Impact of Downstream Supply Chain Dynamics on Patient Access to Oncology Medicines

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ABSTRACT

Access to cancer medicines remains a significant challenge in many Low- and Middle-Income Countries (LMICs), limiting patients' ability to receive timely and affordable treatment. This study aims to analyze the impact of the pharmaceutical downstream supply chain on patient access to oncology medicines in LMICs using a system dynamics approach. A comprehensive causal loop diagram (CLD) was developed to map the complex interactions between stakeholders in the downstream value chain. The CLD was constructed using qualitative data from interviews with a pharmaceutical company's experts and validated with insights from a World Health Organization (WHO) technical report. The analysis revealed several critical reinforcing and balancing loops influencing the affordability and availability of cancer medicines, including market scale, competition, insurance support, and inventory management. The study identified a crucial trade-off between availability and affordability, and hypothesized the existence of a potential optimal markup point that could maximize patient access. Furthermore, the study explored the roles and interests of various stakeholders, such as manufacturers, distributors, healthcare providers, insurers, and governments, in shaping the downstream supply chain dynamics. To validate the reference model, the study proposed the categories of data that would be needed to build a quantitative system dynamics model in the future. This research underscores the importance of adopting a holistic, system-level understanding of the downstream supply chain dynamics to develop effective strategies for increasing patient access to life-saving cancer treatments in LMICs.

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1 Introduction

1.1 Motivation

The United Nations (The Office of the High Commissioner for Human Rights, n.d.) and World Health Organization (World Health Organization, 2022) have described health as a human right, requiring access to timely, acceptable, and affordable healthcare and providing for the underlying determinants of health, including safe drinking water, sanitation, food, housing, and health education. The general concept of access represents the degree of fit between the clients and the system (Penchansky & Thomas, 1981). The set of more specific areas of fit between the patient and the healthcare system are availability, accessibility, accommodation, affordability, and acceptability.

Each country assesses the value of healthcare in different ways and has different priorities based on the local situation. Relevant factors include its overall wealth, the stability of its economy, the distribution of funds to healthcare, the existence of a national health system and how it is set up, the level of personal health insurance in the country, and the average income and available means of its citizens. There are many countries where funding levels for several or all these elements are inadequate. Both the private and public sector share the responsibility to work together to build accessible health systems (Sharma et al., 2021).

The sponsor company (PharmaCo) is a multinational healthcare company with differentiated medicines in oncology, immunology, infectious diseases, ophthalmology, and diseases of the central nervous system. Their access to medicine strategy focuses on understanding local barriers to access (Access to Medicine Foundation, n.d.).

PharmaCo has publicly identified “Improving access to healthcare” as the core element of its business strategy. The company is actively developing new approaches to how they price their medicines, and they are working with governments that are keen to invest in strong and resilient healthcare systems. They identified Affordability, defined as economical access to healthcare, as a Corporate Access Goal during a presentation at Pharma Day 2023, an annual investors’ event (PharmaCo, 2023). Affordability was highlighted as one of the opportunities to remove barriers and substantially increase patients’ access to their products, along with Capacity enablement and Partnerships, as described in Figure 1.

Figure 1

Corporate Access Goal – Affordability

Access levers	Inclusive clinical trials	Regulatory filing & reimbursement	Affordability	Capacity enablement	Partnerships
Mid-term outcomes	Support health equity and diversity in our clinical research and trials	Substantial acceleration of regulatory filling & reimbursement approval	Support development of new, integrated and tailored affordability solutions for different population	Support infrastructure development through external partnerships	Mobilize partnerships with global/regional organizations to solve a gap in local care

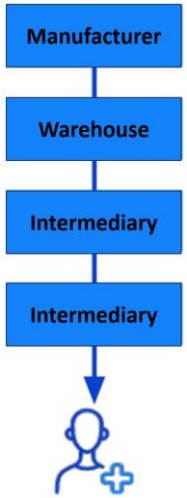
Note: From PharmaCo's Presentation

1.2 Problem Statement and Research Questions

The pharmaceutical supply chain contains multiple levels and many players. As a product moves along the supply chain from manufacturer to patient, the product transfers ownership to various stakeholders, including Warehouses and Intermediaries such as Wholesalers, Distributors, Hospitals, Clinics, and Pharmacies, that take responsibility for the movement of products, as described in Figure 2 (MIT, 2023). The cost of sourcing, storing, and distributing these products often results in a markup on the products' cost and is passed on to the next player in the supply chain as the products' price. In addition to the distribution markups, health systems are complex, with various payers and insurance schemes. The distribution markups and healthcare pricing often lack transparency and can lead to society's inability to access necessary treatment options.

