

# Medicines Shortages and the Perception of Healthcare Professionals working in hospitals: an Italian Case Study

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Conceptualization, A.Z., and U.M.M.; methodology, U.M.M.; investigation, A.Z. and M.P.; data curation, A.Z., M.P.; writing—original draft preparation, A.Z., U.M.M.; writing—review and editing, U.M.M., C.D., F.C.; visualization, M.P., C.D., S.V.; supervision, C.D. and F.C. All authors have read and agreed to the published version of the manuscript.

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## Abstract

Background. The medicines' shortage has arisen as a global crisis, which jeopardizes the continuity of care and overloads for pharmacists and healthcare professionals. Purpose. The paper aims 1) to determine the therapeutic classes mostly affected by shortages in pre-COVID scenario and investigate their impact; 2) to collect the perception of physicians and nurses on shortages to assess the effect on clinical practice and to improve interprofessional collaboration. Methods. A 16-question survey developed by hospital pharmacists was administered to physicians and nurses at Presidio Ospedaliero Luigi Sacco in Milan (Italy). Discussion. A total of 148 medicinal products were reported as unavailable by 58 interviewees. Since in 66% of cases therapeutic alternatives are available, healthcare professionals did not perceive them as so critical since effect on patients can be mitigate by effective interprofessional collaboration. Conclusion. Risk assessment and management of shortages should be based on a bottom-up approach that takes in consideration the ward operability and the perception of healthcare professionals.

## Keywords

Shortages; hospital pharmacy; therapeutic switch; perception; physicians, nurse.

## 1 Introduction

The shortage of medicines has increased worldwide, reducing the ability of national healthcare systems to find solutions to ensure patients' access to pharmacological therapies.<sup>1-3</sup> The shortages can be traced to supply-related causes (e.g., manufacturing issues, regulatory issues, distribution) and demand-related ones (e.g., parallel trade, price and reimbursement policies, tendering).<sup>4</sup> Moreover, extraordinary natural or geopolitical events [e.g., Coronavirus (COVID-19) pandemic, Brexit] have shown to have a strong impact on the productive capacity of the pharmaceutical companies and on the patients' access to therapies. The fragmentation of the National regulatory frameworks may be also a cause of medicine shortage due to market distortion caused by different reimbursement and price policies price at the EU level.<sup>5-8</sup> In fact, the heterogenicity of the National legislation in the different healthcare systems around world limit the develop of an emergency plan to solve the shortage issue, often with a potential negative impact on the daily activity of health care in different countries.<sup>4</sup>

Shortages impacts significantly on the continuity of care and patients' access to therapies and generate additional management loads for all healthcare professionals (HCP; e.g., physicians, pharmacists, nurses).<sup>7,9,10</sup> In this context, the role of pharmacists in both hospital and community pharmacies is frequently crucial in finding feasible therapeutic alternatives to administer to patients.<sup>11,12</sup> As reported by the Royal Dutch Pharmacists Association Farmanco® platform, the continuity of care for patients has been ensured in about 90% of the medicine shortages by the medicine substitution with therapeutic alternatives.<sup>12</sup> However, if therapeutic alternatives are not available on the market, treatment discontinuation, or onset of adverse effects due to the reduced medication adherence, can occur.<sup>7</sup> In this context, both effective and quick communications among the HCP and the application of risk assessment/management strategies have been crucial for effective reduction of the shortage

impacts on public health. To support HCP in their prevention and mitigation activities, EU regulatory authorities are intensifying their efforts in alleviating the root causes of shortages and improving communication through the pharmaceutical distribution chain.<sup>4,13</sup> However, there is an urgent need for improving the strategies to assess the impact of the drug shortages on the operability of healthcare structures and to speed up the communication through HCP working in the same healthcare setting.<sup>7,9,10, 14-17</sup> However, the HCP preparedness is not only influenced by the existence of specific procedures, but also by how critical HCP perceives the problem during the working day. Indeed, physicians and nurses working in the wards may not be aware of many medicines' shortages due to the tireless activities of the hospital pharmacists for mitigating them, or they can be aware only when it is too late to avoid therapy discontinuation.<sup>11</sup>

The paper aims to investigate the impact of shortages on the operability of the hospital wards and how physicians and nurses perceive the issue. Overall, the works also intend to promote the interprofessional collaboration providing useful data for establishing rational strategies in preventing/management of shortages in hospital settings. In this light, a survey was designed to collect data on the therapeutic classes perceived as the most affected by shortages over 2019, the frequency and the duration of the shortages in specific wards, and the strategies adopted to maintain the continuity of care. The Presidio Ospedaliero Luigi Sacco (Hospital) in Milan (Italy) was used as a model. It is a medium hospital structure in the context of the Lombardy healthcare system (about 500 beds, 70,000 hospital admissions/year). The availability in the same hospital of several multi-specialist wards served by the same pharmacy permitted investigating the perception of physicians and nurses on shortages without bias due to differences in medicine supply by wholesalers/manufacturers. Moreover, in the Presidio Ospedaliero Luigi Sacco, the intra-hospital medicines' supply management varies based on the medicine type. In many cases,

requests are sent by the nurses to the hospital pharmacists for refilling the medicines' ward stocks. The medicines' ward stocks are established according to the ward needs in terms of medicines commonly used for treating inpatients or outpatients. On the other side, critical medicines in terms of clinical activity, treated disease, or cost (e.g., chemotherapy medicines, antibiotics) are managed centrally by the hospital pharmacy. In this case, the request is directly submitted to the hospital pharmacists by the prescriber. Unlike requests for refilling ward stocks, it should include information on the treated patient and the dose regimen. Starting from such information, the hospital pharmacists verify the prescription appropriateness based on the hospital formulary and clinical guidelines before supplying the medicines.

