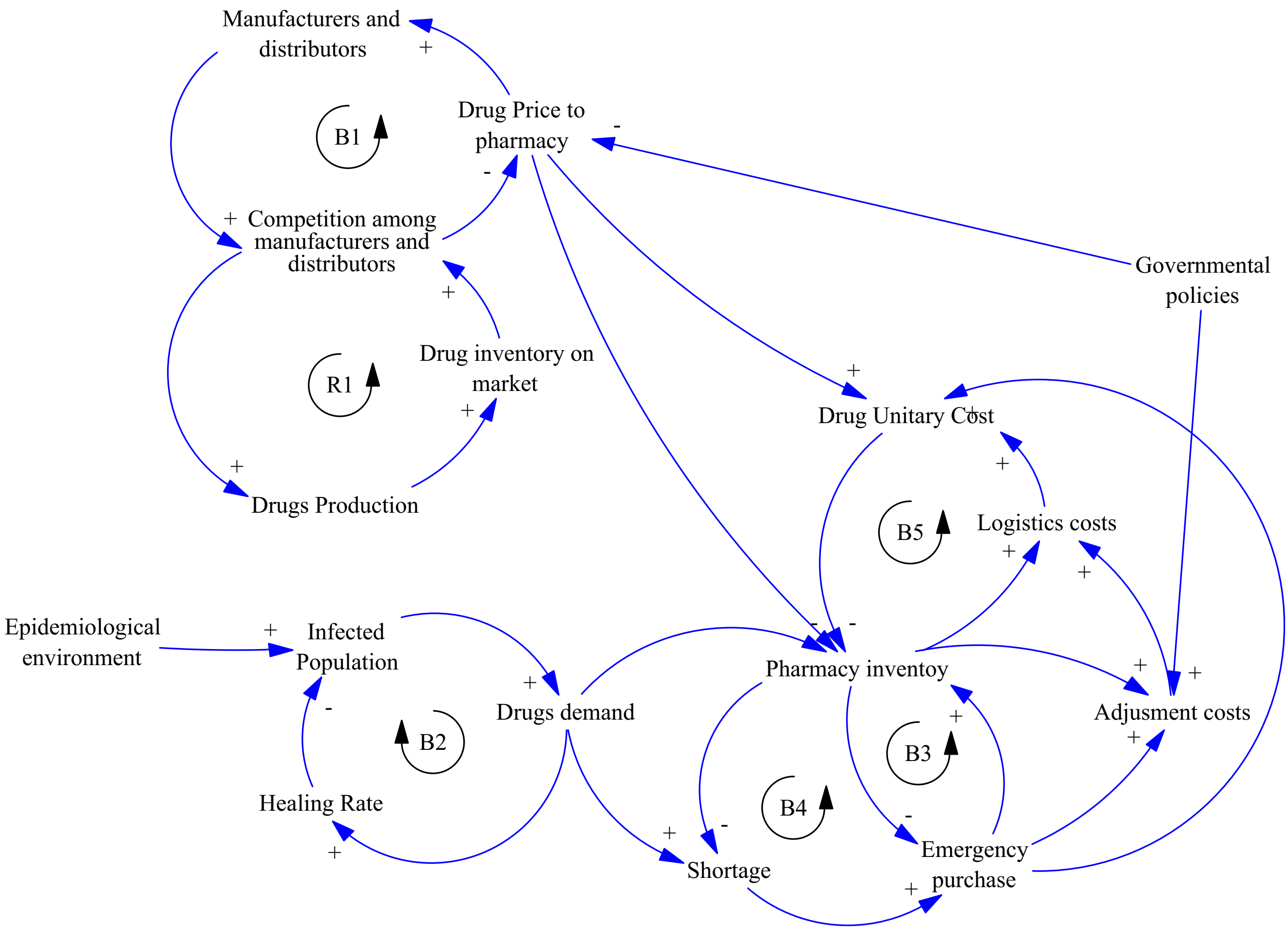


Fig. 5 Causal loop diagram for pharmaceuticals supply chain

A balance feedback process (B2) is driven in the demand of medicines. The infected population is influenced by the epidemiological environment, the increasing of infected population increases the drugs demand and this increasing demand generates and increasing healing rate. Finally, an increasing of the healing rate generates a reduction of the infected population.