Figure 2

PharmaCo's Downstream Supply Chain



Note. From 2023-24 MIT Supply Chain Management Blended Program Capstone Proposals by MIT (2023).

Transparency, which refers to the overall visibility of the supply chain, presents a challenge within the pharmaceutical sector. Enhanced visibility of the downstream network can support PharmaCo's understanding of each stakeholder's contribution. The comprehensive study of the downstream supply chain is required, including an understanding of the physical movement of goods, financial transactions, information sharing, and the unique contributions of each participant in creating value along the chain. This approach can be used later, as PharmaCo plans to assess the impact of the levels of collaboration and integration among those players on price, affordability, and access to medicines.

In that context, this project seeks to address the following questions:

1. How can we best describe PharmaCo's downstream supply chain in a LMIC and understand the role of key stakeholders in enabling patients' ability to access products?
2. How can analytical modeling enable stakeholders to understand the structure and dynamics of the supply chain system to increase patients' ability to access products?
3. How can stakeholders engage in shaping the supply chain system to increase patients' ability to access products?

1.3 Project Goals and Expected Outcomes

The primary goal of this project is to enhance PharmaCo's understanding of its downstream supply chain in Low- and Middle-Income Countries (LMICs). LMICs are classified by the World Bank based on Gross National Income. There are 137 countries in the LMIC category, representing 63% of the total number of countries in the world (Lencucha & Neupane, 2022). This exploration will study the physical, information, and financial flows specific to the selected country and analyze dynamics of downstream supply chain relationships and their influence on patients' ability to access products. In addition, we will introduce a balanced methodology — comprehensive yet practical — for mapping this supply chain and understand the dynamics of the system into causal diagrams described in Section 2. This methodology can then be adapted and applied to other LMICs. With these insights, PharmaCo can engage stakeholders more effectively, using the findings as evidence to develop customized access strategies for each country.

To achieve our goals, we hypothesize that the product and patient journey map developed by PharmaCo will help us identify the key stakeholders and enable us to map the physical and information flows of the downstream supply chain. In addition, with the help of country experts (whether from PharmaCo or third parties), we intend to complete the financial flow by collecting and analyzing data related to cost, volume, capacity, geographic factors, national regulations, incentives, and local entities involved. Third, we expect that the data collected directly and/or estimated indirectly will be sufficiently

accurate to enable this analysis. Finally, we hypothesize that the methodology used to understand the downstream supply chain of the selected country can be applied and scaled to serve as a representative model for other countries.

For the purposes of this study, the downstream supply chain is defined as starting from the “port” and extending to either the “pre-administration” stage or the “administration” stage. The “port” is where medicines are received through transportation terminals like seaports or airports and are ready for further distribution within the country. Medication “administration” refers to the direct application of a prescribed medication — whether by injection, inhalation, ingestion, or other means — to the body of the individual by an individual legally authorized to do so (Washington Department of Social and Health Services, n.d.). “Pre-administration” refers to the steps preceding the administration of a medication to a patient. Excluded from this scope are the manufacturer, the wide PharmaCo network of upstream suppliers, health insurance processes, patient involvement, and product disposal.

According to the World Health Organization (2020), the term “pharmaceutical product” is often used interchangeably with “drug,” “medicine," or “pharmaceutical.” In the scope of this research, the term “product” will be employed with a similar definition.

The expected outcomes of the project are:

- A downstream supply chain map for a selected country, to understand the value added, markups, taxes, objectives, and incentives of key stakeholders.
- Model of relevant variables relationship to understand downstream supply chain dynamics.
- Description of the methodology applied, and data used, to enable country affiliates to adapt and conduct a similar study in other countries in the future.

By applying the playbook to understand the downstream supply chain, PharmaCo will be well equipped to identify and implement access strategies tailored to their LMIC markets.

2 State of the Practice

A comprehensive understanding of the downstream supply chain, including the connections between key stakeholders, their individual contributions, and their impact on the overall pharmaceutical ecosystem is an important and required step in evaluating patient access to healthcare.