## **2 Method**

The study was conducted between January and December 2019 by hospital pharmacists working at the Presidio Ospedaliero Luigi Sacco (Milan, Italy). A questionnaire of 16 questions was submitted to physicians, medical residents, and nurses who decided to join the study. All healthcare professionals working full-time in the wards of the hospital.

The survey (Appendix A) was divided into two categories: the first category is dedicated only to identification questions, then the second category included questions about the phenomenon. The first part of the survey is constituted by four open-ended questions focused on the identification of the HCP, the hospital in which the interviewee works, the hospital wards in which he/she worked, and his/her role. Questions 5-16 are closed questions, dedicated to the actual interview to quantify, and estimate the problem of drug shortages. Specifically, in Question 5 the HCP was asked if he/she has ever found himself/herself in the condition of having to prescribe a medicine that was not found to be available at the hospital pharmacy. Question 6 was devised to quantify the number of lacking molecules over time

and in the benchmark timeframe (12 months) to estimate the shortages' extent the interviewee had to face in the last week, month, semester, or year. Questions 7, 8, and 9 were focused on recording the therapeutic classes and the molecules most subject to shortages according to the experience and perception of the HCP. The medicines reported by the interviewee were classified based on the ATC classification system. Questions from 10 to 13 were focused on the shortage impact of the specific medicines on the ward activities. The interviewees were asked to report if they knew therapeutic alternatives when they became aware of the shortage, what discomfort caused the lack of the medicine to clinical activities, what relevance had this impact, and if it has ever been verified that the shortage has never been resolved and if so in which case. Questions 14-16 are included to investigate how much interviewees knew the activities of the hospital pharmacy and to establish a starting point to increase collaboration and cooperation. The data were fully managed and analyzed by using JMP®14 (SAS Institute, Cary, NC, USA). The study protocol was approved by the Hospital's Health Department.

Although a harmonized definition of shortage has not been applied in the EU yet (De Weerdt et al., 2015), in this manuscript the term “shortage” referred to the definition provided in the latest HMA/EMA guidelines.<sup>4</sup> In this context, it is worth noting that the shortage of medicines does not preclude the existence of therapeutically equivalents or analogs in the Italian market. For such study, pharmaceutically equivalent (PE) means a medicinal product that contains the same active ingredient(s), is identical in strength, and has the same dosage form and route of administration to another reference product; therapeutically equivalent (TE) means a medicinal product that is pharmaceutically equivalent and bioequivalent to another to such a degree that their effects, with respect to both efficacy and safety, are essentially the same;<sup>18,19</sup> therapeutically analog (TA) means a medicinal product that can be

neither pharmaceutically nor therapeutically equivalent to a reference product, but can be switched with it by the prescriber.

### 3 Results

#### 3.1 *Medicines affected by shortages*

At the end of the data collection, 58 interviews were completed in 14 different wards of the Hospital. The interviewed cohorts resulted in 40% of the full-time physicians and nurses of the hospital staff. In total, 44 physicians, 4 medical residents, and 10 nurses were interviewed. More than nine HCP were interviewed in each hospital wards, exception made for gastroenterology (n = 1), immunohematology and transfusion medicine (n = 7), neurology (n = 9), oncology (n = 2), and pediatrics (n = 6). Ninety percent of the interviewees reported being aware of the unavailability of medicines in the wards. Unlike residents and nurses, only 74.1% of physicians declared to experience the prescription of medicine in shortages in the early past.

A total of 148 medicinal products, containing 49 different drug substances, were reported to be unavailable by interviewees. Physicians reported a mean of 2.0 unavailable medicines per interview, whereas residents and nurses up to 3.75, and 4.1 items per interview, respectively. Figure 1 shows the number of medicines that are perceived as in shortage by professionals of the different wards. The reported unavailability of medicines mainly involved wards of infectious diseases (the percentage included data from the three different infectious disease wards present in the Hospital), and respiratory medicine; on the contrary emergency and oncology units seemed marginally affected by shortages.

Therapeutic classes mostly affected by unavailability according to the interviewees' experiences (Questions 7 and 8) are reported in Figure 2. Antibacterials (35.1%) and corticosteroids for systemic use (13.5%) resulted in the therapeutic classes mostly affected by

shortages according to the interviewees' perception. Among the antibacterials, the most frequently reported APIs were the combination of piperacillin/tazobactam (42.3%), ceftazidime (19.2%), and ampicillin (15.3%). methylprednisolone injections (20, 40 mg) were the most reported among steroids (75%). Focusing the attention on ATC level II C09 (4.1%), all reported medicines were sartans (i.e., valsartan, irbesartan), which were in shortages worldwide due to the manufacturing issues related to the possible presence of nitrosamine impurities in the API source.<sup>18</sup> Moreover, it is noteworthy that most of the reported medicines were formulated as parenteral dosage forms (iv: 76.4%; im: 2.0%; sc: 1.4%), whereas the remaining 20.3% were oral dosage forms.