Figure 4 shows the causal loop diagram of pharmacies. The variables used are:

- Pharmacy inventory: refers to the quantity of medicines available in the pharmacy
- Emergency purchase: when there aren't enough medicines on the inventory and the patient needs the medicine at a specific time
- Logistics costs: indicates the cost incurred by the workers at the pharmacy and hospital
- Adjustment costs: indicates the cost incurred with the adjustments of medicines
- Governmental policies: indicates the legal regulation and policies
- Shortage: refers to the quantity of medicines that can't be satisfied with the stock hold by pharmacies or hospitals

Table 1 Medicine statistics

Medicine	D Type	Mean	SD	PS	EI	% L	R	OQ	LZ
ACETAMINOFENE X 500 MG TABLET	Normal	4430.00	551.00	150	Between 6 and 12%	Max 1%	5336	392	8
ACETYL SALICYLIC ACID X 100 MG TABLET	Normal	254.30	53.00	133	Between 6 and 12%	Max 1%	341	62	13
ADRENALINE 1 MG SLN INJEC	Normal	182.95	95.60	1282	Between 6 and 12%	Max 1%	339	55	4
AMLODIPINE 5 MG TABLET	Normal	377.00	99.20	290	Between 6 and 12%	Max 1%	540	33	20
AMOXICILLIN 500 MG TABLET	Normal	27.40	29.60	1589	Between 6 and 12%	Max 1%	76	7	12

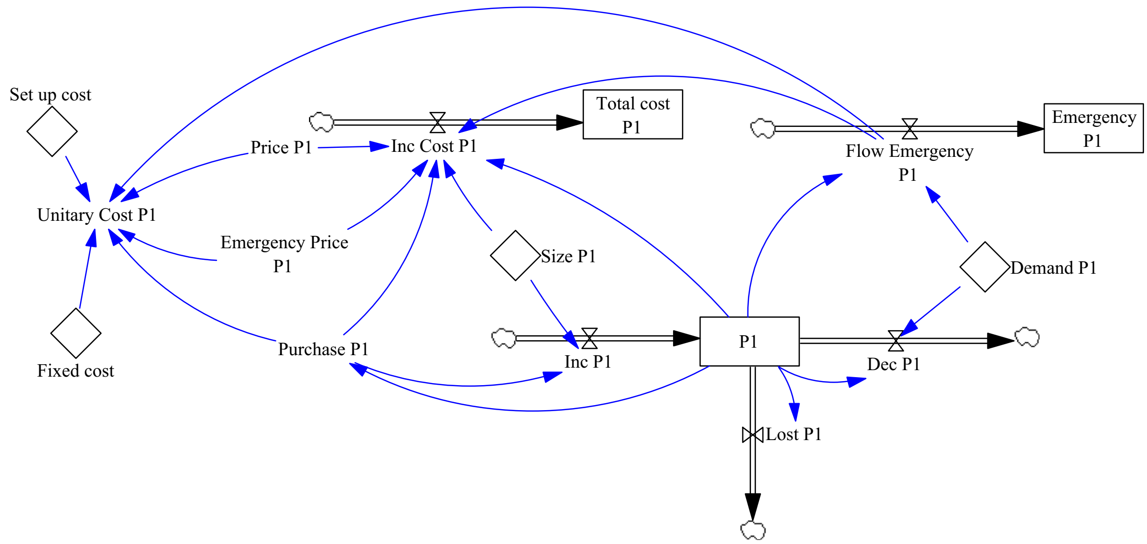


Fig. 6 Forrester diagram for medicine 1

- Drug unitary cost: refers to the final cost of medicines

Internal processes and the definition of the final cost of medicines are dominated by three balance cycles (B3, B4 and B5). Higher level of inventor on pharmacy produce higher logistics costs driven by a balance cycle (B5), if the logistics costs increases, the drug unitary cost also increases, but if the unitary cost increase the pharmacy inventory is reduced due to budget constraints. On the other hand, higher inventory levels produce less shortages with a balance cycle (B4), and the increase of shortages produces an increasing in the emergency purchases, but if the inventory levels increases the emergency purchases decreases, also the increase of emergency purchases increases the inventory levels (B3) Higher inventory levels and emergency purchases generates higher adjustment costs. This adjustment costs are also influenced positively by governmental policies, an increasing the adjustment costs produces an increase in the logistics costs. Finally, higher number of emergency purchases produces higher drug unitary costs.

