Stakeholder involvement in drug inventory policies

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Abstract

This paper experimentally investigates the relationships among three major stakeholders involved in drug inventory management at Intensive Care Units (ICUs), namely: i) nurses, who in person manage drug orders and carry out storage operations, ii) clinicians, who choose the therapy and shape demand, and iii) the hospital management, who is in charge of the economic sustainability of the hospital. As a case study, we consider the ICU ward of a major Italian public hospital and we focus on antibiotics. We exploit a previously developed Mixed Integer Linear Programming model which decides, for each drug, when and how much to order, and we improve it by adding different sets of constraints to represent each stakeholders' point of view. By solving three generalized models, each of which ties the satisfaction of a single stakeholder to different thresholds, we explore the mutual effects of taking explicitly into account different perspectives within the inventory policy. We implemented an instance generator, built on the basis of empirical probability distributions extracted from a large set of observed historical data and representing the decision flow ruling drugs prescription. An extensive set of computational experiments has been carried out on a set of realistic instances provided by the generator. Results based on our test case not only provide computational evidence to intuitive relations among stakeholders, but also suggest possible levels of compromise. Improved stakeholder satisfaction would also benefit the patient, the

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passive stakeholder who is the ultimate subject of the caring process.

Keywords: hospital logistics, drug inventory policy, stakeholder involvement

1. Introduction

Drug logistics optimization is often advocated as an effective leverage to contain healthcare costs, whose steady increase in industrialized countries poses a challenge to decision makers [1]. However, cost reduction should not be the only priority of health care organizations since several stakeholders are involved in the care process and their point of view should be accounted for. In particular, this study is concerned with the drug inventory policies of the Intensive Care Unit (ICU) ward at a large public hospital in Italy, focusing on the different perspectives of the principal stakeholders involved in drug management.

Worldwide, ICUs represent a unique environment [2] due to the following key-features: (*i*) severe clinical conditions of patients, (*ii*) extreme variability in patients' Length of Stay (LoS) [3], (*iii*) the potential for rapid evolution of patients' clinical conditions, that may worsen very quickly, (*iv*) a limited number of ward beds, (*v*) stock-out prevention, since drug supply should always cover drug demand. These features make it complex to prevent inventory understocking and overstocking, which are particularly ineffective in hospitals for the following reasons. Drugs understocking leads to physicians' dissatisfaction and negatively impacts on the operational performance, causing workflow disruptions such as surgeries delays or cancellations. In the specific context of ICU, understocking is even more disruptive, potentially causing patient's death if a drug shortage prevented the timely delivery of a therapy to a critical patient [4]. For this reason stock-outs at ICUs are faced by rush orders, although this is very expensive. On the other hand, overstocking may lead to drug obsolescence, spoilage, and depreciation. Moreover, it often implies long and frequent inventory operations, which keep nurses from patient care. Uncontrolled overstocking is also opposed by the hospital management in charge of the financial sustainability of the hospital (management, hereafter), as it increases carrying costs and it is related to a suboptimal use of budget. This is particularly true in the ICU setting where high-priced pharmaceuticals are typically used. At the same time, though, stock value on the ward is not perceived as a direct financial cost as it is in logistics settings other than health care; indeed, reducing inventory is one of the goals of lean manufacturing. At ICUs, on the contrary, patient care and service level are prioritized with respect to inventory cost containment. In addition, hidden stocks are often kept on the ward as a means to prevent drug shortages. Therefore, tailored inventory policies are needed, that are able to contain understocking and overstocking while ensuring the quality of care.

Based on these observations, we recently proposed a Mixed Integer Linear Programming (MILP) optimization model [5] to implement an inventory policy aiming to: (*i*) reduce the nurse's burden due to drug orders management (lowering the number of orders in the planning period), (*ii*) increase service regularity in drug orders management (for each drug, the same quantity is ordered every time an order is triggered for that drug), (*iii*) contain overstocking by controlling the value of stock, i.e. the monetary value corresponding to the cost of the drugs stored daily on the ward, while (*iv*) preventing understocking and (*v*) incorporating storage constraints. This policy prioritizes patients, since the time nurses save on drug supply management can be redirected to patient care, whereas reducing inventory costs is a secondary objective. This basic model was then integrated to include, one at a time, the perspective of the three main stakeholders also involved in the process, namely nurses, management, and clinicians, and in so doing we laid the ground for the current analysis. Indeed, in this study we proceed a step further as we explore the relationships existing among these stakeholders with the aim of capturing the independencies and interdependencies that hold between them. To reach this goal, we examine the effects that imposing one of the perspectives has on the other two. The trade-offs possibly resulting from the consideration of a perspective with respect to the basic model are evaluated on a realistic data set that is based on a reliable representation of the drug demand generation process. Specifically, we generated a set of random instances representing a meaningful sample of the demand patterns. A first subset is used to set the *levels of desirability* a solution should exhibit when considering each stakeholder's perspective. Then, the other subset is used to computationally verify the robustness of such levels when used to solve instances coming from different demand realization. Finally, for each stakeholder at a time, a certain level of desirability is imposed and the effects are examined from the perspective of each of the other two.

The rest of the paper is organized as follows. Section 2 introduces the drug inventory problem at ICUs and the main stakeholders involved in the process; in Section 3 the relevant literature is recalled; Section 4 is devoted to our research methodology and the mathematical models on which it is based are provided; Section 5 describes the decision process mirrored by the instance generator that is used to build the testbeds. The computational experimentation is described in Section 6, where results are reported and discussed, while conclusions are drawn in Section 7.

2. Problem description

This study concerns antibiotics inventory policies at an ICU. Antibiotics have been chosen as they are crucial drugs in ICUs [6]. Specifically, patients admitted at ICUs are critically ill and while hospitalized most experience infections, often a sepsi, potentially severe, that must be treated by antibiotics. As a whole, antibiotics thus represent a significant fraction of the ICU's drug consumption, although each therapy is tailored on the individual case and must adapt to ever changing conditions also due to antibiotic resistance. Even though they are not necessarily the most expensive drugs present at ICUs, i.e., most antifungal drugs are more costly, they pose a challenge to the inventory manager as their demand is intermittent and irregular, they are not interchangeable, and drug unavailability causes life threatening suspension of therapy. Furthermore, we could access the information regarding the microbiology tests that patients had experienced during their stay as well as the prescribed antibiotic therapy according to the medical staff. This allowed us to replicate the realization of several demand pattern and to build realistic benchmarks, as described in Section 5. All these reasons motivated our choice to elect antibiotics as the drug family in our study. We believe that the approach we propose can be extended to other drugs with similar characteristics. On the other hand, drugs with stationary demand, whose consumption can be approximated by known statistical distributions can be managed by means of inventory policies well discussed in the literature [7] and are not contemplated in this study.

At the ICU in our case study drugs inventory is organized as follows, which is also representative of most ICUs in Italy. Nurses are in charge of drug orders, a very frequent and time-consuming task which keeps them from patients attendance that in ICUs is a 24h task, preferably according to a care continuity policy. Each day, one of the nurses on duty on the morning shift checks the stock levels and potentially issues an order. Since each nurse is personally responsible for a few patients, two at the time in our study, inventory management tasks disrupt continuity of care. The following time constraints hold: lead time is one day but on Saturday, as drugs ordered on Saturday will be available on Monday; urgent orders have few hours lead time but are restricted to cope with stock out emergencies. At present, the ward lacks a formal demand forecasting system and data are spread over heterogeneous information systems that do not share data. Therefore, orders are often based on nurses experience; an educated guess is made, given the current patient population, and overstocking is used to face sudden therapy switches. Indeed, when clinicians suspect the presence of microorganisms, an empirical medical treatment (ET) begins based on broad-spectrum antibiotics and a clinical test request is issued to the microbiology laboratory. If test results confirm infection, a targeted medical treatment starts, consisting of antibiotics targeted to the identified microorganisms [4], but a therapy switch may occur in case of antibiotic resistance. Management monitors drug expenses and may issue a warning in case of budget overrun.

Drugs are stored in a cabinet located in the inpatient room for prompt use and in other shelving and cabinets for storage. The subset of drugs we focus on are located in the inpatient room medicine cabinet, where each drug has its own dedicated storage space and a shared space as well. Some drugs may have specific requirements, such as low temperature, in which case they are stored in a dedicated space in the drug fridge of the ward. On these premises, drugs are partitioned in groups where drugs in the same group share a dedicated storage unit. Knapsack-like constraints describe such capacity restrictions in the mathematical model.