The perception of the interviewees about medicines unavailability varied based on the clinical activities carried out in the wards (Figure 3). The antibacterials were more frequently reported in infectious diseases and respiratory medicine wards, whereas they were not in cardiac surgery. The pattern also differed among wards in which similar activities were performed (e.g., infectious diseases ward I, II, III). For example, the shortages of anthelmintics (P02) were reported only in infection diseases II ward and not in infection diseases I and III. This is due to the specialization of the wards in treating different types of infections and, consequently different medicines were used.

### **3.2 Duration of shortages**

In 88% of cases, the interviewed physicians or nurses declared to have been in the condition to prescribe/request a medicine which turned out to be unavailable at the hospital pharmacy (Question 5). This data is comparable to the data of the literature.<sup>7,20,21</sup> However, it is noteworthy that 20% of the interviewees declared that they did not experience any shortages affecting their working activities within a year. For other interviewees, the longer the time of reference, the higher the number of perceived drug shortages (Figure 4). In particular, 34.5%



of the interviewees declared that they had prescribed/requested in the last week up to 5 medicines that resulted unavailable at the hospital pharmacy, whereas the percentage reached 58.6% considering 6 months before the interview. About 27.6% of them reported that they experienced between 6 and 10 unavailable medicines during the same period. No significant differences were observed comparing the 6-month and 1-year period (27.6% vs 24.1%), whereas 3.5% of interviewees had to face shortages of 11-20 medications in the year before the interview (i.e., 2018).

In most of the cases, the unavailability was resolved within two and eight weeks according to both physicians and nurses. However, the shortage has never been resolved in 17% of cases. All those medicinal products are still lacking due to manufacturing or marketing issues (Table 1). In three cases (e.g., cefepime 2G vials, ceftazidime 1G vials, labetalol 5mg vials), the medicines' unavailability induces the prescriber to switch them with therapeutic alternatives available on the Italian market. The patients were treated with a TA with a different API, having the same IV-level of ATC code (e.g., ceftriaxone), or strength (e.g., cefepime). However, in most cases, no therapeutic alternatives are available on the Italian market (i.e., PE, TA, TE), and importation from abroad was mandatory to ensure the patients' access to therapies. Fortunately, 6 of 7 imported medicines are PEs and, therefore, the efficacy/safety profile of the treatment was not significantly affected.

### ***3.3 Availability of therapeutic alternatives***

In 66% of cases, HCP reported that they were aware of possible therapeutic alternatives when they knew medicine was in shortage. It is worth noting that the higher HCP awareness was founded in the wards most affected by shortages. Indeed, the availability of therapeutic alternatives has been known by more than 90% of HCP working in infectious diseases and respiratory medicine wards. Indeed, the HCP substituted the medicine in shortages with a

generic product in 11.4% of cases, with a medicinal product with the same API strength but different dosage form in 8.6% of cases, with a different dosage in 14.3% of cases, and with a product containing API of the same therapeutic class in the 65.7%. Moreover, the substitution with alternatives was not judged critical by the healthcare professionals for the patients, since only 34% of the interviewees declared that their clinical activity was significantly altered by the therapeutic switch due to the unavailability of the medicine. In this context, the main issues reported by the interviewees were related to the therapeutic substitution itself (53.3%), to the delay or the block in the therapy administration to patients (13.3%), and the need for closer monitoring of patients' condition (6.7%). The 3.9% of interviewees also declared that the substitution resulted in a worsening of patient care and treatment. For example, the unavailability of interferon for a few weeks in the ward of immunohematology and transfusion medicine resulted in a block of the treatment of patients affected by myeloproliferative neoplasm.

### ***3.4 Shortages effects on the operability of hospital wards***

Most of the interviewees considered not relevant (13.7%) or not very relevant (39.2%) the impact of adopted actions on their work and the ward operability. As previously discussed, the presence of PE or TE on the market allowed the HCP to change patient treatment without interacting with the hospital pharmacists or prejudicing patients' continuity of care.

On the contrary, in 41.2% of the cases, the operability was significantly affected by the shortages because the healthcare professional had to wait for the hospital pharmacy to obtain supplies from distributors.

Finally, in the 5.9% of cases, the impact was judged very relevant for the procedures needed for requiring the authorization of the AIFA for the importation of a therapeutic analog from abroad. Seventy-five percent of physicians and 100% of nurses declared to be aware of

the procedures for obtaining the AIFA authorization to import a temporarily lacking medicine from abroad. Indeed, based on the current Italian regulatory framework, a hospital or community pharmacy cannot import independently a medicinal product from abroad like in other EU countries.<sup>7</sup> The importation of medicinal products has to be authorized by the AIFA only in the presence of a request of a physician for specific patients. In this light, the cooperation between the hospital pharmacy and the physicians is critical for speeding up the importation of essential medicines in shortages. In this context, interviewees confirmed the importance of the cooperation between wards and hospital pharmacists in the management of critical issues. Moreover, they appeared satisfied with the existing communication: indeed, their satisfaction is scored 3.78 units on a scale of 0-5; 29.9% of the answers were at the highest level of satisfaction, none indicated a value lower than 2.