A detailed study focusing on relevant areas to achieve our goal of understanding downstream set-up and impact on affordability and availability is needed. The complexity of the project proposal requires analyzing patient access frameworks, access to medicines, particularly in LMICs, and the details of the pharmaceutical supply chain – differences between sectors, distribution channels, payment schemes, and pricing components.

2.1 Access to Healthcare

2.1.1 Definition of Access

Patient access to healthcare has been conceptualized in many ways. The broader concept of access to medical care has been discussed and has evolved over the past 50 years.

Ideally, individuals should have access to healthcare at the time and place needed, through a well-defined and known point of entry and system to use medical services, ensuring equal access that is proportional and appropriate to the individual needs (Freeborn & Greenlick, 1973). In this context, access is defined as the utilization of healthcare, qualified by the requirement for care (Waters, 2000). The term “access” has also been used to denote the ability of the population at risk to seek and obtain care (Aday & Andersen, 1974).

Access to healthcare can be perceived as a function of supply and demand, where access is a product of supply factors like the geographical placement, accessibility, cost, and suitability of services; and demand factors such as the disease burden, the individual's knowledge, attitudes, and self-care practices (Aday & Andersen, 1974; Culyer & Wagstaff, 1993; Mooney, 1983).

Another perspective on access is to view it as the degree of fit between the characteristics of the healthcare delivery system and characteristics of the population (Penchansky & Thomas, 1981; Aday & Andersen, 1974). Access is understood as the interface between potential users and healthcare resources.

2.1.2 Access Frameworks

Studies exploring the concept and definition of access have been complemented by investigations seeking to understand the dimensions of access, which examined relevant aspects such as barriers, difficulties, and facilitators. The Alma Ata Declaration (World Health Organization, 1978) was a

groundbreaking document to address the urgent need for comprehensive and accessible primary healthcare around the world. Since then, the global health landscape has evolved, marked by contributions from multiple sectors, including World Health Organization (WHO), governments, healthcare professionals, the private sector, communities, academia, and researchers.

Aday and Andersen (1974) introduced a basic framework for investigating access to medical care, involving health policy, characteristics of the at-risk population, characteristics of the health delivery system, utilization of health services, and consumer satisfaction. The disaggregation of access into geographic, economic, and social dimensions allows for more operational actions by examining specific determinants of access to care.

The general concept of access by Penchansky and Thomas (1981) summarizes a set of more specific areas of fit between patient and health system—the dimensions of access—described as follows:

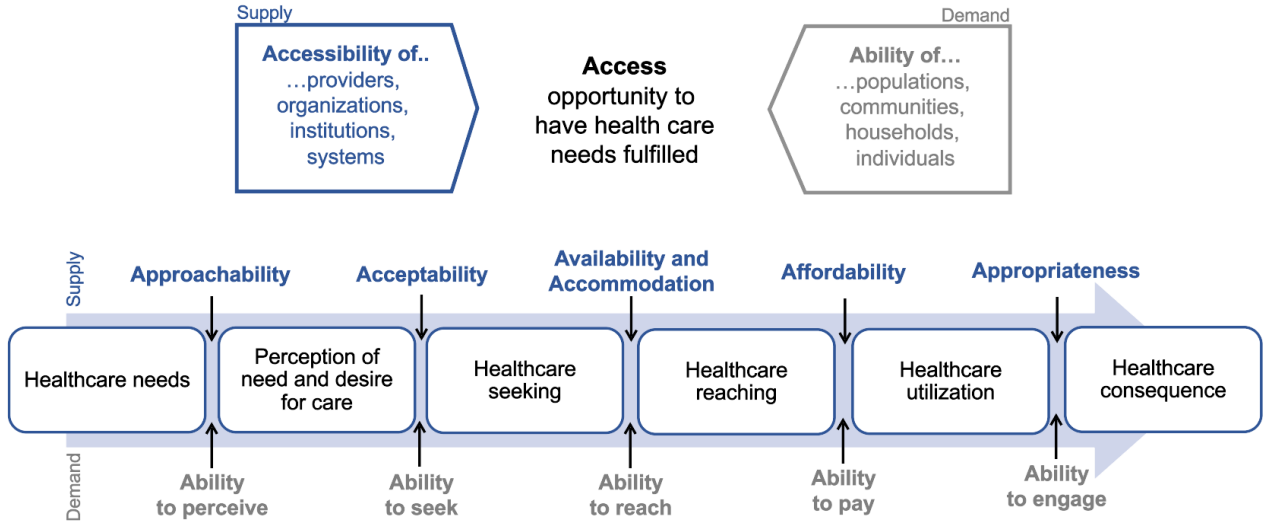
- *Availability* refers to the adequacy of the supply of healthcare services and resources (facilities, health workers, drugs, and equipment), taking into account the demand by type of need.
- *Accessibility* involves the geographical and financial aspects of reaching healthcare services, considering the proximity of facilities to the population, transportation options, travel time, and cost.
- *Accommodation* refers to the way the supply resources are organized to accept clients, including service hours, waiting times, and the appropriateness of healthcare practices.
- *Affordability* (financial accessibility) involves the ability of individuals to pay for healthcare services. It considers the costs of services, including insurance coverage, out-of-pocket expenses, patients' income, and the presence of financial barriers. It also covers the client's perception of worth relative to the total cost and willingness to pay.
- *Acceptability* assesses cultural and social aspects of healthcare, incorporating elements such as the attitudes, expectations, and preferences of both clients and providers. This dimension recognizes that patient satisfaction and adherence to healthcare recommendations are influenced by the acceptability of services provided, specifically how responsive health service providers are to the users and communities.