3. Related works

One of the distinguishing features of inventory in hospitals with respect to industrial settings is the existence of a plurality of stakeholders [8]. In addition, business strategies may be different from hospital to hospital and a deep understanding of processes and activities involved in hospital logistics is necessary [9]. However, despite its unique features, only a few studies have addressed inventory problems in hospital logistics with a focus on stakeholders. Among these, [10] investigates collaborative arrangements existing among pharmaceutical manufacturers, wholesalers, and public hospitals in Australian hospital supply chains. However, it reports that pharmacy departments are less prone with respect to departments that manage other materials to outsourcing arrangements, such as vendor managed inventory practices and the like. This suggests that additional stakeholders who are active at the point of use should be involved in the decision making process. Conflicts arise when stakeholders have different goals for efficiency management since they disagree on what constitutes efficiency and how to achieve it [11]. However, only a limited number of empirical studies investigates how conflicting interests and power relationships between stakeholders influence the design of inventory systems in health services. We recall in particular the stakeholder analysis in [12], which discusses the (re)shaping of an inventory system in use at the central pharmacy of a hospital. The literature [13] suggests that, in health care settings, stock levels tend to reflect the levels caregivers consider desirable for patient care and often seem to be more politically and experience-based driven rather than supported by data-driven quantitative methods. As observed in [12], within hospital logistics the outcome of an inventory policy is highly influenced by the expectations and the perceptions different stakeholders have of these outcomes. Indeed, the majority of studies on hospital logistics assume the point of view of the material managers and optimize a single criterion related to cost, using concepts and paradigms inspired by inventory theory in manufacturing. We refer the reader to [1] for a recent review on hospital logistics in general and to [7] for a focus on pharmaceuticals inventory management. This may lead to the situation where policies are proposed that can hardly be put into practice, as they are opposed by the people who should act accordingly [12].

Finally, we provide a brief review of the methodologies available to address multi-objective multi-stakeholder problems and we motivate our choice of using MILP models in the current study. Increasing attention to the economic costs and limited resources compel health care organizations to introduce quantitative methods to attempt to optimize the complex processes arising in hospital logistics where decisions are especially characterized by uncertainties, high stakes, urgency, and disputes [14]. The choice of the most suitable method is by no way an easy task, since it has to take into account the specific issues of the context addressed. In such a setting, Multiple Criteria Decision Aid (MCDA) provides a widespread and useful tool allowing for multiple objectives and for the involvement of different stakeholders. De Montis et al. [15] reviews a wide range of methods among which we mention those based on the use of a single synthesizing criterion such as Multiple-Attribute Value Theory (MAVT) or Multiple-Attribute Utility Theory (MAUT) [16] [17], Analytic Hierarchy Process (AHP) [18], and Evaluation Matrix (Evamix) [19], outranking methods such as Electre III [20], Regime [21] and Novel Approach to Imprecise Assessment and Decision Environments (NAIADE) [22], and finally mixed integer programming-based methods possibly incorporating negotiation processes, such as Multi-Objective Programming (MOP) [23] and Goal Programming (GP) [24],[25].

In [15] a list of quality criteria is proposed to compare MCDA methods, assessing their strengths and weaknesses, and suggesting the proper method to address a specific problem. There, the comparison is tailored for environmental problems in which multiple criteria are usually present, but the proposed analysis is general enough to extend to the health care setting. Quality criteria are grouped in three categories concerning: (*i*) operational components, (*ii*) applicability in the user context, and (*iii*) applicability considering problem structure. Among the operational components, interdependence of criteria plays a crucial role and methods can be grouped accordingly, depending on whether they allow for comparability of criteria or not. In regard to the applicability of the MCDA methods to the user context, the main criteria that should hopefully be considered in the health care setting are project constraints and problem structuring. Specifically in our case, project constraints may refer to the impact of introducing stakeholders' perspective on solution times required by more constrained models with respect to the basic one and to the detriment of solution quality with respect to the solution of the less constrained basic model. On the other hand, the quality criteria a MCDA method should encompass in order to capture the structure of a problem in a health care setting, should include: the possibility to include more than one decision maker (stakeholder participation), transparency in the decision making process, and actor communication to foster the interactions between possibly opposing parties. Finally, among the criteria relevant to the applicability of the selected MCDA method considering problem structure, in our setting, the scalability of the method and its applicability to a different ward/hospital surely deserve consideration.

One of the aims of our study is an improved understanding of the relationships existing among stakeholders. Consequently, we cannot make any a priori assumption regarding the independence vs interdependence nature of the involved stakeholders. Thus, according to the classification proposed in [15], the most suitable method to address our inventory problem would be AHP because it allows for interdependence of perspectives and stakeholder participation. However, AHP requires a complete ranking of the solutions which is unaffordable in our case, because of the very large size of the solution space.

Based on these observations, we addressed the multi-objective multi-stakeholder hospital logistic problem that we have previously introduced in Section 2 using the MILP based method hereafter presented.

4. Methodology

Stakeholder involvement in decision making within the environmental sector has been proliferate, however it has raised some concerns about the quality of the solutions thus obtained. Some ([26] and [27]) argue that stakeholders might be guided by political expediency rather than by solution quality and that they often make inadequate use of scientific information. Surprisingly, the literature gives evidence [28] of a very limited number of contributions reporting on the quality of solutions obtained by stakeholder involvement. However, regardless of the quality of such solutions, there are several motivations to include stakeholders in decision making, among which we mention capacity building and social learning, conflicts resolution and networking [29], [30], [31]. Indeed, stakeholder involvement might be of paramount importance in identifying solutions that result from a negotiation process and are thus sharable by the different actors. This is particularly true in the health care sector where reaching an equilibrium among the parties might be very challenging. Interestingly, the results of a survey work [32] reporting the outcomes of bringing stakeholders to the decision table in a remarkable number of case studies allow us to conclude that, in the majority of the cases, the decisions thus obtained: (*i*) are cost-effective with respect to alternatives imposed by a single decision maker, (*ii*) allow the increase of joint gains among the parties, and (*iii*) give evidence that stakeholders contribute new ideas and make use of objective scientific information and expertise.

Motivated by these results, we started a program at an ICU to foster an integrated and holistic way to define inventory policies. The project consists of the following steps: (*i*) identification of the stakeholders; (*ii*) design of optimization models; and finally, (*iii*) discussion with the stakeholders about solutions obtained.

The first step was crucial and time-consuming: a plurality of potential stakeholders to be involved in the process were interviewed and ultimately three were acknowledged to play a pivotal role, namely the head nurse, the hospital's management, and the clinicians, while others, such as the manager and the staff of the hospital pharmacy, ESTAR, i.e. the public drug supplier agency, and the students of the medical school, were dropped. Indeed, none of them is an active decision maker at this stage of the decision process. While the three active stakeholders agree upon the importance of minimizing the order frequency and reducing the time-consuming management of drug orders, each of them has their own perspective, possibly conflicting with the others. Each of them thus, defines a desirability criterion each solution should be measured against to be considered acceptable. Specifically, nurses in charge of order management, besides minimizing the number of order events, favor homogeneous orders in terms of the number of different drugs involved in each order. This would allow them to allot in advance a constant portion of their shift to accomplish drug orders related tasks and to better plan their activities. Indeed, the time required to store drugs into cabinets and update the system data (so far on paper) mainly depends on the number of different drugs involved in the order rather than on the number of boxes, so they would like to keep this number steady. On the other side, the management aims at minimizing the total quantity of drugs ordered in excess with respect to demand, possibly weighted by coefficients that reflect the importance of drugs, such as their cost or their perishability - in this study we used the total financial cost of drugs supplied. Finally, clinicians are interested in maximizing the daily variety of drugs involved in broad-spectrum therapy so as to reduce the latency of therapy switching due to patient's resistance to the currently prescribed antibiotic.

In step (*ii*) of the project, first a basic model was designed to take into account all the operational constraints at the ward; then, perspective-wise, the basic model was equipped with additional constraints relevant to a specific stakeholder's perspective. The complete models have already been the subject of a conference paper [5], but for readers sake we report them in the following.

