The optimization of drug distribution processes for citizens and users during pandemics

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Abstract: Of the drug distribution models implemented in the Italian National Healthcare Service provided to guarantee the administration of medication, the drug distribution performed through the hospital channel is an operative strategy that allows for savings in the public expenditure, but often creates higher social costs for patients and caregivers. This distribution model leads to high access to hospitals which, during pandemics, amplifies the risk of contagion, making these healthcare facilities a place where epidemics could spread and negatively affect high-risk patients. Considering their extensive local presence, primary care services and community pharmacies could play an active role to reach patients and ensure the proper distribution of drugs. Based on the differences in these two distribution models, a prescriptive tool could provide suggestions for the institutional decision-making process. When performed by different stakeholders (i.e., policy makers, health authorities or agencies), it could define which drugs should be distributed by primary care pharmacies for the treatment of chronic diseases and provide an answer to critical issues in case of future pandemic situations and healthcare emergencies. Prescriptive data analyses are known as the best methods for formulating prescriptions in the distribution field and constrained optimization sets the values of decision variables to achieve specific objectives, such as a reduction in the number of visitors to the hospital setting. Grounded on previous research in this field, the present study proposes a decision-support tool based on a constrained optimization model, establishing which drugs currently dispensed by hospital pharmacies should be distributed by primary care pharmacies. This approach allows for limiting crowding and balances the distribution costs to guarantee equal access to care for patients. The model structure and the possible decision-making outputs reached by applying the prescriptive tool are discussed and the "what-if" analysis is used to ensure the robustness of the simulation approach.

Keywords: Supply chain design; Optimization; Decision support systems.

I. INTRODUCTION

Literature evidence [1] showed the pharmaceutical supply chain comprised of a set of different players: manufacturers, including pharmaceutical companies, but also laboratories and co-manufacturers, wholesalers, distributors, brokers, customers, logistics providers, and regulatory agencies [2]. This supply chain is a very complex one [1], especially with regards to communication and coordination between the many parties. In addition, the definition of the distribution models could also be driven by contextual factors, such as the features of the medication (often subjected to cold chain), service requirements, available distribution channels, demand properties, and legislation restrictions [3]. Providing a high level of service to all the final users (citizens and patients) could be considered to be the main task of the drugs supply chain, evaluating that needs and requirements are often not investigated [4].

Taking into consideration the entire drug management process, the distribution phase appears to be the most relevant one for users and society in general, involving both patients and their caregivers. The adherence to the pharmaceutical prescribed strategy could be affected and influenced by the facility and efficiency of the distribution process and, from the patients' point of view, the therapeutic effectiveness should be supported by a structured and easy- to-manage distribution model, while reducing any treatment switches [5]. Considering the caregivers' point of view, a well-conceived and designed drug distribution network could help reduce supply and delivery times, focusing the efforts on direct patient support, communication issues and the overall management of disease. Several variables, such as the length of the treatment, the innovativeness of the therapy or the administration modalities, could impact the delivery of specialized medication to the patients. Furthermore, the need to monitor the occurrence of adverse events, also with the support of highly specialized healthcare professionals, could influence treatment management, considering that, at the same time, some medications could be administered at home with the support and monitoring of caregivers and families [6].

In a context such as the one described above, different types of drug distribution models and strategies were proposed and implemented by the Italian National Healthcare Service (NHS). They tried to meet the needs of patients and caregivers, and to ensure the highest level of service, while containing costs and addressing ethical concerns. In the Italian context, one approach that is characterized by centralization and called "Direct Distribution" is related to distributing drugs directly through the hospital channel, leading to cost savings related to the treatment management, but often resulting in higher social expenses for both patients and caregivers. On the other hand, to guarantee a more capillary distribution of drugs and to enhance proximity to patients, there is another model in the Italian context whereby primary care and local pharmacies ensure the administration of drugs. This model is called "Distribution Through Pharmacies on Behalf of Hospitals".