#### **4 Discussion**

The percentage of HCP working in the Hospital that answered the survey and their good distribution through the hospital wards allowed to provide a realistic representation of the perception of hospital medical staff. Ninety percent of interviewees declared to have to face unavailability in the year before the interview. Such a percentage decreases to 75% considering only the physicians' answers. The nurses reported a higher number of unavailable medicines in comparison to physicians. These findings seem due to the different roles in the medicines' management in the wards, not to the different expertise. Indeed, the interviewed nurses were directly involved in the management of the ward medicines stocks, and actively cooperated with both the physicians and the hospital pharmacists. Based on the survey results, nurses reached a good level of knowledge of the medicines' shortages within their working daily life since they are involved both in sending the requests for refilling ward stocks and in administering the medicines to the patients. Therefore, they could know in

advance about issues in the continuity of care due to shortages or temporary unavailability and they could fix the problem by requesting therapeutic alternatives such as generics. On the contrary, a physician was often aware of the medicines' shortage only at the late moment. Therefore, the physicians might be informed when its impact on the continuity of care could not be avoided. However, such a difference in the shortage perception between physicians and nurses might be a bias due to the higher percentage of interviewed physicians than nurses. It can be a limitation of the study, although the nurses (max 1-2) in charge of the management of medicines' stock and of interacting with the hospital pharmacy is generally lower than physicians working in the hospital wards.

The different shortage perception between physicians and nurses also agrees with the fact that most medicines reported to be in shortages were managed by the wards in stock-refill mode. Indeed, 77,6% of API of unavailable medicines were supplied by the hospital pharmacy by nurse request for refilling the ward stocks. Such a higher frequency of perceived shortages suggested that the stock-refill mode in intra-hospital inventory management seems less effective than centralized systems in mitigating promptly the negative effects of shortages on the wards' daily activities. When centralized inventory management and/or unit-dose prescription system is adopted in the hospital, the collaboration among HCP is closer and more frequent. It facilitates the exchange of knowledge and improves the hospital resilience to a shortage. Moreover, it is noteworthy that the physicians' perception of shortages is higher in those using the unit-dose prescription system. Indeed, they (n=21) reported an average of 3.1 unavailable medicines per interview versus a mean of 1.6 reported by colleagues (n = 23) that prescribed only medicines managed by stock-refill mode. Such evidence suggests that the difference of shortage perception between physicians and nurses seemed not related to the expertise of the healthcare professionals, but its involvement in the

medicine supply from the hospital pharmacy to the ward. The higher the involvement of the healthcare professional, the higher its awareness of potential or existing shortages.

However, it is noteworthy that, although a centralized medicines' supply would provide better management of hospital inventory and shortage mitigation by the hospital pharmacists, it cannot be widely applied in hospitals worldwide since the lack of appropriate IT infrastructures (e.g., middle-income countries). In high-income countries, the two supply management models also coexist, like the example provided by this study.

It is interesting noting that interviewees' answers differ from data available in the literature.<sup>20,22</sup> Indeed, their perception of the problem extent did not match the real trends. The number of shortages in the Italian market increased from 1690 to 2223 items from November 2018 to August 2019, according to the AIFA list of medicine shortages.<sup>22</sup> A similar scenario emerged from the surveys in other European Countries.<sup>15,20,23</sup> On the contrary, in this study, the shortages reported by physicians and nurses appeared relatively limited. The 96.5% of interviewees declared to remember less than 10 unavailable medicines they had to face within the year before the survey (i.e., 2018). As shown in Figure 3, no apparent increase in shortages was observable comparing the HCP perception on shortages in short period (e.g., within a week and a month) versus a longer one (e.g., within a semester and a year). Such a perception gap can be due to the important role of the hospital pharmacists in preventing and mitigating the impact of shortages on daily clinical activities. Surely, the adoption of risk assessment and management strategies by the hospital pharmacists allowed to postpone the negative effects on the continuity of care.<sup>16,17</sup> For example, rational programming of the hospital pharmacy stocks of medicines and their therapeutic alternatives based on the estimated shortage impact of a medicine permitted to ensure a constant supply to the hospital wards up to weeks or months even if the medicines

were not available on the market.<sup>16</sup> The hospital pharmacists need to assess information about possible/ongoing shortages in real-time to anticipate and minimize the critical issues through stocks and to establish good communication among the different HCP. Indeed, the hospital pharmacists have to provide updated information on possible and ongoing unavailabilities to allow nurses to rationalize the medicines' stocks of the hospital wards and physicians to adopt the most appropriate clinical decisions to ensure the continuity of care of patients. The actions adopted by hospital pharmacists should be rationalized based on the real needs of hospital wards. The results of the study highlight that both types of medicines and clinical activities carried out in the hospital wards influenced how HCP perceive the unavailability of medicine. The HCP working in the hospital wards affected mostly by shortages seemed the most experienced in the management of the shortages and the therapeutic substitutions. Moreover, the obtained results confirmed what was reported in the literature: antibiotics and parenteral dosage forms were the most referred therapeutic classes, and dosage forms affected by shortages.<sup>15,16,23,24</sup> However, the results also highlighted that interviewees were often aware of possible therapeutic alternatives containing different API of the same therapeutic class (i.e., same levels III or IV of ATC code). In this context, the substitution is frequently judged not so critical to be carried out at the patient bedside. However, in some cases, a different dosage form or strength had to be used. Here again, the hospital pharmacists have also an important role in the switching procedures, especially when products should be manipulated<sup>25</sup> or should be delivered in combination with other medicines to which the compatibility has not been evaluated in advance.<sup>26</sup>