4.1. The basic optimization model

Our model reflects a single-echelon, point-of-use, inventory policy with constant reorder quantity and compulsory demand coverage [7]. Let us consider a given planning horizon, a set of drugs, and the parameters listed in Table 1. The basic model, as well as the perspective-aware ones, determine for each drug when the drug is to be ordered and the quantity to be ordered every time an order of that drug is triggered in the planning horizon. The main variables concern stock level of each drug at the end of each day of the planning period, the order quantity of each drug, and the order events schedule. The mathematical notation and variables are summarized in Tables 1 and 2.

$$\min \quad M \sum_{d \in D} \sum_{w \in W} \upsilon_{dw} + \sum_{f \in F} \sum_{d \in D} \sum_{w \in W} c^f s^f_{dw} \tag{1}$$

$$s^f_{01} = l^f - q^f_{01} \qquad \forall f \in F \tag{2}$$

$$s^f_{0w} = s^f_{6,w-1} - q^f_{0w} \qquad \forall f \in F,\ \forall w \geq 2 \tag{3}$$

$$s^f_{dw} = s^f_{d-1,w} - q^f_{dw} + U^f y^f_{d-1,w} \qquad \forall f \in F,\ \forall d \in D, d \neq 0,\ \forall w \in W \tag{4}$$

$$s^f_{dw} \leq U^f \left(C^f + x^f_{dw} \right) \qquad \forall f \in F,\ \forall d \in D,\ \forall w \in W \tag{5}$$

$$x^f_{dw} \leq \overline{C}^f \qquad \forall f \in F,\ \forall d \in D,\ \forall w \in W \tag{6}$$

$$\sum_{f \in F_g} V^f x^f_{dw} \leq \overline{V}_g \qquad \forall g \in G,\ \forall d \in D,\ \forall w \in W \tag{7}$$

$$\sum_{f \in F} c^f s^f_{dw} \leq B_{dw} \qquad \forall d \in D,\ \forall w \in W \tag{8}$$

$$\upsilon_{dw} = 0 \qquad d = 6,\ \forall w \in W \tag{9}$$

$$\Delta^f \leq \Gamma^f \qquad \forall f \in F \tag{10}$$

$$y^f_{dw} \leq \Gamma^f \nu^f_{dw} \qquad \forall f \in F,\ \forall d \in D,\ \forall w \in W \tag{11}$$

$$y^f_{dw} \leq \Delta^f \qquad \forall f \in F,\ \forall d \in D,\ \forall w \in W \tag{12}$$

$$y^f_{dw} \geq \Delta^f - \Gamma^f (1 - \nu^f_{dw}) \qquad \forall f \in F,\ \forall d \in D,\ \forall w \in W \tag{13}$$

$$\nu^f_{dw} \leq \upsilon_{dw} \qquad \forall f \in F,\ \forall d \in D,\ \forall w \in W \tag{14}$$

Table 1: Sets and parameters

F	set of drugs (indexed by f)
G	set of drug groups (indexed by g) - drugs in a group share the same storage unit
$F_g \subseteq F$	set of drugs in group $g \in G$
$D = \{0, \cdots, 6\}$	ordered set of days (indexed by d, 0 corresponds to Sunday, 1 to Monday etc)
W	set of weeks (indexed by w, with $w \geq 1$)
q^f_{dw}	demand of drug f on day d week w (number of doses)
U^f	number of doses in each box of drug f
c^f	cost of each dose of drug f
B_{dw}	maximum monetary value of the stock on day d week w
l^f	doses of drug f on the ward at time 0
C^f	capacity of storage unit devoted to drug f (number of boxes)
$\overline{C}^f$	maximum number of boxes of drug f in shared storage unit
V^f	drug f box volume in number of units in shared storage
$\overline{V}_g$	shared storage capacity of group g (number of storage units)
$\Gamma^f = C^f + \overline{C}^f$	upper bound on the total number of boxes of drug f in stock.

Table 2: Variables

s^f_{dw}	stock level of drug f in number of doses at the end of day d week w
y^f_{dw}	order quantity of drug f in number of boxes on day d week w
ν^f_{dw}	equal to 1 if an order of drug f occurs on day d week w; 0 otherwise
υ_{dw}	equal to 1 if an order occurs on day d week w; 0 otherwise
Δ^f	order quantity of drug f, expressed in number of boxes
x^f_{dw}	number of boxes of drug f in shared storage unit on day d week w.

$$y_{dw}^{f} \in N \qquad \forall f \in F,\ \forall d \in D,\ \forall w \in W \tag{15}$$

$$x_{dw}^{f} \in N \qquad \forall f \in F,\ \forall d \in D,\ \forall w \in W \tag{16}$$

$$\upsilon_{dw} \in \{0,1\} \qquad \forall d \in D,\ \forall w \in W \tag{17}$$

$$\nu_{dw}^{f} \in \{0,1\} \qquad \forall f \in F,\ \forall d \in D,\ \forall w \in W \tag{18}$$

$$s_{dw}^{f} \geq 0 \qquad \forall f \in F,\ \forall d \in D,\ \forall w \in W \tag{19}$$

The objective function of the basic model (1) is a hierarchical one, that first minimizes the number of order events and, at a lower level, hinders overstocking by minimizing the sum of daily stock value.

The constraints describing the operations at ward, at the core of the basic model, can be grouped into: (i) flow conservation constraints on the stock level of drugs; (ii) storage constraints - dedicated and shared storage; (iii) budget constraints; (iv) constraints on regularity of orders; and finally, (v) constraints on variable domain.

Specifically, constraints (2)-(4) are classical flow conservation constraints regulating the stock level for each drug depending on the day considered, i.e. on the first day of the planning horizon (2), on week days (4), and on Sunday (3) when no regular order is received from the hospital pharmacy because of reduced opening hours. They guarantee that for each drug and for each day, the stock level on the ward of that drug at the end of the day is equal to the stock level at the end of the previous day plus the quantity of drug that has possibly arrived on that day minus the consumption of that drug for that day. These constraints mirror the weak lot-sizing formulation [33]. Demand is assumed to be known in the whole programming period, in the sense that the forecast is assumed to be realized, which is a common assumption in the literature [34]. This assumption clearly guarantees that all demand is met by regular orders. Nevertheless, out of stock situations may occur and are resolved by emergency orders. These can be placed anytime but are quite expensive. While we can disregard them by now, we will consider them in a future study, where the present model will be used as a black box in a rolling horizon framework.

Constraints (5)-(7) impose that the quantity of drugs daily stored in dedicated as well as in shared space does not exceed capacity. Capacity is expressed in number of boxes or in volume according to the type of storage considered.

Constraint (8) guarantees that the cost of drugs stocked at the end of a day does not exceed a given amount which we informally refer to as the *daily budget*: it is meant to prevent overstocking due to orders consolidation at the beginning of the period.

Constraints (9)-(14) guarantee that for each drug the same lot size is used every time that drug is ordered. In addition, they manage the order event variables ensuring that the variable related to an order event on a given day is equal to one if at least one drug is ordered on that day.

Finally, constraints (15)-(19) define variable domain.

So called *stakeholder perspective-aware models* are obtained by enriching the basic model with a set of constraints characterizing the degree of satisfaction of each stakeholder, Nurses (see 4.2.1), Management (see 4.2.2), and Clinicians (see 4.2.3). In so doing, we refer to a generic set of instances I, not to be confused with the training or the test instances introduced later on, and to the mean level of flexibility.

4.2. Stakeholder aware models

4.2.1. Nurse perspective

To take into account nurses' perspective, we define, for each instance $i \in I$:

$$\upsilon_{\max}^{(i)} = \max_{d\in D, w\in W} \sum_{f\in F} \nu_{dw}^{f(i)} \quad \text{as well as} \quad \upsilon_{\min}^{(i)} = \min_{\substack{d\in D, w\in W,\\ \text{s.t. } \upsilon_{dw}^{(i)}=1}} \sum_{f\in F} \nu_{dw}^{f(i)}$$

where $\nu_{dw}^{f(i)}$ and $\upsilon_{dw}^{(i)}$ refer to the value of variables ν_{dw}^{f} and υ_{dw} in the optimal solution of instance $i \in I$, so that $\upsilon_{\max}^{(i)}$ and $\upsilon_{\min}^{(i)}$ denote respectively the maximum and the minimum number of drugs present in a single order over the planning period when model is run on instance i. Since nurses consider orders as homogeneous when the difference between $\upsilon_{\max}^{(i)}$ and $\upsilon_{\min}^{(i)}$ is low, i.e., the number of different drugs is almost steady in all the orders, the average difference over the set of instances I is computed as

$$\overline{\upsilon} = \left\lceil \sum_{i \in I} (\upsilon_{\max}^{(i)} - \upsilon_{\min}^{(i)})/|I| \right\rceil$$

The model enriched with nurses perspective is then:

$$\min \quad M \sum_{d \in D} \sum_{w \in W} \upsilon_{dw} + \sum_{f \in F} \sum_{d \in D} \sum_{w \in W} c^f s_{dw}^f$$

s.t.

Constraints (2) – (19)

$$\sum_{f \in F} \nu_{dw}^f \leq \upsilon_{\max} \qquad \forall d \in D,\ \forall w \in W$$

$$\upsilon_{\min} \leq \sum_{f \in F} \nu_{dw}^f + |F|(1 - \upsilon_{dw}) \qquad \forall d \in D,\ \forall w \in W$$

$$\upsilon_{\max} - \upsilon_{\min} \leq \overline{\upsilon}$$

where $\overline{\upsilon}$ is the parameter denoting the mean level of flexibility.