The COVID-19 pandemic highlighted the criticalities and weaknesses of the centralised distribution models where Hospital pharmacies were the centre of the distribution network, especially in comparison with alternative distribution networks. Direct Distribution, which is characterized by direct access to hospital facilities, amplified the risk of contagion and may have contributed to making hospitals a culprit in the spread of COVID-19. Due to a strong national production structure, which constitutes a significant portion of Italian gross domestic product, no drug shortages were experienced, and it was possible to guarantee the right to treatment for all the patients, even during the pandemic, a period in which many industrial settings experienced great upheaval in their supply chains. However, a new health emergency could negatively impact the patients' right to treatment [7], considering the limits of the current distribution network, designed, in most of the cases, to be a centralized model in which the nodes are represented by specialists and hospital pharmacies. On the other hand, a decentralized distribution network in which general practitioners, primary care providers and community pharmacies would temporarily return to play a leading role in distribution would be more robust and resilient [8].

Moving on from these premises, drug distribution issues are therefore becoming a relevant topic, not only for the NHS actors (healthcare providers, hospitals and community/primary care pharmacists, drugs and technologies producers), but also for society, which is the sum of families/caregivers and patients/healthcare system users. Defining an efficient and well-structured drug supply chain could cover the operative interest of the players involved in the processes of decision-making and defining strategies but taking on a more comprehensive perspective could answer to the practical issues of those who are directly involved in the supplying of drugs. In addition, considering the social, epidemiological, demographic and cultural factors that result in an increased demand for healthcare services and a strong need for lengthy and expensive treatments, all the National Healthcare Services (NHSs) are invited worldwide to act in order to ensure their economic sustainability and affordability.

Focusing on chronic disease, which represents the second greatest concern of global health, as it is responsible for 70% of deaths worldwide and consumes a large part of economic resources while demanding the definition of a new paradigm of care (Tang & Smith., 2016), the present research is devoted to investigating the different available distribution models to understand which drugs among those currently dispensed by hospital pharmacies could be transferred to the territorial setting for primary care and community pharmacies distribution in the occurrence of a future pandemic or health emergency, with the aim to ensure a high level of service to patients. The current paper adopts an optimization approach and develops a tool that is able to support the decision-making process [9].

The final goal is to provide both practical and theoretical contributions. In practical terms, this paper aims at encouraging healthcare organizations and policy makers to develop more resilient and local drug supply chains and distribution networks. This study could also have some theoretical implications considering the fields of optimization and healthcare analytics, opening the avenues for future research in the field of advanced optimization techniques that could be applied to a wide range of healthcare challenges.

The research questions that were identified to achieve the outlined objectives are as follows:

RQ1: Which drugs currently dispensed by hospital pharmacies to treat chronic diseases could be distributed instead by primary care providers and community pharmacies during a pandemic or healthcare emergency?

RQ2: From both a financial and social perspective, which model would be the most appropriate and what effects would it have on the number of hospital visits in terms of social impact and spending costs?

The paper is organized as follows. First, the context of the Italian drug supply chain is outlined to clarify its characteristics and literature on the drug distribution chain models is outlined. Then, the proposed model and decision-support system developed to answer the the

RQs are presented. Lastly, a discussion and conclusions are drawn.

II. CONTEXT

A. The Italian Drug Supply Chain

In the Italian context, the distribution of drugs through the hospital channel (called "Direct Distribution") is defined as a strategy which allows for economic savings in the management of medications, leading to higher social costs for patients and caregivers. According to the definition of the Italian Ministry of Health, this model was designed to dispense drugs to patients through hospital facilities for self-administration at home, allowing for direct control over medicine consumption, since the prescription and provisions are based on hospital resources. Furthermore, the direct purchase by Hospitals allows for the application of transfer prices, reserved for, by Italian law, Public Institutions. Prices could be further reduced thanks also to tender procedures. The regulation of Direct Distribution (DD) is generally set by a Regional Therapeutic Handbook, which is a comprehensive guide that lists drugs provided and reimbursed by the Healthcare Service. It also includes the guidelines related to the prescriptive activities. This tool also shows which drugs are considered necessary to guarantee the continuity of care after the hospital discharge, determining a connection between the hospital setting and the patient's home., At the same time, however, it contributes to the care shift from the hospital setting to the primary care and territorial level, defining the hospital-territory drugs list. Moving the distribution of drugs between these two organizational settings aims at ensuring a balance, not only by considering social and ethical issues, adopting the double perspective of the healthcare system and the citizens/users, but also by ensuring an improvement in delivery services to adapt and contain the governance of drugs expenditure. Within the DD model, agreements could be reached with primary care pharmacies on the distribution account to reach patients in their proximity. Applying this model, defined as "Distribution Through Pharmacies on Behalf of Hospital" (DTPH), drugs are distributed to patients through community pharmacies, while the hospitals control the purchase of medications, limiting expenditure thanks to the discounts gained due to centralized purchasing by the Hospitals.