The overall data suggested a good resilience of the healthcare professionals to the medicines' unavailability in the hospital wards. Only in 47.1% of the cases, the wards operability was slowed down due to the supplying of TEs/TAs from wholesalers and/or manufacturers, or due to the importation from abroad. It should be underlined that the

perception of physicians and nurses about this latter aspect seemed to be distorted in comparison to the real complexity of the procedure. Indeed, most of the activities were performed by the hospital pharmacy. While only 5.9% of the responders evidenced this problem, the hospital pharmacy had to import therapeutic analogs marketed abroad in the case of 59% molecules without therapeutic alternatives: in these cases, the average timing of import and delivery of medicines from abroad was about four/five weeks.

Finally, the results highlighted 17% of the medicines which unavailability has not been solved yet. Some of them were voluntary withdrawals by the Marketing Authorization Holder, others have been shortages due to manufacturing issues.<sup>27</sup> In this case, the only solutions to ensure continuity of care were the importation of a therapeutic alternative. Not all these molecules are still unavailable in the Italian market nowadays. To ensure the supply of Italian hospitals, the supply of lysine acetylsalicylate 500mg vials (N02BA01), bleomycin 15mg vials (L01DC01), mitomycin 40mg vials (L01DC03) has been strictly governed by AIFA by the application of a specific quota.

## **5 Conclusion**

The survey highlighted a good awareness of the interviewees on the criticisms connected with the medicines' shortages. However, the results suggested that nurses involved in the management of medicines have a better perception of the problem than physicians probably due to the more frequent contact with the hospital pharmacists. However, the overall results demonstrated a good resilience of all HCP in managing the medicines' unavailability. In most of the cases, the unavailability of medicine was overcome by substituting with a therapeutic analog directly at the patient bedside, without affecting the wards' operability and the continuity of care. The cooperation between the hospital pharmacy and healthcare professionals should be strengthened by creating and adopting procedures to rationalize the

risk assessment and management of shortages based on the real features and needs of the wards of the hospital. In this context, the development of new management technologies and knowledge sharing are desirable. For example, the application of the unit-dose prescription system and the centralized supply management by the hospital pharmacy will be useful to improve the awareness and reactivity of healthcare professionals in preventing and mitigating shortages. In this light, the survey appears a proof-of-concept for the routine communication among healthcare professionals to enhance the collaboration among hospital workers and to identify the therapeutic classes that needed to be strictly monitored based on the clinical activity of each hospital ward.



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## Tables

**Table 1.** List of medicines affected by shortages that have never been resolved, the root causes, the date of shortage beginning, and the advice to HCP reported in the shortages list of the Italian Medicines Agency (AIFA, 2020). PE: Pharmaceutically equivalent; TE: therapeutically equivalent; TA: therapeutic analog.

Medicinal products	ATC	Date of shortage beginning	Shortage causes	Italian therapeutic alternatives (PE, TE, TA)	Advice for healthcare professionals	Therapeutic alternative used
Fructose diphosphate 5G vials	C01EB07	09/01/2019	Marketing suspension	No	Importation of TA	TA (Fructose diphosphate 10G vials)
Ceftazidime 1G vials	J01DD02	01/08/2016	Manufacturing issues	Yes	Substitution with TA	TA (Ceftriaxone 1G vials; J01DD04)
Cefepime 2G vials	J01DE01	14/10/2015	Manufacturing issues	Yes	Substitution with TA	TA (Cefepime 1G vials)
Labetalol 5mg vials	C07AG01	15/08/2013	Marketing cessation	Yes	Substitution with TA	TE
Sodium nitroprusside 100mg vials	C02DD01	18/07/2018	Marketing cessation	No	Importation of TA	PE

Diazepam 10mg vials	N05BA01	01/05/2018	Manufacturing issues	No	Importation authorization to MAH	PE
Lysine acetylsalicylate 500mg vials	N02BA01	24/05/2019	Manufacturing issues	No	Importation of TA	PE
Bleomycin 15mg vials	L01DC01	24/05/2019	Manufacturing issues	No	Importation of TA	PE
Mitomycin 40mg vials	L01DC03	03/06/2019	Manufacturing issues	No	Importation of TA	PE

## Figure captions

**Figure 1.** Percentage of medicines containing different drug substances reported as unavailable in the different wards of the Hospital.