4.2.2. Hospital Management perspective

The management is in charge of the financial sustainability of the hospital and would like to spend on drugs no more than the value of what will be consumed in the whole period. Given $b^f = \lceil \sum_{d \in D} \sum_{w \in W} q_{dw}^f / U^f \rceil$ as a lower bound on drug f boxes required to satisfy demand and w^f as the weight associated with drug f (we will use the cost in the computational experiments), the average weighted number of boxes ordered in excess with respect to the demand over all instances in I is:

$$\overline{\gamma} = \frac{1}{|I|} \sum_{i \in I} \sum_{f \in F} w_f \big(\sum_{d \in D} \sum_{w \in W} y_{dw}^{f(i)} - b^f \big)$$

The model enriched with management perspective is then:

$$\min \quad M \sum_{d \in D} \sum_{w \in W} \upsilon_{dw} + \sum_{f \in F} \sum_{d \in D} \sum_{w \in W} c^f s^f_{dw}$$

s.t.

Constraints $(2) - (19)$

$$\sum_{f \in F} w_f \big(\sum_{d \in D} \sum_{w \in W} y^f_{dw} - b^f \big) \leq \overline{\gamma}$$

where $\overline{\gamma}$ is the parameter denoting the mean level of flexibility. Note that both management's criterion and the second term of the objective function are concerned with stock levels, but they capture different aspects of the inventory policy. Management's utility depends on the monetary value of the stock on the last day of the planning horizon, while the second component of the objective function of the basic model addresses the sum over the whole period of the value in stock at the end of each day. Therefore, the first is concerned with *what has been ordered* over the entire period, while the second also considers *when orders have been placed*, thus accounting for *carrying costs*. Indeed, since the primary objective is the minimization of order events, tackling orders frequency, drugs tend to be ordered well ahead of consumption to allow order consolidation. Therefore, an upper bound to daily stock value is required, i.e., the daily budget constraint, to avoid excessive order consolidation - think of a single order placed on the first day and covering the demand of the whole planning period: such an event, if allowed, provides the possibility of having a zero drug supply available for the final day of test period, thus maximizing the management utility but also increasing carrying costs. A just-in-time order policy, which closes the gap between ordering time and consumption time as much as possible, would keep carrying costs to their minimum and push the management utility towards the maximum, since it would reduce the amount of drugs in stock on the last day of the period. At the same time, though, it would increase order frequency, thus deteriorating our main objective function. Moreover, note that order regularity (regarding the order quantity of each drug) further constrains the amount in stock on the last day when orders are consolidated. In summary, these criteria are all strongly related but also mutually conflicting. Therefore some form of compromise must be sought after.

4.2.3. Clinician perspective

Denote $F^e \subseteq F$ as the set of equivalent drugs in broad-spectrum therapy; n^f as drug f daily dosage; $T = \{T^j, T^j \subseteq F^e\}$ as a set of therapies where each T^j is a subset of drugs in F^e; K as the daily target number of available therapies. We compute how many days in the planning period, averaged over I, stock exhibits the desired variety in terms of equivalent therapies, namely $\overline{\delta}$.

The model enriched with clinicians perspective is then:

$$\min \quad M \sum_{d \in D} \sum_{w \in W} \upsilon_{dw} + \sum_{f \in F} \sum_{d \in D} \sum_{w \in W} c^f s^f_{dw}$$

s.t.

Constraints $(2) - (19)$

$$\alpha^f_{dw} \leq s^f_{dw}/n^f \qquad \forall f \in F^e,\ \forall d \in D,\ \forall w \in W$$

$$\beta^{T^j}_{dw} = L(\alpha^f_{dw} \text{ with } f \in T^j) \qquad \forall T^j \subseteq T,\ \forall d \in D,\ \forall w \in W$$

$$\lambda_{dw} \leq \sum_{j: T^j \subseteq T} \beta^{T^j}_{dw}/K \qquad \forall d \in D,\ \forall w \in W$$

$$\sum_{d \in D} \sum_{w \in W} \lambda_{dw} \geq \overline{\delta}$$

where α^f_{dw} is a binary variable equal to one when a surplus of at least n^f doses of drug $f \in F^e$ is present on day d week w and zero otherwise; $\beta^{T^j}_{dw}$ is a binary variable equal to one when therapy T^j is available on day d week w while λ_{dw} is a binary variable equal to one when at least K therapies in T are available in surplus on day d week w. Variables $\beta^{T^j}_{dw}$ are the results of a logic function ($\vee$ and $\wedge$ operators) of the drugs involved in therapy T^j that can be linearized in standard way.

4.3. Assessing stakeholder interactions

In order to experimentally evaluate the trade-offs arising when model (1)-(19) is enriched with stakeholder perspectives, we assume that a set I of instances is available, where I is a meaningful sample of representative drug demand realizations in the planning horizon. In this study we consider a four week period, i.e. a time empirically set as the shortest period long enough to capture the variability of the patient LoS as well as repeated occurrences of similar patients. Then, we propose a two-phase method where the first phase is a learning phase, while the other is a validation phase. Specifically, set I is arranged in two subsets, namely a training set I_t to learn and a validation set I_v to validate the model. In the learning phase, we solve the basic model (1)-(19) for each instance in I_t and record the three values representing the perspectives of the three stakeholders. The average value of each criterion over I_t can be computed. Then, perspective by perspective, model (1)-(19) is tightened by a constraint which imposes that the value of the considered criterion does not deviate *too much* from the average value of the same criterion computed over the set I_t. Specifically, we can manage this latter constraint (and quantify *too much*) with three increasing levels of flexibility: low, medium, high, i.e., when flexibility is low, the constraint is tighter. The aim of the training phase is thus to evaluate the impact of taking into account stakeholder perspectives on solution quality. The validation phase of the method aims to evaluate the robustness of average values computed on set I_t when used to solve instances of set I_v. Accordingly, for each instance in I_v, perspective by perspective, the three perspective-aware models are solved using as threshold the value computed on set I_t properly adjusted by means of a flexibility level. Section 5 provides details on the instance generator that was developed to build set I.

Finally, in the last phase of the project, the solutions have been delivered to the ICU Director thus providing him quantitative results allowing a negotiation process to commence with all the stakeholders. The ICU Director has the responsibility of deciding whether advocating the role of stakeholders is sustainable or not in terms of detriment of solution quality with respect to the solution obtained by means of the basic model.

5. Realistic Instances Generator

Data collection has been a major concern in this study. We have been observing the ward for one month and could collect daily prescriptions only for that period since prescriptions were recorded on paper only. In addition, we could access patients records over the past 5 years, but data were not fully reliable as information was often incomplete. Moreover, patients information were spread among several information systems that did not communicate and the same patient was associated to different identifiers in different systems. During the project, the ward had been subject to a major reorganization which has modified the number of beds, thus affecting demand levels. Therefore, historical demand, as is, was not sufficient to support the experiments. Furthermore, particularly at ICUs, strong correlations among different drugs involved in the same therapy can be observed, so we discarded the idea of building an empirical distribution for each drug on its own, based on its own historical demand. The only constant in the observation period and beyond is the procedure that rules decision making when prescribing antibiotics (the drugs this study is concerned with). We discussed such decision making process with clinicians to devise the possible outcomes of each step where a decision is made, and roughly estimated their empirical distributions, which has been refined by double checking with historical patient records. This process lies at the heart of the instance generator we set up to provide a reliable representation of how demand is deployed over time at the ICU ward. This relies on the realistic representation of the patients flow process (from patient admission to discharge, through the different stages of health conditions evolution) in order to yield the drug consumption for each day of the planning horizon. In our experiments such period is four weeks, long enough to cover the whole hospital stay of most of the patients. With the support of the clinical staff, the daily budget has been estimated as a percentage of the average monetary value of the drugs consumed in a day. In the following, we provide further insight into the construction of the generator.

First, an abstract representation of the ward as a system is needed, together with historical data collection to estimate the empirical probability distributions of the main events ruling the system.

ICU patients are characterized by critical conditions and high mortality rate, often correlated to infections. According to guidelines, when clinicians suspect an infection is present, a microbiology laboratory test is issued and an ET is started [4] until results are returned from the lab. ET is broad spectrum, covering the most likely microorganisms. The ongoing treatment is reviewed in case of clinical deterioration and drug resistance. This process yields a highly irregular demand due to laboratory response lead time and to frequent therapy switchings for the same patient.