Levesque et al. (2013) have defined access as the opportunity to identify healthcare needs; seek healthcare services; reach, obtain, or use healthcare services; and ultimately have the need for services fulfilled. The conceptual framework for healthcare access, seen in Figure 3 (Levesque et al., 2013), is built on previous conceptualizations capturing supply-side and demand-side determinants. This framework integrates the five dimensions of accessibility proposed by Penchansky and Thomas (1981), with the five

corresponding abilities of individuals interacting with these dimensions to generate access (ability to perceive, ability to seek, ability to reach, ability to pay, and ability to engage). Levesque et al. (2013) suggest that, especially when assessing equity, access should consider resource allocation in relation to social and health needs. This concept includes broad dimensions and determinants that incorporate both demand and supply-side factors. It facilitates the operationalization of access throughout the entire process of obtaining care and benefiting from services. They introduce the term "Approachability" (Levesque et al., 2013), related to first, people facing health needs being able to identify that some form of services exist, and second, those services being reachable and having an impact on people's health. They also introduce the term "Appropriateness" (Levesque et al., 2013; Frenk & White, 1992) to denote the fit between services and clients need.

Figure 3

Conceptual framework of access to healthcare



Note. Adapted from "Patient-centered access to health care: conceptualizing access at the interface of health systems and populations," by Levesque, J.F., Harris, M.F., and Russell, G., 2013, *International Journal for Equity in Health,* 12(1), 4-5 (https://doi.org/10.1186/1475-9276-12-18).

The access to healthcare remains a complex issue, characterized by diverse concepts, interpretations, and frameworks. Often the dimensions of access are interconnected. They impact each other and can manifest at different stages during an illness' care (Levesque et al., 2013; Hornbrook et al., 1985). Consequently, measuring access is a challenging task.

Various indicators are available for measuring whether people receive services based on perceived needs. "However, a true assessment of access requires the combination of all these measures

to truly judge whether the characteristics of services, providers and systems are aligned with people, households and communities' capabilities" (Levesque et al., 2013, p. 8).

2.2 Medicines Access and Healthcare in LMICs

Our work aims to map the downstream supply chain in a Low- and Middle-Income country and identify the stakeholders and their contributions. We seek a high-level understanding of their contribution to access, limiting the scope mainly to supply-side factors related to affordability and availability of oncology medicines used to treat and manage cancer. The specific medicines selected by PharmaCo's team for this study are part of breast cancer treatment. The assumptions used for this analysis will be described to help similar future investigations in other locations.

2.2.1 Essential Medicines and Oncology

Essential medicines are defined by WHO as those that satisfy the priority healthcare needs of a specific population. According to WHO, the products listed on the World Health Organization Model List of Essential Medicines (WHO EML) should be always available in adequate amounts, be affordable, and have a proven efficacy, quality, and safety (World Health Organization, 2023). The total number of medicines in 2023 is 502 (World Health Organization, 2023). Medicines are an important part of cancer treatment for both curative and non-curative intent. At least 62 cancer medicines are classified as essential (Jenei et al., 2022).