Over the years, the two distribution models have been developed widely in all Italian regions to achieve the full application of the hospital-territory drugs handbook described above and, consequently, to guarantee public service delivery to the advantage of citizens and society. It also controls, public expenditure and generates the possibility to reallocate the obtained savings. Distribution on behalf of hospitals has developed consistently over a decade and is widespread in the various regional territories, guaranteeing continuity of care through the creation of a therapeutic area between intensive care (hospital) and chronic care (territorial medicine). In addition, this distribution model could facilitate access to medicines for some categories of patients, safeguarding the financial management of the National Healthcare Service. By developing and supporting the provision of drugs by ensuring proximity, the territorial setting is also enhanced by the development of local care. This is also to be carried out according to future indications supported by the PNRR - Mission 6, which regards proximity networks and telemedicine structures for territorial health care. These aspects are also relevant and explicit concerning the reorganisation of territorial medicine that is supported and defined due to the publication of the Ministerial Decree 77/2022.

In 2021, the primary care and territorial pharmaceutical expenditure for both the public and private sectors amounted to 32.2 billion euros, an increase of 3.5% in comparison with the previous year. The costwas a significant part of the national health expenditure, affecting 1.9% of the gross domestic product. The expenditure on a national level for drugs dispensed through the alternative distribution models, i.e., DD and DTP of product categories A, H and C, reached 8.7 billion, amounted to 74.7% for DD expenditure, with the remaining 25.3% for DTP (OSMED2021 Report).

The DD and the process to directly provide pharmaceutical assistance to specific categories of high-risk and chronic patients has been introduced at the essential levels of assistance to make continuity of care more homogenous and accessible to Italians in all regions. On the other hand, the increase in DD expenditure (i.e., in direct distribution and within the distribution through pharmacies on behalf of the hospital) and the decrease in the Conventional distribution expenditure (considering the expenditure for drugs generated within the network of territorial pharmacies) in a stable deficit for the former (whose maximum is abundantly exceeded each year) and surplus for the second, increases the need for continuous monitoring of these two elements to ensure a growing efficiency of investment choices in innovation.

B. Drug distribution chain optimization models

The objective of strategically addressing the optimization of the distribution flow in order to reach the desired service level without cost overrunning was considered in the Italian context by Constantino et al. [10]. Constantino et al. (2010) propose a Mixed Integer Linear Programming (MILP) problem considering two alternative objective functions under a set of constraints that consider capacity, demand, existence and structural constraints is proposed. As the Italian pharmaceutical market is characterized by a slow dynamic and given the strategic aim of the model, the optimization model considers a time horizon of 1-3 years. Even though the work develops a model for strategic optimization that considers the hospitals, pharmacies and patients, it overlooks the DTP model and the accesses issue in terms of social impact. In fact, the work by Constantino et al. (2010) is interested in the distribution chain side of the supply chain, rather than in the patient side.

Outside of Italy, focusing on the patient side of the distribution chain, other research considered drug distribution and, in particular, the pharmacy site selection problem as to where to assign the limited doses of drugs to different pharmacies in order to best benefit society and provide fair access (e.g. [11], [12], in particular after the advent of pandemics, given the raised interest in the topic (e.g. [13], [14].

To maximize access in the target population, Singh et al. (2015) propose a hybrid optimization model that identifies ZIP code areas for the pharmacy-based distribution of antiviral drugs, which are critical for early pandemic control. The objective function focuses on the expected number of persons willing to obtain antiviral drugs from the nearest dispensing point. On the one hand, the authors propose a web-based distribution decision support tool for decision makers that uses a map to visually represent the output of the optimization helping the Healthcare Services and demonstrates that independent pharmacies are essential for increasing expected access. On the other hand, even if the proposed model is applied to the case of Texas, the work is limited, as it overlooks the number of available antiviral drug doses and the capacity of individual pharmacies, limiting the research's validity.

The optimization model proposed by Zhang, Dai and Han (2017) assigns optimized amounts of antiviral drug for each pharmacy maximizing the access, based on distance, and social and spatial imbalances, , under a minimum volume constraint, through integer linear programming. The access is approximated by the distance, the pharmacies' reputation and the scale and number of drugs-stores in the area. Again, the capacity of the pharmacies is not considered, limiting the practical applicability of the model.