Real data have been collected covering a 5 year period regarding patients admission and discharge at the ward, their clinical severity and microbiology laboratories data, i.e. for each patient for whom a request has been issued, the drug which is most likely to stop infection. We identified the main critical events whose outcome determines the ward state transition and therefore drug demand. The ward state is described, in turn, by the state of the hospitalized patient, if any, at each of its 8 beds. The empirical probabilities of such event outcomes have been computed based on the historical data. Main events include daily admission at ward and patient clinical condition severity at admission. At patient level, drug demand day by day is dictated by clinical evaluation and evolution of patient condition from admission to either death or discharge. This is modeled as a path along a flowchart with stochastic decision steps representing the outcome of a stochastic event, such as, for example, the LoS in case of no infection or, in case of infection, the antibiogram laboratory response, the development of antibiotic resistance, the clinician choice regarding the broad spectrum therapy, and the response of the patient to the therapy. The flowchart modeling the evolution of a typical ICU patient is sketched in Figure 1. Each event with multiple outcomes is depicted as a diamond. For example, at admission a patient is classified according to the severity of its conditions: supported by the ICU clinicians we partitioned patients into 6 classes with homogeneous characteristics. The specific patient class is the outcome of the diamond block labeled *Patient type*. After LoS days, the patient may leave the ward towards a subintensive care unit or a regular hospital bed or because of decease. Likewise, a patient without infection typically spends on the ward a period from a minimum of one day to a maximum LoS depending on the patient class, i.e. ranging from 4 to 9 days, while any period out of this interval is considered an outlier. As far as we are concerned, the only relevant information in this branch of the flow chart is the patient LoS, not the causes of dismissal or death. Those not affected by an infection correspond to an occupied bed with no impact on the demand for antibiotics. Again, all such parameters are based on collected patients records and have been validated with ICU clinicians.

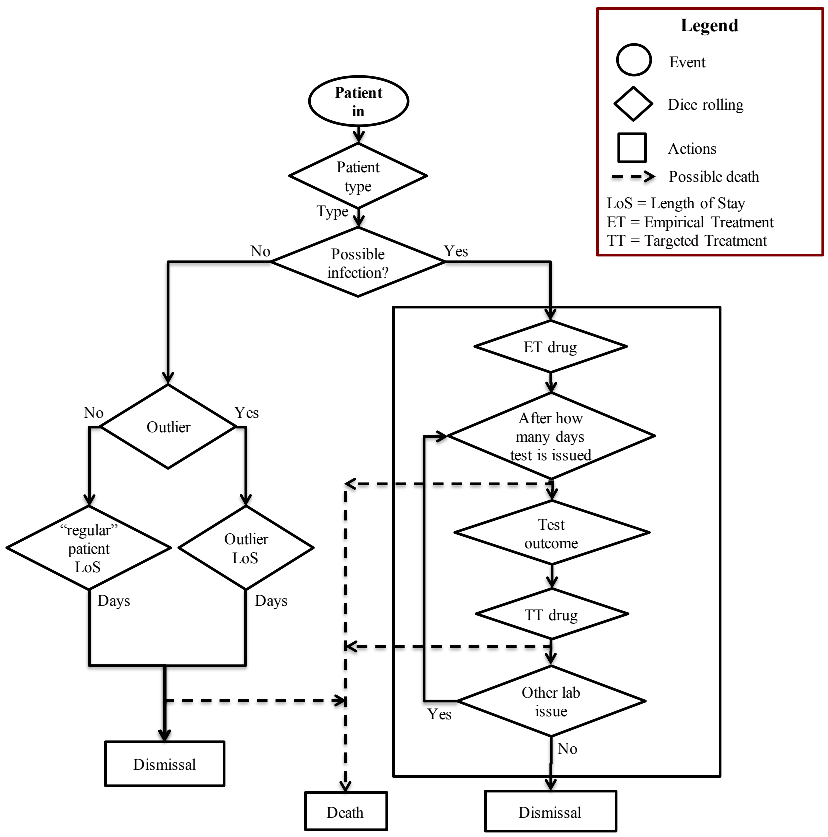

Figure 1: Patient probability driven flowchart.

The individual patient daily drug prescriptions sum up to yield the daily ward drug demand: the generator carries on the process on a monthly period and returns one instance. To provide a realistic representation of patient flow, we start the simulation a week before day one of the planning period with an empty ward which becomes populated as time goes bye, so that on day one the number of occupied beds is close to the average.

6. Computational results

The computational experimentation aims to investigate the relations among stakeholders. Models were coded in Python and solved by the IBM ILOG CPLEX 12.7 solver on a MacBook Pro equipped with Intel Core i5 cpu. A total of 1000 runs were executed obtained by combining 100 demand instances with 10 versions of the model, i.e., the basic model and the 9 perspective-aware versions given by imposing the three different levels of satisfaction with the three stakeholders. The running times of the perspective-aware models have been marginally affected with respect to the basic model ones and the average time is 35 seconds. Realistic data are available upon request, while historical data are sensitive information and cannot be distributed.

6.1. Setting the thresholds of satisfaction

First, 100 instances have been generated as described in Section 5 to yield the above mentioned set I. Then, the training set I_t was built by picking at random 50 instances chosen from I. The satisfaction levels for each stakeholder have been computed by solving the basic model on I_t, yielding a set of 50 values for each stakeholder, say N_t for the nurses, C_t for clinicians and D_t for the management. The thresholds have been computed as in [5], namely, the average μ has been considered as the medium value of N_t, C_t and D_t, respectively, while the other two values have been set as $\mu \pm \delta$ where δ is the standard deviation of N_t, C_t and D_t. Table 3 reports the values used in our experiments.

For consistency, the results are presented by coding the three levels as *low*, *medium*, and *high flexibility* (denoted as L, M, H, respectively, in all figures)

Table 3: Stakeholders thresholds for nurses, clinicians, and management.

Flexibility	Nurses # drugs per order max-min	Clinicians # days with ≥ 3 ET drugs in stock	Management € spent - € demand
Low	3	28	35
Medium	5	24	285
High	7	20	620

with respect to the satisfaction constraint, meaning that, for example, low flexibility enforces high satisfaction level. Intuitively, this mirrors the impact on the feasible region which becomes more constrained (less flexible) when satisfaction is enforced to be high.

We assess the impact of constraining the satisfaction level of one stakeholder on the other two. Therefore, we build one perspective-aware model for each stakeholder at a time, ensuring its aforementioned satisfaction levels by setting the associated threshold on the constraints that represent the stakeholder satisfaction in the MILP model. Such perspective-aware models have been solved for the training set I_t as well as on the validation set $I_v = I \setminus I_t$ and the levels of satisfaction of the other stakeholders have been recorded as the percentage gap with respect to the unconstrained model. In order to provide a reference point for the following discussion of computational results, we solved 9 models, each of which constraints the satisfaction level of one stakeholder at one of the three above mentioned thresholds. Figure 2 depicts, for each such case, the distribution over the training set of the percentual gap of the stakeholder satisfaction variation with respect to the basic model.

6.2. Stakeholders interactions

As mentioned, taking each stakeholder one at a time, we constrained its satisfaction and computed the impact on a second stakeholder satisfaction by solving the perspective-aware model. In particular, the impact is quantified as the percentage gap with respect to the satisfaction level the second stakeholder

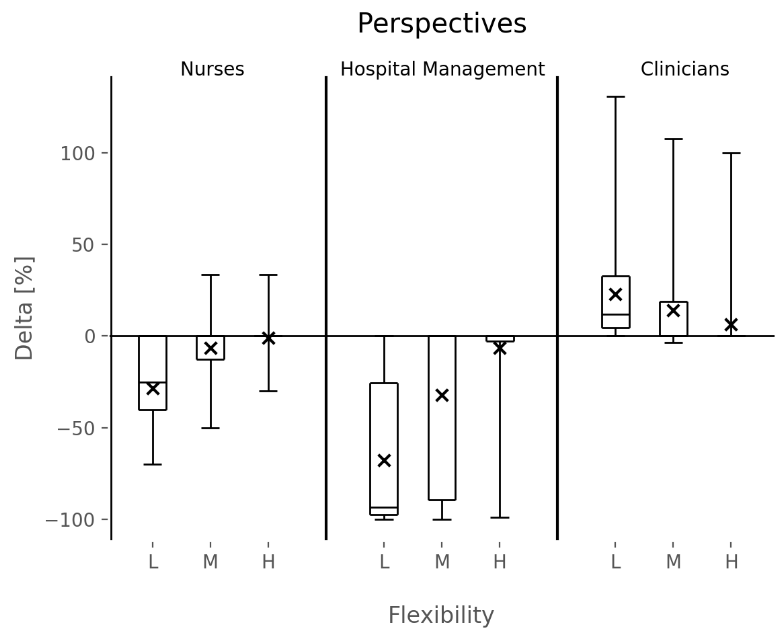

Figure 2: Stakeholders satisfaction degrees with respect to the basic model (in %), evaluated on the training set.

scored in the unconstrained model. Results are depicted as boxplots, showing on the left the values on I_t and on the right those on I_v, for each of the three flexibility levels Low, Medium, and High. By comparing the boxplots on the two sides we can assess the general validity of thresholds, which is the highest the more the results on the validation set (right part) look like those on the training set (left part) in each figure (from 3 onwards).