**Figure 2.** Medicines affected by shortages in the different wards classified based on ATC level II. ATC level II codes: A02, drugs for acid related disorders; B06, other hematological agents; C01, cardiac therapy; C02, antihypertensives; C03, diuretics; C09, agents acting on the renin-angiotensin system; G04, urologicals; H02, corticosteroids for systemic use; J01, antibacterials for systemic use; J06, immune sera and immunoglobulins; L03, immunostimulants; N02, analgesics; N03, antiepileptics; N05, psycholeptics; N06, psychoanaleptics; N07, other nervous system drugs; P02, anthelmintics; R06, antihistamines for systemic use. “Other” included ATC level II with only one medicinal product reported, namely: A01, stomatological preparations; B01, antithrombotic agents; B05, blood substitutes and perfusion solutions; G03, sex hormones and modulators of the genital system; H01, pituitary and hypothalamic hormones and analogs; J02, antimycotics for systemic use; P01, antiprotozoals.

**Figure 3.** Therapeutic classes most frequently reported in hospital wards with more than nine interviewees.

**Figure 4.** The number of medicines perceived as deficient by interviewees in the reference period.

## **Supplemental online material**

**Appendix A.** Survey for physicians and nurses working in the hospital clinical units about the phenomenon of medicines' shortage.

Figure 1 [Click here to access/download;Figure;Figure 1.pdf](#)

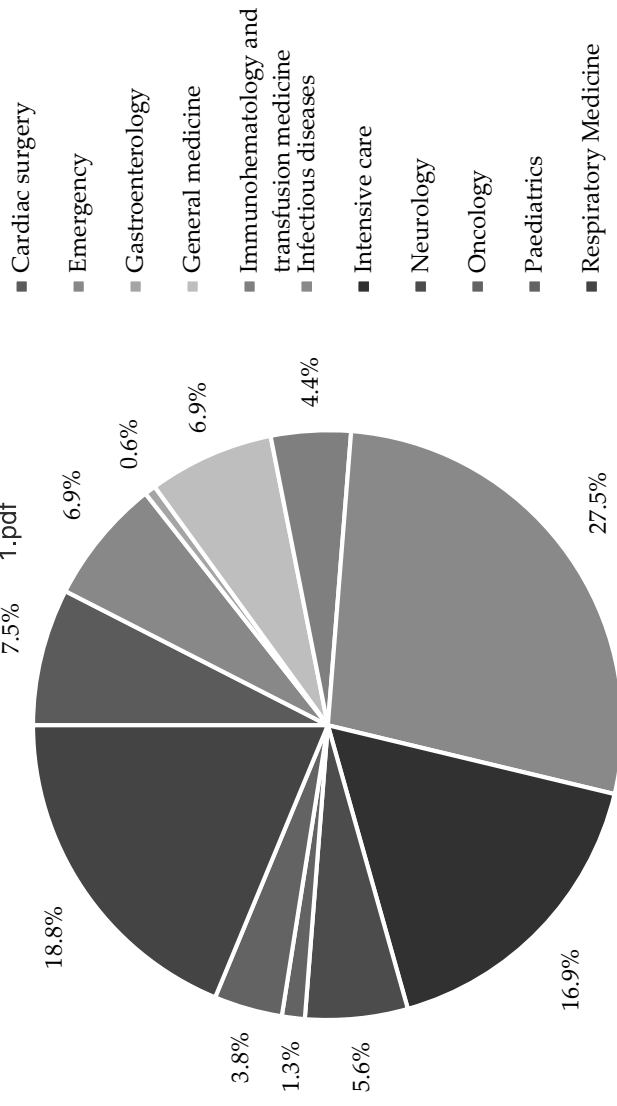
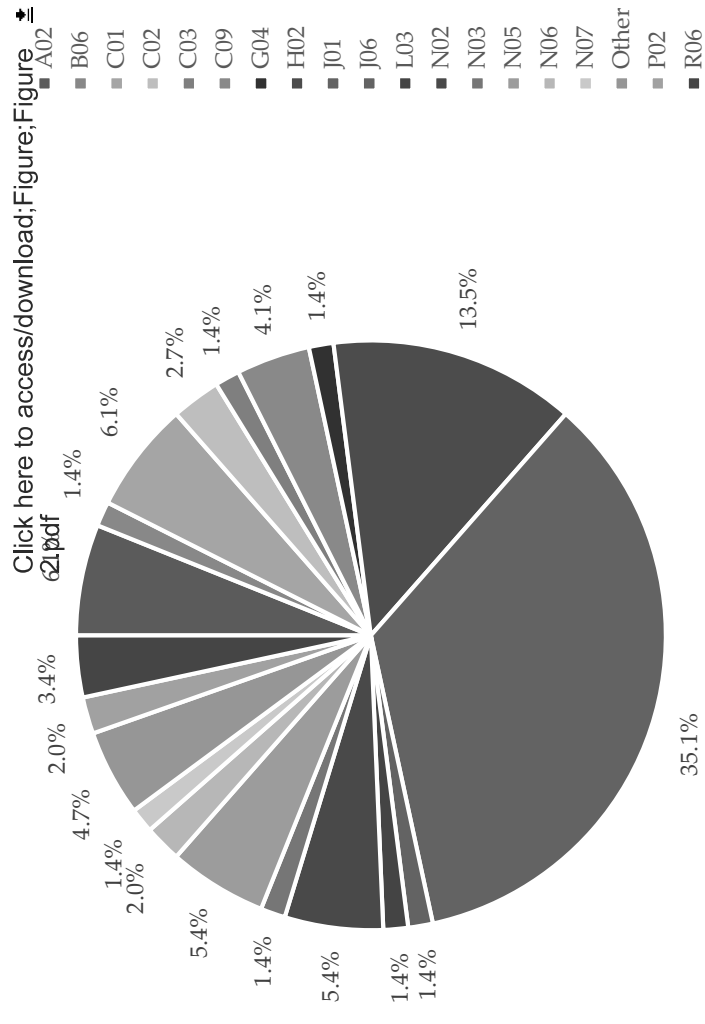