The work by Risanger et al. [13], extending the work by Singh et al. (2015), selects pharmacy points of covid-test dispensing to provide equitable and easy access to all, differentiating from traditional health care facility location problems. The developed MILP optimization model considers a willingness-to-travel function, based on exponentially decaying fraction of the population and distance, mapping areas with ZIP codes. Also in this case, the capacity of pharmacies is not considered, limiting the matching of testing capacity with the testing demand [14].

Similarly, Emu et al. [15] propose an algorithm based on the combination of clustering and MILP to optimize the distribution of vaccines in a given geographical region and taking into consideration priority groups and travelling distance. Their proposal identifies a number of facilities but does not consider the pharmacies in the existing network.

The efficiency of the mass dispensing of medical services, such as vaccines or drugs, during health emergencies can be increased creating emergency points, called "points of dispensing" [14]. Based on the review on existing literature on location-allocation models for points of dispensing during public health emergencies, Alghanmi et al. (2022) conclude that demand for services will depend on country and population.

As recent literature on drug distribution is paying attention to the willingness to travel and assumed the need of focusing on countries when developing such optimization models, a gap emerges. Moreover, none of the revised works has considered drug distribution, overlooking a 'drug selection' activity. Hence, this work aims to propose a model for drug distribution specific for the Italian context that takes into account the country's character and that considers the access issue, as well as the capacity constraint of points of dispensing.

III. THE PROPOSED MODEL AND DECISION SUPPORT SYSTEM

The present work proposes the combination of mixed integer programming models that consider the possibility of exploiting the DTP model, combined with the DD one, to identify from among the list of drugs that are currently in DD which ones should be distributed by pharmacies on behalf of the hospitals (DTP), and decision support tools, with the aim of reducing the accesses issue.

One combination is aimed at pursuing the economic objective, while the other one is aimed at reducing distance between patients and points of dispensing.

After loading the data sets reporting the drugs distribution data (a flat table reporting year, point of consumption, drug, volume, cost, point of dispensing), the decision maker is first asked to set the maximum level of accesses to the hospitals through the slider (*Max*), as the primary objective that will be pursued by means of a constraint of the model. Then, the decision maker is asked to decide whether to pursue primarily a cost minimization (model 1) or a dispensing distance minimization (model 2). The choice will activate alternatively one integer linear programming models. For both models, the notations are reported by Table 1.

TABLE I. NOTATIONS

x_i	Drug *i* in DD, Boolean
y_i	Drug *i* in DTP, Boolean
h_{ik}	Link between the hospital in area *k* distributing drug *i* in DD to patient *j*, Boolean
p_{im}	Link between the pharmacy in area *m* distributing drug *i* in DPT, Boolean
$Dist_{j,k}$	Cost attributed to distance from area *j* to area *k*
$Dist_{j,m}$	Cost attributed to distance from area *j* to area *m*
$Cost_i$	Cost of distributing drug *i* in DTP

Vol_{tot}	Volume of all drugs
$Vol_{i,j}$	Volume of drug *i* administered to patients in area *j*
Max	Maximum objective volume in DD
I	Set of considered drugs, $i \in I$
J	Set of considered patients, $j \in J$
K	Set of considered hospitals, $k \in K$
M	Set of considered pharmacies, $m \in M$

A. Model 1

The variables considered by this model (x_i and y_i) represent the alternative distribution of drug *i* to the DD or DTP.

The costs minimized by the objective function (1) are the costs that the hospital will pay the pharmacies for distributing the drug using the DTP model. The cost for directly distributing the drug is considered null.

$$\min \Sigma_i \left(Cost_i \cdot y_i \right) \tag{1}$$

The constraints ensure that all drugs are assigned one distribution model (2) and the maximum access to the hospital is ensured (4). Non negativity of the considered variables in ensured by (5).

$$\Sigma_i \Sigma_j (x_i + y_i) \cdot vol_{ij} \geq vol_{tot} \tag{2}$$

$$\Sigma_i \Sigma_j \, x_i \cdot vol_{ij} \leq Max \tag{3}$$

$$x_i \, , y_i = 0,1 \tag{4}$$

B. Model 2

The minimization pursued by the objective function (5) regards the distances that the patients should travel between their location and the points of dispensing, either the hospital or the pharmacy, to obtain drugs.