The boxplots in Figures 3-6 refer to the case when nurses satisfaction is constrained, i.e., the number of different drugs in the orders can vary at most by 3, 5 or 7, respectively. The number of order events is not affected (see Figure 3). A possible explanation is that a steady number of drugs on different orders may often be accomplished by changing the order date with respect to another schedule, usually anticipating them, which also explains stock value marginal increase (see Figure 4). In both Figures (3-4), the boxplots on the right part marginally differ from those on the left, confirming that thresholds coming from I_t hold also for I_v. Concerning the impact on the management (Figure 5), as just mentioned order regularity could be attained by rescheduling certain orders and potentially distributing them with a different schedule in the time period, potentially resulting in additional extra orders for some drugs as well as in fewer extra orders for others, because of the constant lot size constraints (9-14). Therefore, the impact on the management may be mixed. However, each whisker in the boxplots of Figure 5, when present, on the top or on the bottom, is due to one instance. Moreover, the instances in the box are affected by the satisfaction constraint by at most 4%. Therefore, imposing nurse satisfaction is likely to be easily tolerated by the management. Regarding the impact on clinicians (Figure 6), very few instances show a negative impact of high nurses satisfaction (low flexibility) and its amount is limited and restricted to very few instances. As a general conclusion, these results suggest that a certain degree of regularity in the orders composition can be enforced without disrupting the other stakeholders nor affecting the main objectives. This is not straightforward and could not have been anticipated; moreover, it indirectly benefits the patients as nurses potentially have more time to devote to patients interaction.

Now let us look at the consequences of constraining the management satisfaction. According to such preferences, orders should closely follow the demand pattern and since demand is highly variable it comes as no surprise that the number of order events increases for low and medium flexibility, i.e., high satisfaction (see Figure 7). On the other hand, when orders closely follow demand and adapt to it, stock value along the period can be reduced, as shown in Figure 8. We expect an increased variability in orders, and indeed results (see Figure 9) show that nurse satisfaction may be marginally affected. Since orders stick more closely to demand, additional drugs availability for a therapy switch decreases, which affects clinicians (see Figure 10). In general, results suggest that strictly embracing the management perspective may harm the other stakeholders, and thus it is not advisable.

Finally, we address clinicians satisfaction. Recall that taking clinicians' side leads to increasing overstocking of those drugs involved in the ET. Extra stock allows more flexibility in placing the orders (an order can not be postponed if stock level is below the incoming demand, while it can be issued anytime as long as stock level is above). Indeed, the number of order events is unaffected (see Figure 11) while we observe a marginal increase in stock value in Figure 12. The order regularity (nurses perspective, Figure 13) is episodically affected (only few instances) and often in a positive manner. Regarding the impact on the management, one would expect that overstocking implies additional extra orders, since drugs that are ordered to edge against a potential demand change often do not get actually consumed. This occurs for instances in I_t, while the effect is milder on I_v and it is limited to few instances (Figure 14).

As a whole, we can conclude that thresholds proved rather robust and a low level of satisfaction can be enforced for each single stakeholder without major disruption. The results suggest that strong relations exist among the degree of satisfaction of the three different stakeholders: indeed, a high satisfaction level for one stakeholder potentially entails benefits as well as detriment to the others, depending on the specific instance. Specifically, nurses' high satisfaction does not conflict with the other stakeholders, therefore their perspective can be prioritized without impacting the other two. This policy is worth considering, on patients behalf, as nurses would gain extra time to devote to patients care. To further assess the intuition that the three stakeholders cannot be fully satisfied at the same time, we solved the 100 instances with respect to the additional configuration where each stakeholder‘s satisfaction is tied to its highest level (low flexibility case). The results confirmed the intuition: 52 over 100 instances did not admit any feasible solution, while feasibility was achieved on the remaining instances to the detriment of solution quality, i.e. the number of order events increased on average by 31.9% with a peak of 175%. This gives evidence that stakeholder preferences should be prioritized. Indeed, an ongoing study [35] is devoted to select the principal stakeholder by means of well assessed quantitative methodologies.

We believe that the above findings can help decision makers in the related negotiation process. During the third phase of the project these conclusions will be delivered to the ICU Director, presented to the stakeholders, and discussed with them under his supervision. Should a strategy come up as a result of the discussion, our models can be customized to take that strategy into account and measure the potential outcomes, in terms of order events, stock value, and satisfaction, on a what-if basis, thus providing a versatile decision support tool to the decision maker.

7. Conclusions and work in progress

The aim of this research was to experimentally investigate the potential interdependence relationships between the different stakeholders who are involved, with different roles, in the drug inventory management at an ICU ward, namely nurses, clinicians and management. This study relies upon an MILP model recently developed which optimally schedules orders events (when and how much to order), taking into account real (storage capacity) and realistic (budget related) constraints. We evaluated the effects of imposing different levels of satisfaction of one stakeholder on the satisfaction levels of the others. A realistic instance generator was implemented to yield a training set of instances on which thresholds of satisfaction are computed, as well as a test set of instances on which these levels have been imposed before solving the model. Results indicate a few lessons that can be learned, some more intuitive than others. The main result is that reasonable satisfaction levels can be set without major impairment to other stakeholders, especially in case of nurses satisfaction who are the most concerned with attending the patients. Such practices should be encouraged whenever they go in favor of the patient who, while not being an active stakeholder, is the ultimate subject of the caring process.

The results obtained are thus encouraging and allow us to return interesting findings to the stakeholders. Finally, we observe that the approach proposed seems to be scalable provided that the lot-sizing based model, i.e., the basic model without orders regularity constraints, is tightened as described. In addition, ICU wards are usually characterized by a limited number of beds, thus the computational efficiency of the approach seems not to be a critical issue. At the same time, applying this approach to other ICU settings would be interesting and valuable.

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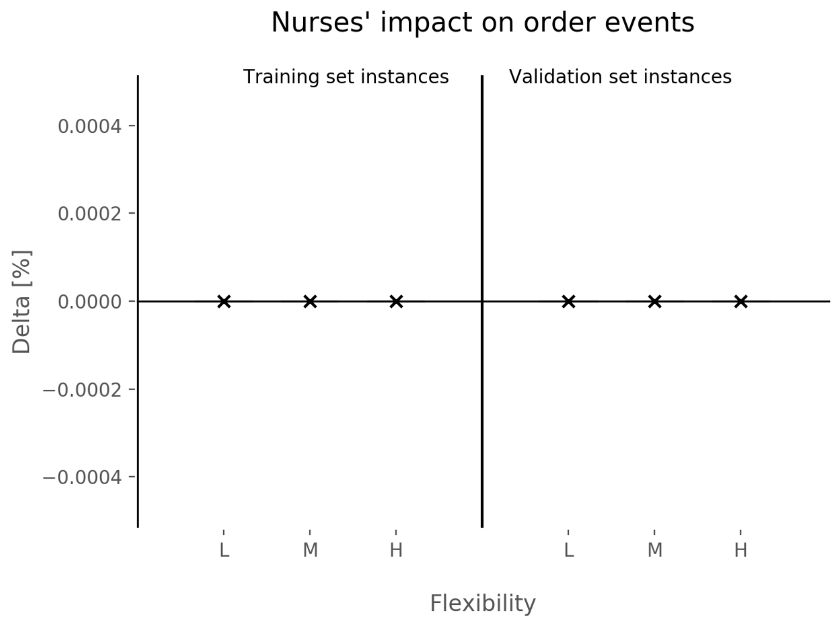

Figure 3: Effects of the satisfaction degree of nurses on the number of order events, with respect to the basic model (in %).

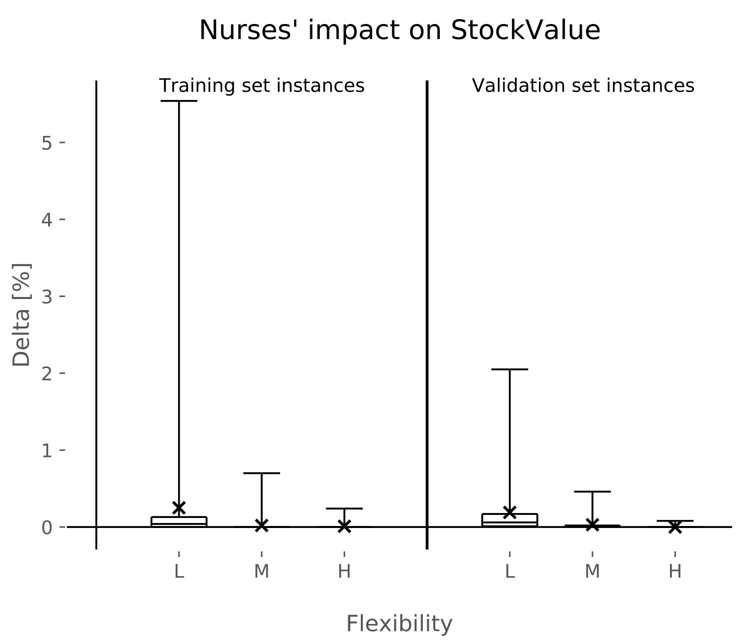

Figure 4: Effects of the satisfaction degree of nurses on stock value, with respect to the basic model (in %).