Figure 5 shows the integration of the specific causal loop diagrams shown in Figs. 2, 3 and 4, and represents all the relationships in the pharmaceuticals supply chain. Higher selling price from manufacturers produce less inventory levels, also this increment generates higher unitary cost of medicines, but this selling price is regulated or reduced by governmental policies. Finally, with higher demand of medicines generates major shortages and reduce the inventory levels.

Data sources

Data were obtained from the administrative health databases of the hospital and from public databases. The model requires five categories of data: consumption of medicines, selling prices from manufacturers and sellers, lot size of medicines and legal regulation of prices.

Consumption of medicines: each patient arrives at the clinic and requires a specific medicine or set of medicines. The data used for the model require the total amount of consumption of each type of medicine in each month. Consumptions were obtained from the databases for a range of three years. Daily consumption was aggregated into monthly, to obtain the total amount of medicines that must be available in a single period. For each type of medicine and its consumption, a goodness of fit test was developed.

Legal regulation of prices: The health care system is regulated by local regulation policies. Hospitals can define the final price of a medicine given to a patient, but this cannot exceed the maximum price defined by legal regulation. This is public available information.

Lot size of medicines: Each manufacturer and seller have its own lot size of medicines. This information is given to the hospital.

Selling prices: Each manufacturer and seller has its own selling price, and this is given to the hospital during each period of time.

System model structure

The system dynamics simulation model was developed using Vensim V6.2. As our purpose is to study the behavior of the total cost of administration of medicines, we select the delta time (DT) as monthly during an interval of a year (12 months). We select five (5) items of medicines that share the same space in the storage area and that can be provided by two different

Table 2 Description of variables

Name	Description	Type	Equation	Units
Demand P1	Parameter that generates the demand	Auxiliary Variable	INTEGER(RANDOM NORMAL(3591, 5954, 4430, 551, 1000))	Units of medicine 1
Emergency P1	Acummulation of emergency purchases	Stock	Flow Emergency P1	Units of medicine 1
Flow Ememrgency P1	Present the flows of emergency purchases	Flow	MAX(0, Demand P1-P1)	Units of medicine 1
Dec P1	Units of medicine use to satisfy the demand	Flow	MIN(Demand P1, P1)	Units of medicine 1
P1	Units on inventory of medicine 1	Stock	Inc P1-Dec P1-Lost P1	Units of medicine 1
Lost P1	Units of medicine on inventory lost	Stock	INTEGER(P1*MIN(RANDOM 0 1(), 0.01))	Units of medicine 1
Inc P1	Flow of units of medicine 1	Flow	Purchase P1*Size P1	Units of medicine 1
Size P1	Number of units of medicine 1 per package	Constant	8	Units per package
Total cost P1	Acummulation of the total costs	Stock	Inc Cost P1	Monetary ($)
Inc Cost P1	Calculation of the costs incurred	FLow	Price P1*(1 + Emergency Price P1)*Flow Emergency P1 + Purchase P1*Price P1 + 210*Size P1 + 0.03*P1	Monetary ($)
Price P1	Price per package of medicine	Constant	150	Monetary ($)/package
Emergency Price P1	Increment of the regular price when a emergency purchase is done	Auxiliary Variable	(RANDOM UNIFORM(8, 12, 2))/100	%
Purchase P1	Units of medicine purchased using the R, Q policy	Auxiliary Variable	IF THEN ELSE(P1 < =5336, 393, 0), RANDOM UNIFORM(1, 2, 1), IF THEN ELSE(P1 < =5336, 393, 0), 0	Units of medicine 1
Fixed cost	Fixed cost due to logistics area	Constant	3000	Monetary ($)/order
Set up cost	Set up cost due to internal and governmental policies	Constant	210	Monetary ($)/unit of medicine
Unitary Cost P1	Unitary cost per medicine	Auxiliary Variable	IF THEN ELSE(Flow Emergency P1+ Purchase P1 > 0, (Flow Emergency P1*Price P1*(1 + Emergency Price P1) + Purchase P1*Price P1)/(Flow Emergency P1 + Purchase P1) + Set up cost+Fixed cost/(Flow Emergency P1) + Fixed cost/(Purchase P1), 0)	Monetary ($)/unit of medicine