$$\min \Sigma_i \Sigma_j \Sigma_k \left(Dist_{jk} \cdot h_{jk} \cdot x_i \right) + \Sigma_i \Sigma_j \Sigma_m \left(Dist_{jm} \cdot p_{jm} \cdot (1\text{-}x_i) \right) \tag{5}$$

The constraints ensure that all drugs are assigned a distribution model (6) and the maximum access to the hospital is ensured (7). The variables of the model are all non negative (8).

$$\Sigma_k \, h_{jk} \cdot x_i \cdot vol_{ij} + \Sigma_m \, p_{ijm} \cdot \left(1\text{-} x_i \right) \cdot vol_{ij} \geq vol_{tot} \quad \forall j \in J \;\; \forall i \in I \tag{6}$$

$$\Sigma_i \Sigma_j \Sigma_k \, h_{jk} \cdot vol_{ij} \;\; \cdot x_i \leq Max \tag{7}$$

$$x_i \, , \, h_{jk} \, , p_{jm} = 0,1 \tag{8}$$

The output of the optimization that will be presented to the decision maker (Figure 1) shows the total cost of distribution, the amount of drugs that are distributed in DD (with the possibility to show the complete list), the list of drugs that are distributed in DTP (with the possibility to show the complete list) and the average distance travelled by patients to reach the point of dispensing. A map of consumption volumes per drug is also presented to help the decision maker understand the geographical distribution of volumes.

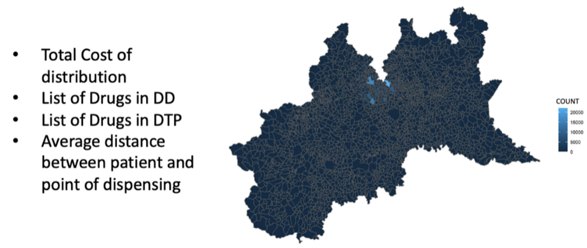

Figure 1. Decision support tool interface design for output

The decision-support interface and tool will be developed via R open software and a Shiny app webpage will provide access to the tool.

Regarding data protection issues that may rise in case of storing data regarding patient locations and consumption of drugs, they will be avoided as the R Shiny app (https://www.shinyapps.io/) is known to be secure by design [16] and will not store the data.

IV. Discussion and Conclusions

The proposed optimization model could allow a decision maker to answer the two RQs. In fact, regarding RQ1, model 1 will provide the lists of drugs to be dispensed by hospital pharmacies (DD) and by primary care and community pharmacies (DTP), in the occurrence of a pandemic or health emergency, i.e., a reduction in the number of accesses to hospitals is needed. Regarding RQ2, model 2 supports the evaluation of how the reduction in the number of hospital accesses will have an effect on social impact, and on the spending, assuming a financial and economic perspective.

Moreover, the proposed decision-support tool could help to generate better performance both from the system's point of view and from the perspective of the patients/users, with the aim of supporting the decision-making process. The drug distribution network redesign, by exploiting the capillarity of primary care and community pharmacies compared with hospital ones, implies a greater possibility for patients, care givers and family members to reach the pharmacy on foot without forcing possibly high-risk subjects to take public transport or alternative services: this faces the problem of social distancing and also responds to the need for environmental sustainability. The improvement of the service could generate positive impacts both for pharmacies and for citizens. Larger orders and an accurate planning with drug manufacturers could ensure on-time deliveries while simultaneously reducing the risk of waiting lists and decreasing the lead time perceived. Therefore, the improvement of the services from the citizens' point of view could be translated into an empowerment of his/her quality of life. Considering a future pandemic situation and crisis, the tool could provide a decision-support system for updating the supply chain design and the drugs involved in a specific drug distribution channel, containing the costs related to the occurred changes as much as possible while ensuring the system's resilience.

Regarding the field of application, the proposed model could be applied in the context of optimizing delivery processes, both within a local context and at a broader level (regional or national), depending on the decision makers' willingness to implement this tool.

Furthermore, the defined model has been applied to chronic diseases but could also be extended to acute diseases and other clinical issues.

The model and the visual decision-support tool is being discussed and applied to the data of the ATS Insubria drug distribution chain, which counts around 19,000 patients and 100 pharmacies. The results of the model application to this practical case will support additional findings as future work.

V. References

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