Access to essential medicines is a fundamental element but is not isolated from the other components of a health system. To understand the downstream medicine distribution, the actors and the interconnections that influence patients' access to healthcare, a system approach is required, considering private and public sectors when appropriate, particularly in LMICs where access to these medicines continues to be inadequate (Jenei et al., 2022).

Cancer, the second leading cause of death globally, is a major public health problem accounting for approximately 10 million deaths worldwide in 2020. By 2030, it is estimated that the annual number of new cancer cases globally will increase to 24 million and that the number of cancer-related deaths will increase to 13 million annually (Ferlay et al., 2020b). The greatest burden is in LMICs, where 70–80% of deaths occur and are expected to increase for the next decade (Ferlay et al., 2020a; Ferlay et al., 2020b; Mendis et al., 2007; Lopes et al., 2013). This discrepancy is a result of the access gap faced by these countries, where more than half of the cancer medicines listed on the WHO EML remain out of reach (ATOM Coalition, 2023a; Lopes Jr et al., 2013).

2.2.2 Low- and Middle-Income Countries

In general, people in poor countries have less access to health services than those in higher-income countries, and within countries, usually the poor have less access to health services (Peters et al., 2008; De Siqueira Filha et al., 2022). Poverty can be examined as a determinant of illness or health needs, as well as by looking at disparities within the different dimensions of healthcare access. Determinants of health service access occur at the policy or macroenvironmental level, as well as the individual and household levels (Peters et al., 2008). The inverse care law asserts that, when governed by market forces, healthcare resources are distributed inversely to the need (Gottret & Schieber, 2006; Watt, 2018).

Access to medicines is considered fundamental for addressing patient access to healthcare, especially those with chronic diseases who require a reliable supply of affordable medicines (Mendis et al., 2007).

The availability of effective and affordable medicines is crucial for preventing, treating, and managing diseases to avoid morbidity and mortality:

- Availability of medicines, even essential medicines, is still poor in many LMICs, particularly in the public sector (Bigdeli et al., 2015).
- Affordability for patients varies. The price of medicines differs across countries or regions and between the public and private sector (Cameron et al., 2009). The cost is often unaffordable to the patient, especially the poorer, when not covered by universal healthcare schemes.

Barriers on the demand- and supply-side affect access to health services, especially for the poor, as universal access to healthcare programs for their citizens is still lacking in the majority of LMICs (Mendis et al., 2007; Lopes et al., 2013). The healthcare access frameworks can be utilized to analyze and identify the dimensions or aspects of access barriers. Interventions to effectively address these barriers require a combination of actions and effort from multiple stakeholders, including public-private partnerships, and government policies to ensure key medications are consistently available and affordable (Lopes et al., 2013). Effective cancer control requires a holistic approach — not limited to medications. It should consider other resources, such as adequate training, infrastructure, diagnostics, and surgical and radiotherapeutic services (Lopes et al., 2013).

Improving patients' ability to access healthcare in LMICs is an opportunity for pharmaceutical companies (Access to Medicine Foundation, n.d.). The Access to Medicine Index (Hogerzeil, 2013) has been ranking the world's 20 largest research-based pharmaceutical companies since 2008 according to their efforts to make their products more available, affordable, and accessible in developing countries.

PharmaCo was ranked one of the top 10 in the 2022 report (Access to Medicine Foundation, n.d.). Based on this analysis, improvement in access strategies and expansion for oncology products are described as opportunities for PharmaCo to increase its performance. Aligned with this recommendation, PharmaCo has joined the Access to Oncology Medicines (ATOM) Coalition – a new global initiative that aims to improve access to essential cancer medicines in LMICs (ATOM Coalition, 2023b).

Patient access to healthcare is multi-layered and dynamic. Mapping out the downstream supply chain is critical to understanding the stakeholders' contributions and limitation factors in ensuring equitable access and appropriate use of medicines across various LMIC populations. Data on medicines is fragmented along the health system. As information is a central piece of a systematic approach to access, more structured and transparent connections between information, medicines, and decision-making are required (Bigdeli et al., 2015).