Table 3 Results of validation

Medicine	H0 Result	*P* value
ACETAMINOFENE X 500 MG TABLET	Not rejected	0.52
ACETYL SALICYLIC ACID X 100 MG TABLET	Not rejected	0.13
ADRENALINE 1 MG SLN INJEC	Not rejected	0.23
AMLODIPINE 5 MG TABLET	Not rejected	0.07
AMOXICILLIN 500 MG TABLET	Not rejected	0.32

suppliers, who can deliver the product in 1 to 2 months. Demand can be supplied from the inventory or by an emergency purchase, where the pharmacy must find the medicine in the market, no matter what the selling price is, because the service level must be always 100%.

Following the methodology of system dynamics modeling, it is necessary to classify the variables into auxiliary variables, stock variables or flow variables.

Table 1 shows the medicines selected for this study and their statistical metrics required by the simulation model. The distributions of each of the medicines are presented in Table 1 and are obtained from the data given by the hospital. The first column presents the name of the medicine and the next shows the density probability function (D Type). As the demand for all medicines follows a normal distribution, the mean and the standard deviation (SD) are presented. In the fifth column, we present the normal price of suppliers (PS) followed by the price increment if an emergency purchase is made (EI). (%L) is the percentage of medicine lost, and we can observe from the data that in all cases the losses of medicines do not exceed 1%; this depends on factors like human mistakes or expiry dates (%L). Reorder points defined by the pharmacy in terms of re-order point (R) and order quantity (OQ) are presented, and the last column shows the lot size (LZ).

The simulation model comprises 15 stocks, 25 outflow rates and 35 auxiliary variables. Some other auxiliary variables, stocks and outflow rates have been included to facilitate the calculations and the output analysis. A single model used for medicine 1 is presented in Fig. 6. Also, the description of the main variables used are presented in Table 2. In this table the name of the variables, the description, type, equations and units are presented.

The rate of demand is obtained by using the information presented before; using this information and the reorder point, we obtained the purchases that increase the flows of incoming medicines considering the lot sizing of each of them. Medicines are accumulated, and the inflow rates are the medicine lost and the demand. If there is not enough medicine available, a flow of emergency purchases is used to satisfy the demand. Therefore, we used some auxiliary variables, flows and accumulations to obtain the total unitary cost.

The stocks used refer to the amount of medicine 1 on the inventory that can be reduced by the demand and the amount of product lost. The inventory increases by the total amount of purchases of medicine 1. Also, a stock for emergency prices and the cumulative cost of medicine 1 are used. Finally, an auxiliary variable of the unitary cost for each month is used to calculate all the expenses for the medicine.

Validation

From the results of the simulation output we used a t-student test to validate the simulation model. Hypothesis testing techniques are used to determine if the average results of the simulation model are statistically similar to the real data or not for each type of medicine (final costs considering the uncertainty). The validation process consists in determining if the null hypothesis is not rejected,