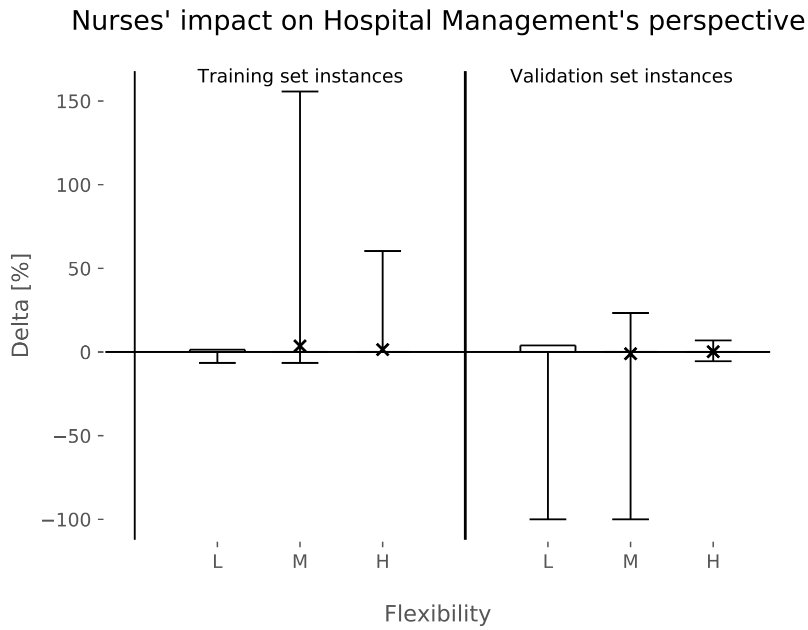

Figure 5: Management satisfaction when nurses satisfaction is constrained, with respect to the basic model (in %).

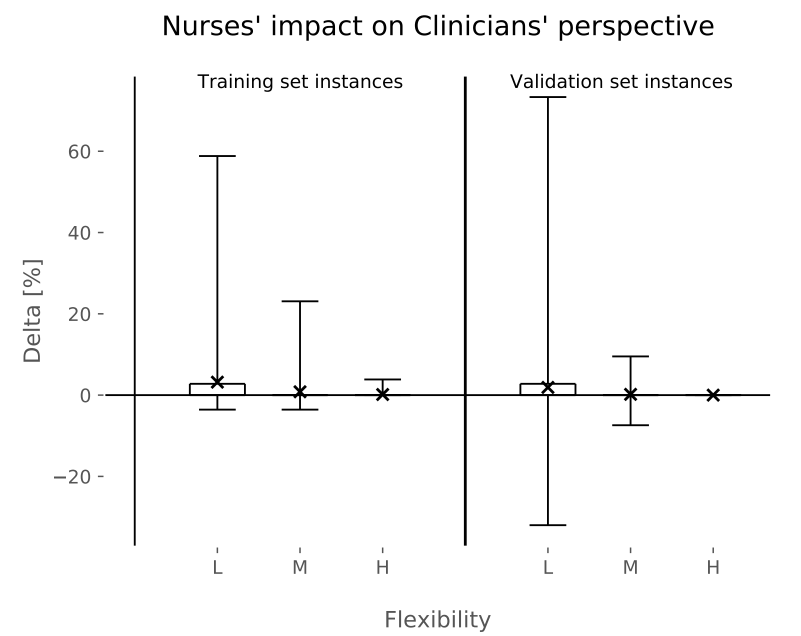

Figure 6: Clinicians satisfaction when nurses satisfaction is constrained, with respect to the basic model (in %).

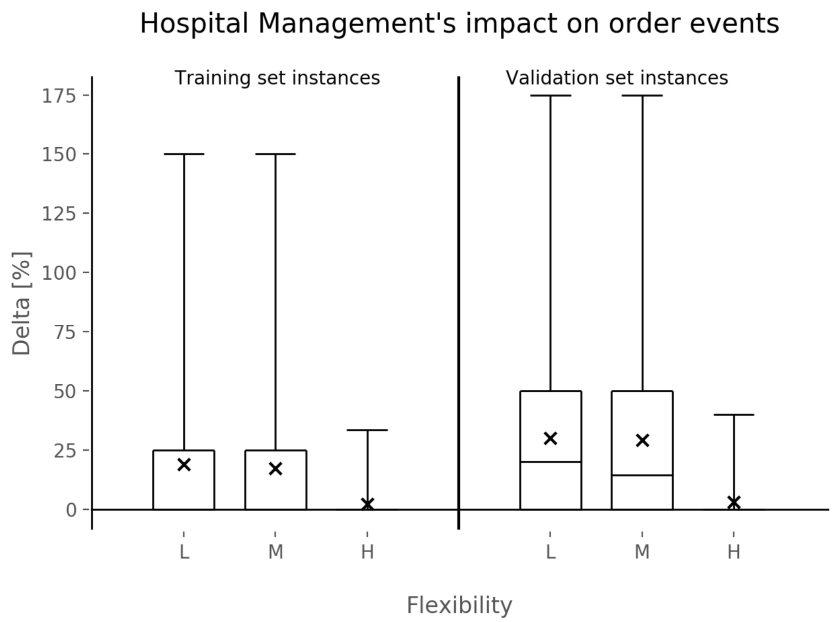

Figure 7: Effects of the satisfaction degree of management on the number of order events, with respect to the basic model (in %).

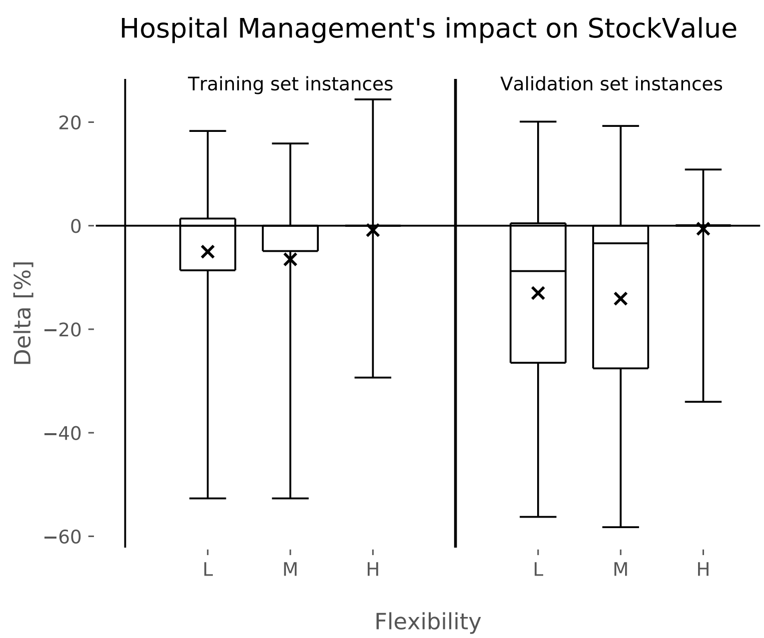

Figure 8: Effects of the satisfaction degree of management on stock value, with respect to the basic model (in %).

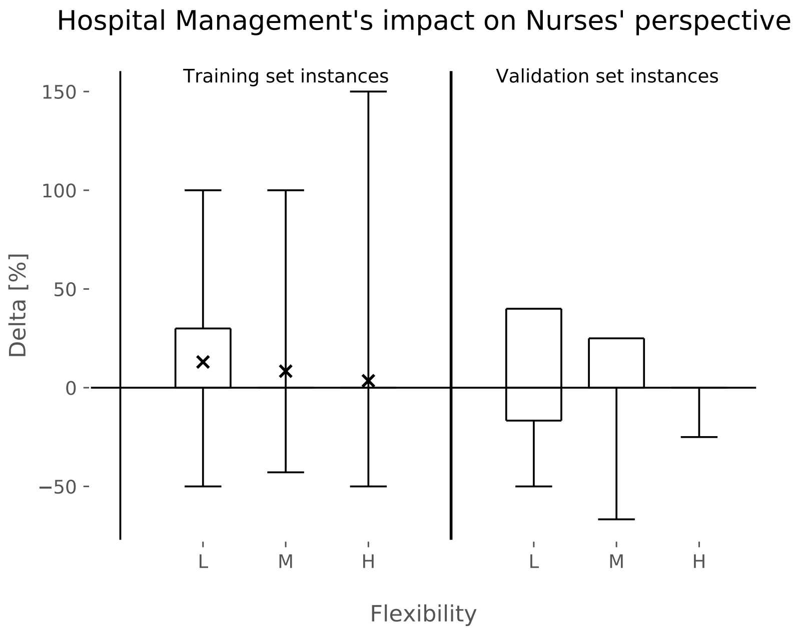

Figure 9: Nurses satisfaction when management satisfaction is constrained, with respect to the basic model (in %).