2.3 Pharmaceutical Downstream Supply Chain

To enable PharmaCo to expand patient reach in LMICs, it is essential to map the downstream supply chain network, identify the key stakeholders, understand their roles and contributions to the supply chain, and examine how they influence the pricing of medicines.

2.3.1 A Generic Pharmaceutical Downstream Supply Chain Network in LMIC

The term "pharmaceutical supply chain" is not clearly defined in literature, but three main classes of terminologies are used to describe it: generic supply chain, pharmaceutical-specific, and healthcare-specific. These terminologies reflect the increasing recognition of the importance of supply chain management in the pharmaceutical and healthcare industries (Narayana et al., 2014).

Downstream pharmaceutical supply chain refers to the supply chain that feeds pharmaceutical manufacturers' "distributors, wholesalers, clinical trial settings, physician offices, and ultimately, patients" (Shelley, 2023, p. 25).

Carter et al. (2015) defines supply chain as a network that is composed of nodes and links. A node is "an establishment which is an agent that has the ability to make decisions and maximize its own gain within the parameters in which it operates (e.g., manufacturers, warehouses, transportation carriers, and financial institutions)." A link is "the connection between two nodes, representing transactions consisting of the flow of materials, information, and/or finance between nodes" (Carter et al., 2015, p. 90).

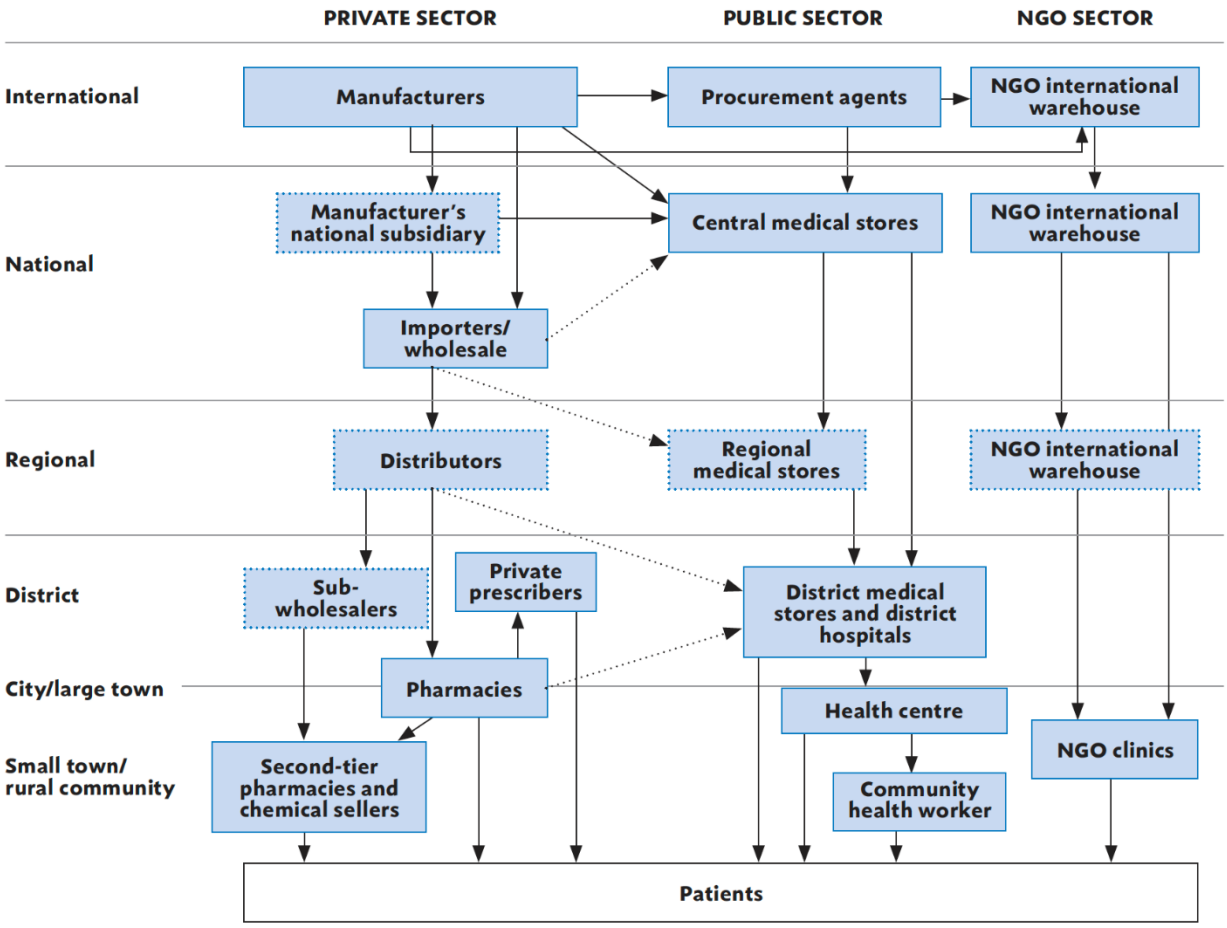
Based on Narayana et al.'s (2014) summary of "various elements of exchange" for the pharmaceutical supply chain, the relevant elements for the three downstream supply chain flows are as follows (Narayana et al., 2014, p. 29):