Figure 2



Click here to access/download;Figure;Figure 3.pdf

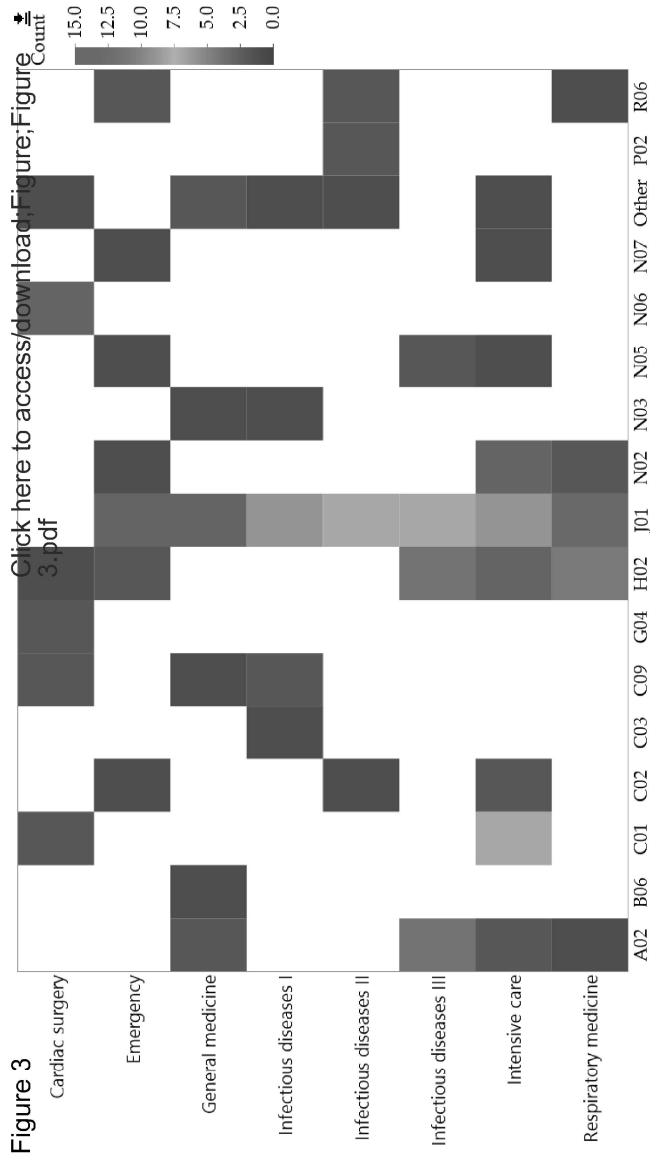
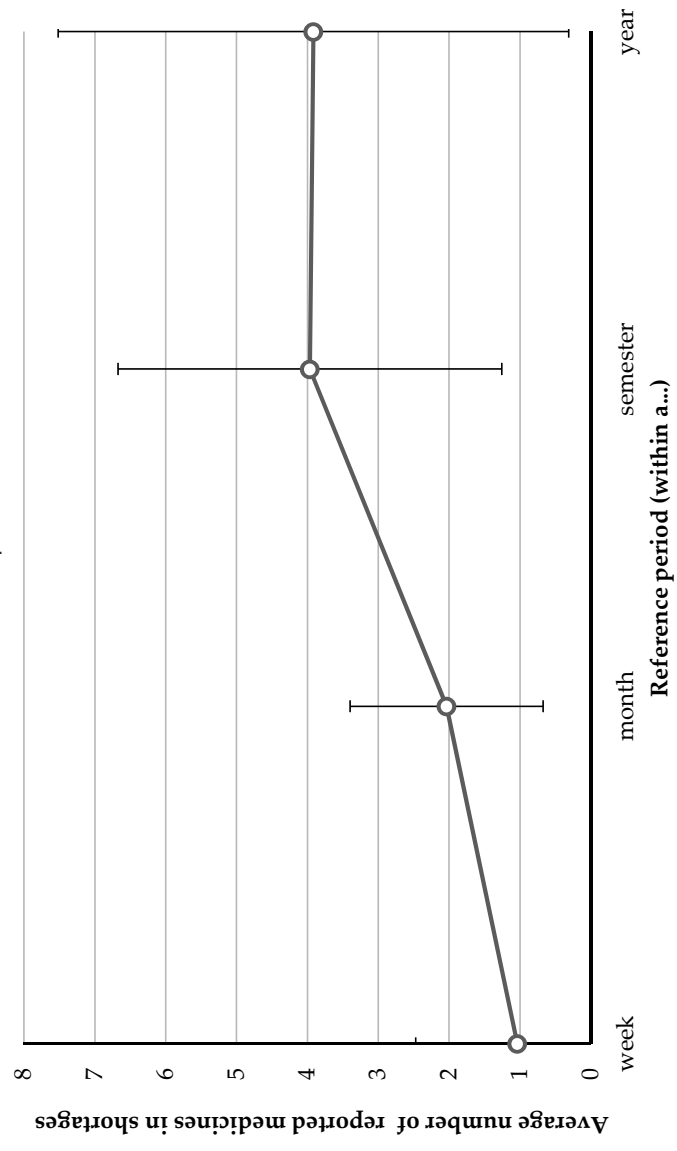