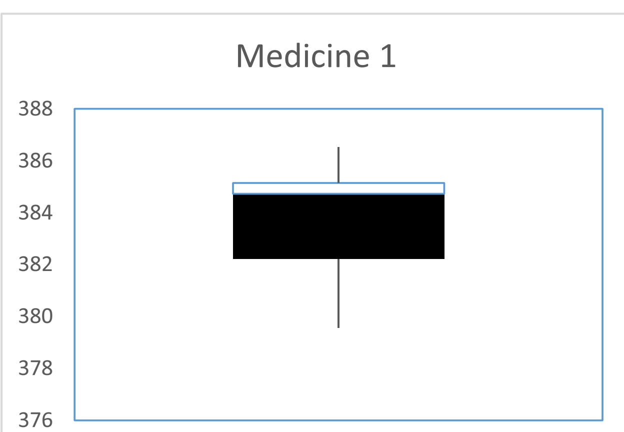


Fig. 7 Box plot medicine 1

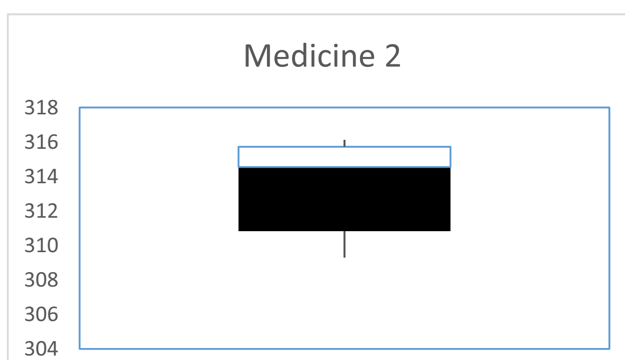


Fig. 8 Box plot medicine 2

Fig. 9 Box plot medicine 3

from which we can conclude that the simulation data is statistically close to the real data (Table 3). We have used for each medicine a confidence level of 95% and the results are provided in Table 2.

From the results presented in Table 2, we can validate the results of the model.

Results and discussion

Figures 7, 8, 9, 10 and 11 show the effect of the medicines' administration in the final unit-dose costs, where the final costs in Colombian pesos are presented in the y-axis.

For medicines 1, 2 and 5 there is a high variation of costs, by contrast with medicines 3 and 4. This is explained by the supplying conditions of the clinic. For these five medicines the final cost increases by 158%, 137%, 41%, 116 and 36% respectively because of the interaction of all the uncertainty and variables. This indicates that each of the medicines has its own behavior and they are affected in different ways by the complexity of the system.

The effect of lead times and the re-order time (r,Q) policy over the planning horizon, coupled with the influence of other factors, creates irregular cost behavior, and their final costs change over time due to different influences. This result can help the hospital to determine the likely expenses and income for a financial

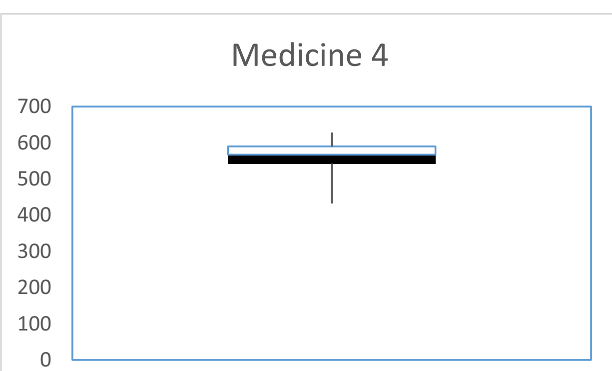


Fig. 10 Box plot medicine 4

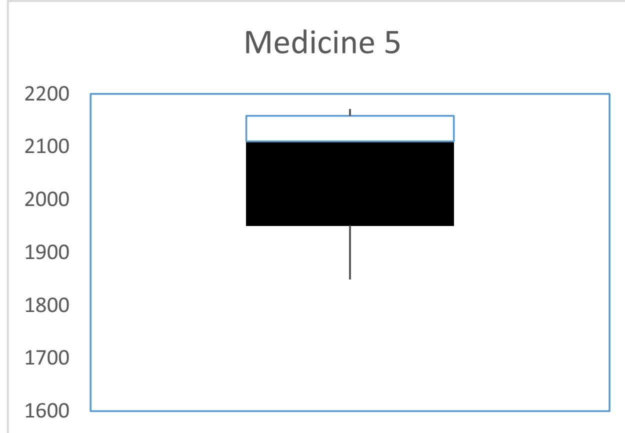


Fig. 11 Box plot medicine 5

planning horizon, but this model cannot determine the final cost of a medical treatment, which is out of the scope of this study.