- Physical (Material) Flow: Pharmaceutical products
- Financial Flow: Sales, budgets, profits, royalties, costs, distribution margins, healthcare finance
- Information Flow:
    - Business process information exchange:
        - Orders, demand forecasts, lead time, sales data, billing, and invoice information
        - Contractual and regulatory information
    - Technical information exchange:
        - Consumer/patient-specific data (healthcare statistics, prescription data)
        - Product-specific data (shelf life)
    - Technological advances in information/data exchange:
        - Product tracking technology (Radio Frequency Identification [RFID], bar-coding)
        - Electronic data interchange, use of internet
        - Information systems (Decision Support System [DSS], accounting systems, Enterprise Resource Planning [ERP])
    - Information coordination/collaboration
        - Improved communication between stakeholders

Yadav et al. (2011) conclude that in the majority of LMICs, medicines are distributed through a combination of public, private, and nongovernmental organizations (NGO). The drug distribution processes of these three channels are often interrelated. However, in several low-income nations, the primary responsibility for distributing medicines falls to government and NGO sectors. Figure 4 from Yadav et al. (2011) describes the typical distribution patterns observed in the private, public, and NGO sectors in LMICs.

Figure 4

Distribution network for essential medicines in the public, private and NGO channels in developing countries



Note. Adapted from "*The World Medicines Situation 2011 — Storage and Supply Chain Management*," by Yadav, P., Tata, H. L., & Babaley, M., 2011, The World Medicines Situation 2011 3rd Edition, p. 4.

Public sector

Yadav et al. (2011) indicate the public sector distribution system is a complex network of warehouses and distribution points that are responsible for getting medicines to patients. The system is typically organized into three tiers: Central medical store (CMS) that serves as the primary warehousing and distribution point, regional stores (RS), and district-level stores (DS). In some countries, there may also be primary and secondary distribution locations. On average, only about 52% of partners primarily use the CMS for storage purposes (Yadav et al., 2011).

They further state that the distribution system is responsible for ensuring that medicines are available to patients at all levels of the health system. This is done by pushing medicines from the central

level down to the district level, or by pulling medicines from the district level up to the health facilities. The choice of which system to use depends on the country's capacity to conduct stock planning and forecasting at each level of the supply chain (Yadav et al., 2011).

Among the eight selected countries Yadav et al. studied, the logistics costs as a percent of stock value varied from 1% to 44%. They receive funding from either the public budget or, in countries where a cost-recovery system exists (predominantly in Francophone nations), through the margins established to determine the selling price (Yadav et al., 2011).

Private sector

Yadav et al. (2011) indicate the private sector distribution of pharmaceuticals involves a complex network of importers, wholesalers, sub-wholesalers, and pharmacies. Pharmaceutical wholesalers play a dual role of distributing and storing medicines to ensure pharmacies are well-stocked to fulfill their everyday needs. In many LMICs, wholesalers often have significant influence over retail pharmacies. When a pharmaceutical manufacturer has a subsidiary in a country, that subsidiary is responsible for product registration. In the absence of a local subsidiary, the importer is responsible for registration as the representative of the manufacturer, which may lead to import monopolization. Wholesalers typically utilize three primary distribution methods: delivery by their own vehicles, delivery by private couriers, and customer pick-up. While the private sector distribution system ensures product availability, especially in urban areas, the distribution margins are often very high (Yadav et al., 2011).