Figure 4 [Click here to access/download;Figure;Figure 4.pdf](#)



**SURVEY FOR HEALTHCARE PROFESSIONALS  
ABOUT THE PHENOMENON OF MEDICINES' SHORTAGE**

**Identification questions**

- 1) Hospital: .....
- 2) Department: .....
- 3) Role: .....
- 4) Healthcare professional: .....

**Cognitive questions**

- 5) Have you ever found in the condition to have to prescribe a medicine that wasn't available at the Hospital Pharmacy?
- ☐ Yes ☐ No
- 6) In the last week how many medicines at the moment of prescription weren't available at the Hospital Pharmacy?
- ☐ 0 ☐ 0-5 ☐ 6-10 ☐ 11-20 ☐ > 20
- In the last month how many medicines at the moment of prescription weren't available at the Hospital Pharmacy?
- ☐ 0 ☐ 0-5 ☐ 6-10 ☐ 11-20 ☐ > 20
- In the last six months how many medicines at the moment of prescription weren't available at the Hospital Pharmacy?
- ☐ 0 ☐ 0-5 ☐ 6-10 ☐ 11-20 ☐ > 20
- In the last year how many medicines at the moment of prescription weren't available at the Hospital Pharmacy?
- ☐ 0 ☐ 0-5 ☐ 6-10 ☐ 11-20 ☐ > 20

1

PATHOLOGY.....

VIA DI SOMMINISTRAZIONE.....

MOLECULE.....

- 9) On average how long the medicines listed in question 8 have not been available?
- A) ☐ 1 week ☐ 2-8 weeks ☐ 2-6 months ☐ 6-12 months ☐ > 12 months
- B) ☐ 1 week ☐ 2-8 weeks ☐ 2-6 months ☐ 6-12 months ☐ > 12 months
- C) ☐ 1 week ☐ 2-8 weeks ☐ 2-6 months ☐ 6-12 months ☐ > 12 months
- D) ☐ 1 week ☐ 2-8 weeks ☐ 2-6 months ☐ 6-12 months ☐ > 12 months
- E) ☐ 1 week ☐ 2-8 weeks ☐ 2-6 months ☐ 6-12 months ☐ > 12 months
- 10) At the time of unavailability of medicines do you know any therapeutic alternatives?
- ☐ Yes ☐ No
- If yes, which?:
- ☐ generic
- ☐ same AI same dosage different pharmaceutical form
- ☐ same AI different dosage
- ☐ different AI same therapeutical class
- 11) Clinical activity has undergone any type of variation caused by the unavailability of the medicine?
- ☐ Yes ☐ No

3

- 7) Based on your experience in the department, which therapeutic classes are most subject to unavailability?

A) .....

B) .....

C) .....

D) .....

- 8) Which medicines that you originally prescribed have been subject to unavailability?

- A) MEDICINE.....  
PATHOLOGY.....  
ROUTE OF ADMINISTRATION.....  
MOLECULE.....
- B) MEDICINE.....  
PATHOLOGY.....  
ROUTE OF ADMINISTRATION.....  
MOLECULE.....
- C) MEDICINE.....  
PATHOLOGY.....  
ROUTE OF ADMINISTRATION.....  
MOLECULE.....
- D) MEDICINE.....  
PATHOLOGY.....  
ROUTE OF ADMINISTRATION.....  
MOLECULE.....
- E) MEDICINE.....

2

If yes, which:

.....

.....

- 12) Overall, what impact had the medicines' unavailability on clinical activity?

- ☐ Not relevant: there was often a generic medicine or a different equivalent pharmaceutical form (e.g. capsules, immediate release tablets)
- ☐ Not very relevant: there was often a therapeutic alternative on the national market but it needed manipulation to adjust the dosage
- ☐ Relevant: in many cases there was no therapeutic alternative and I had to wait for the pharmacy to get supplies from distributors
- ☐ Very relevant: I often had to wait for the AIFA Nulla Osta

- 13) Has it ever happened that the shortage never resolved?

☐ Yes ☐ No

If yes, in which case:

.....

- 14) Do you know that AIFA Nulla Osta is essential for importing a temporarily deficient medicine from abroad?

☐ Yes ☐ No

- 15) Are you satisfied about the communication between Department and Pharmacy in managing critical issues?

☐ zero ☐ one ☐ two ☐ three ☐ four ☐ five

- 16) Do you have any improvements to suggest for the management of the unavailability of medicines?
- .....
- .....

4