With this result, we can observe that for medicines with lower costs like medicines 1, 2 and 4 the final costs are duplicated, meaning that the logistics costs and other external factors have a greater value than the original price of the medicine. This means that the legal regulation of the final costs for medicines may be ignoring these issues in the established policies.

These unit-dose cost variations are highly influenced by external factors such as market prices and expiry dates. Figure 12 presents the behavior of medicine 5. The first figure presents the behavior of the unitary cost during the year (x-axis represents time and y-axis final costs), the second figure contains the behavior of the inventory levels (x-axis represents time and y-axis inventory levels), and the last figure presents the emergency purchases in the same period (x-axis represents time and y-axis emergency purchases).

It can be observed that the final costs of medicines do not have a linear behavior (due to the complexity of the system). Due to the lead times of manufacturers, sometimes there will be no medicine in the inventory (stock = 0), a situation that triggers the purchase of emergency medicine, which increments the cost of the purchase. Also, it can be observed that the final costs do not always have the same influences. For example, in some periods 44% of the final cost is influenced by the stock and 56% is influenced by emergency purchasing, while in some other periods the final price is influenced by purchasing and emergency purchasing in different proportions. Also, we can observe from the figure that in some periods of time the unitary cost is 0, a situation that occurs because in these periods there are no purchases or emergency purchases. In that case, demand is satisfied by the units remaining in the inventory, and for this reason the inventory cost is used in the months when a normal purchase and/or emergency purchase is made.

Finally, and as our objective is to determine the final unit-dose cost of a medicine and the reimbursement value, these values are presented in Fig. 13, which shows the range of the

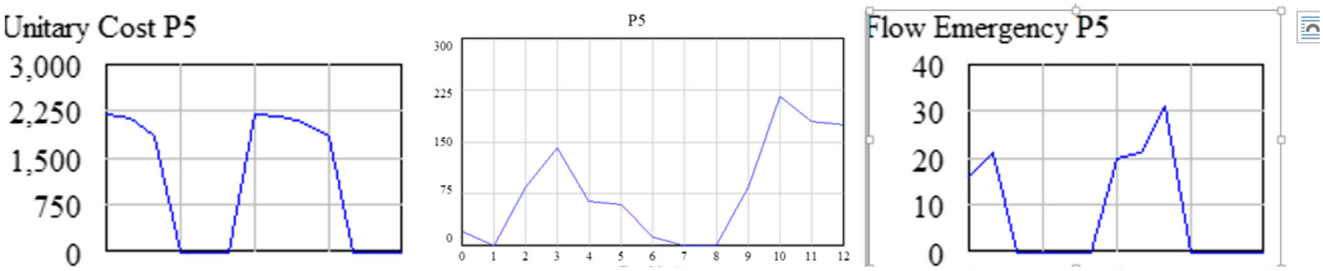


Fig. 12 Behavior of medicine 5

final cost of medicines, where the point is the value of the actual reimbursement approved by the government.

In the cases of medicines 1 and 2, the value of reimbursement is less than the interval value. In the cases of medicines 3, 4 and 5, the value is between the extremal values. We can conclude in the cases of medicines 1 and 2 that there is no scenario in which the hospital can recover the money invested in medicines, or much less generate profits from the administration of medicines. This fact can be explained by the low unit cost of medicines, which makes the internal cost larger than its unit value and therefore does not reach the maximum value of the medicine.

On the other hand, it can be observed that the disbursement values of medicines 3, 4 and 5 are within the range of variation of the price of the drug, which means that there are possible scenarios in which the administration of medicines recovers the value of the drugs and on certain occasions generates some profits from them. However, this does not happen in all cases since there are external elements such as emergency purchases, medicine losses and variations in sales prices that directly affect the final cost of the medication, in addition to the hospital's internal administration.