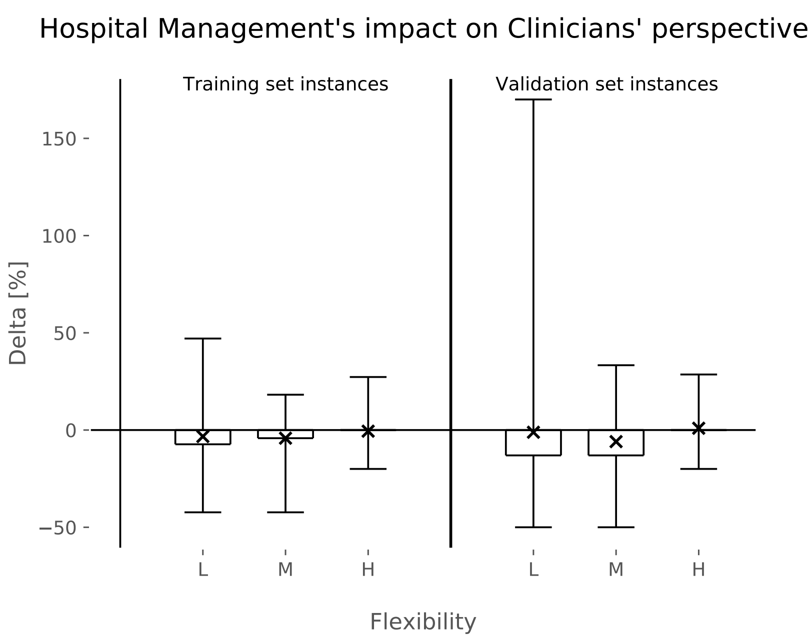

Figure 10: Clinicians satisfaction when management satisfaction is constrained, with respect to the basic model (in %).

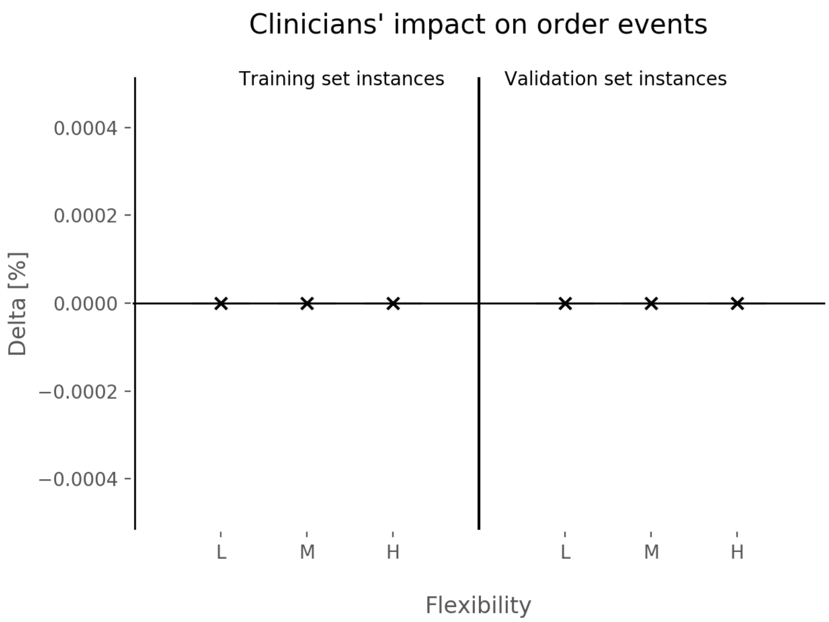

Figure 11: Effects of the satisfaction degree of clinicians on the number of order events, with respect to the basic model (in %).

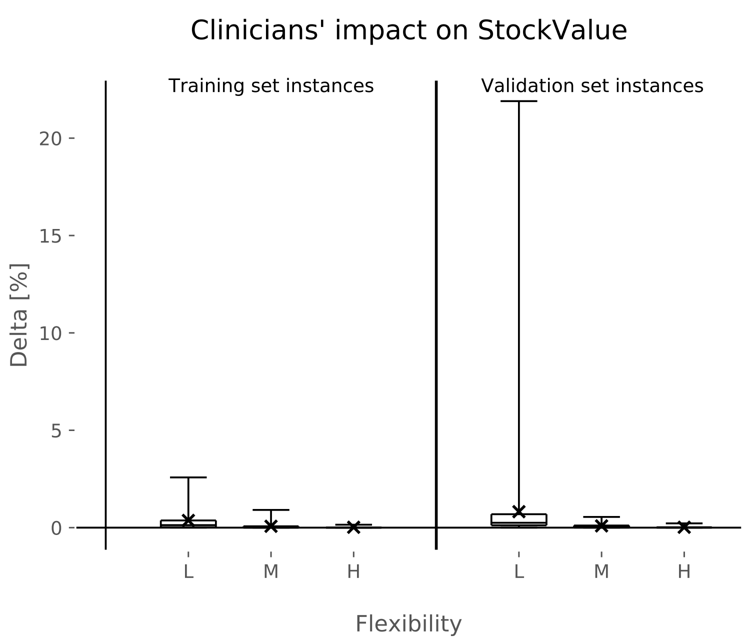

Figure 12: Effects of the satisfaction degree of clinicians on stock value, with respect to the basic model (in %).

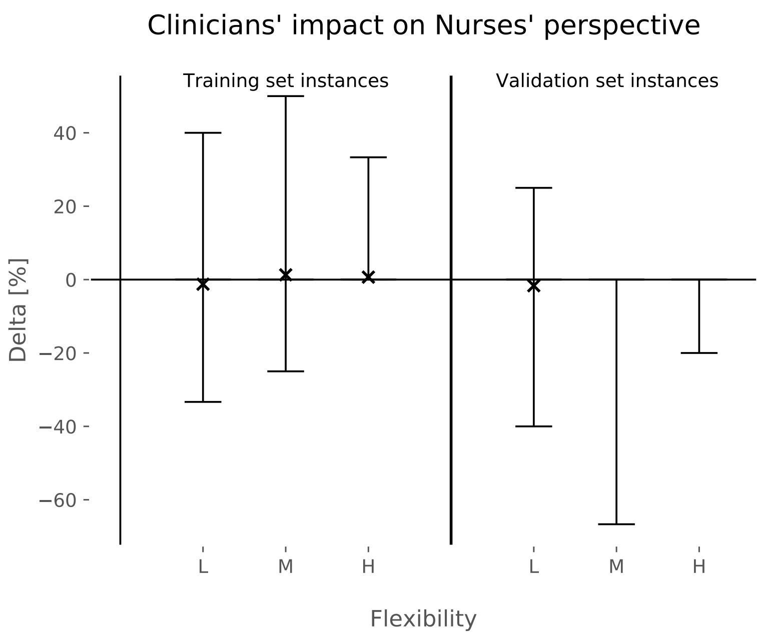

Figure 13: Nurses satisfaction when clinicians satisfaction degree is constrained, with respect to the basic model (in %).

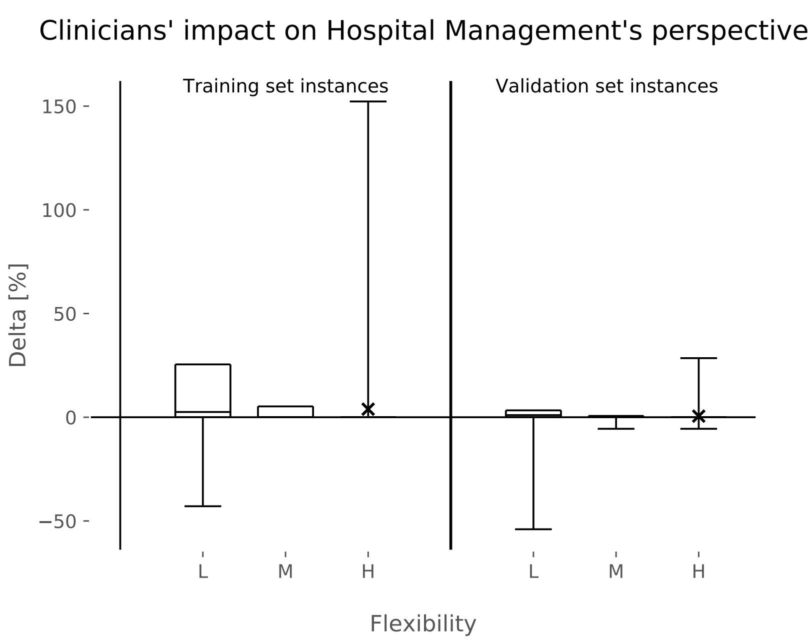

Figure 14: Management satisfaction when clinicians satisfaction degree is constrained, with respect to the basic model (in %).