Sensitive analysis

A sensitive analysis is developed to determine the variation of the final cost due to changes in some variables used in the model. In Fig. 14 the sensitive analysis is presented. This analysis is composed by four variations: (a) a variation of the set-up cost, (b) a variation of the fixed costs, (c) a variation of both parameters, set up cost and fixed cost and (d) a variation of the selling price. The range of variations for the first three cases are from 0 to the maximum value. In the case of the selling price we consider the extreme case in which the selling price of medicine is reduced to the half, this affirmation is not far from reality because there are some cases in which government stablish or reduce the selling prices of medicines to hospitals. Analyzing the behavior between the changes of (a) and (b), we can observe that bigger variations are presented when changes are made with the set-up cost over the fixed cost. Also, and is a consideration that can be made for the hospital is the fact that if both changes are made and the cost are reduced, the reduction over the final cost of the medicine can reach a 28%. Finally, over the graph (d) we can conclude that the reduction over the final cost is mainly driven by the selling price of medicines, this can enhance to public and national governments to analyze and propose policies to control the selling prices.

Conclusions

In this paper, we have presented a system dynamics simulation model to represent the behavior of the final cost of medicines. The model was calibrated and tested based on currently available data on the clinic. We have provided the actual system scenario as part of our analysis because our purpose is to study

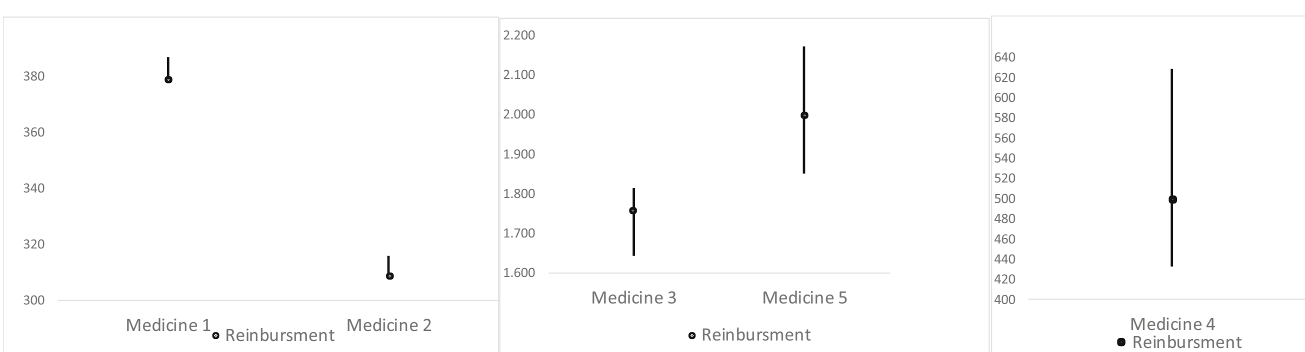


Fig. 13 Reimbursement and range of costs

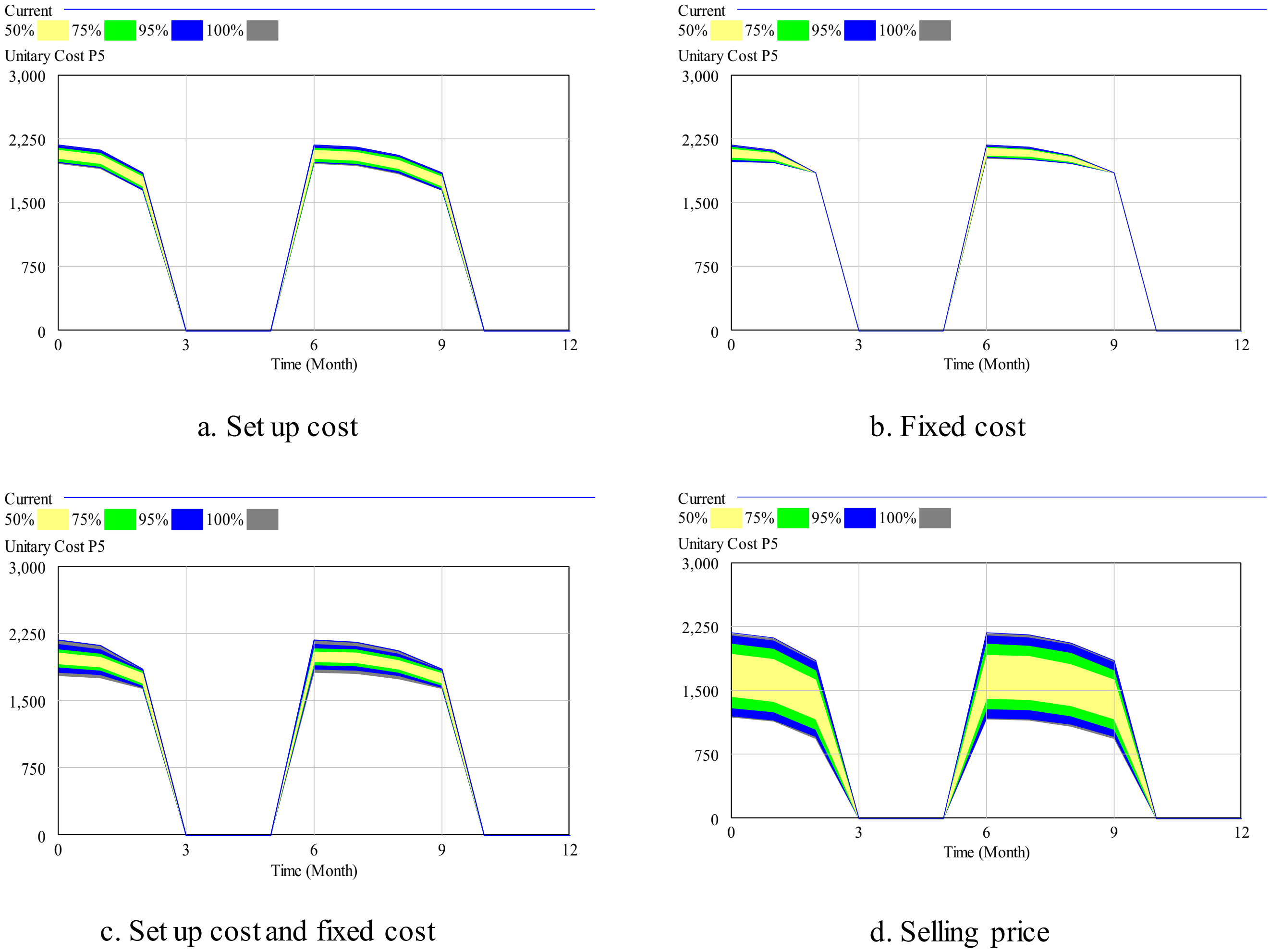


Fig. 14 Sensitive analysis

the behavior of the total cost of medicines. From this study, we can observe that the final cost of medicines is not static and it is affected by different factors.

The healthcare sector, especially the pharmaceuticals sector, in Colombia demands high-quality models for decision support systems in order to understand and optimize processes with the purpose of generating a high-quality level of service and minimizing total operational costs.

As part of our research, we incorporate in the model logistics issues that have not previously been considered in the literature. Therefore, we can observe the real behavior of supplying medicines for patients and the behavior of the final cost of medicines, which is a key aspect because of the legal regulation of the final prices in Colombia. The system dynamics methodology includes the incorporation of causal loops diagrams; this is an advantage of the study because it makes it possible to determine the relationships and feedback between the main variables.

Finally, in this study we present a system dynamics simulation model for the pharmaceuticals supply chain in a clinic in Colombia. Our contribution aims to determine the relations and feedback between variables that affect the system, and the model developed can be used to explore various scenarios that will help decision makers to ensure alignment with the consumption of medicines by patients and to minimize the final cost of medicines. While the simulation model presented in this article is applied to a Colombian hospital, it can be applied also in other pharmaceuticals systems. At the end of the article, we present the reimbursement values, from which it can be concluded that this study could be a first step to determine which the best values are to determine the top of prices considered by legal regulation taking into account the conditions at individual hospitals and uncertainty related.

Future research can include some items that we have not considered, such as economic factors and policies used by companies and pharmacies to fix the prices of medicines. Also, future work will include some optimization policies for the clinic to determine the best quantities and then try to reduce the unit-dose costs. Other future research will include the study of generic drugs, their effectiveness on patient health, and the minimization of total costs.

Compliance with ethical standards

Declaration of interest The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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