NGO and Faith-Based Organizations (FBOs) Sector

Yadav et al. (2011) note that NGOs and Faith-Based Organizations (FBOs) play a significant role in providing essential medicines, particularly in rural areas. The extent of their involvement varies across countries. FBOs typically utilize two primary distribution methods: healthcare facilities either pick up their orders from the FBO's distribution warehouse or submit orders electronically or by phone and receive delivery (Yadav et al., 2011).

2.3.2 Key Stakeholders in the Pharmaceutical Downstream Supply Chain

Based on an analysis of the U.S. healthcare supply chain, Burns (2002) classifies the major players of the healthcare supply chain into five categories: Producers, Purchasers, Providers, Fiscal Intermediaries, and Payers. Table 1, as referenced in works by Yadav et al. (2011), Burns (2002), and Pitta & Laric (2004), presents a comprehensive summary of stakeholders as outlined in the literature, structured according to Burns' (2002) framework.

Table 1

Overview of the stakeholders in pharmaceutical downstream supply chain

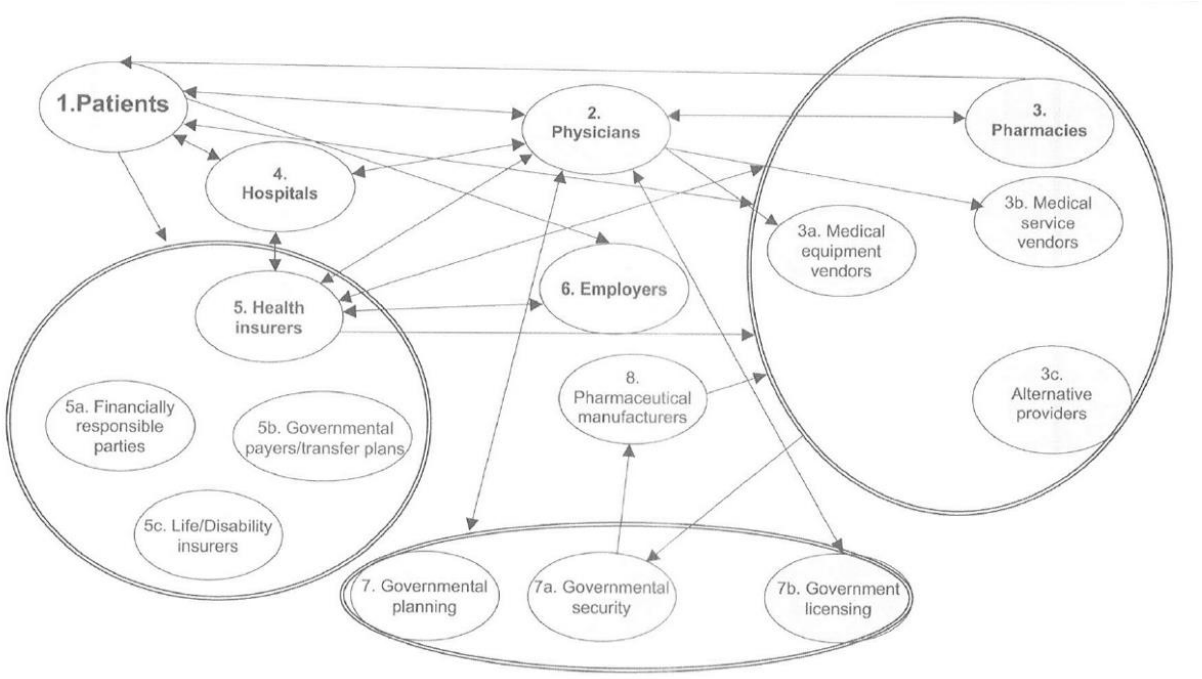
Stakeholders	Sectors	Coverage
Producers		
Manufacturers	Public, Private	International
Manufacturer's Central medical stores national subsidiary	Public, Private	National
Purchasers (resellers)		
Procurement agents	Public	International
NGO international warehouse	NGO	International, National, Regional
Central medical stores (CMS)	Public	National
Importers/wholesalers	Public, Private	National
Distributors	Public, Private	Regional
Regional medical stores	Public	Regional
Sub-wholesalers	Public, Private	District
Group purchasing organizations	Not specified	Not specified
Providers		
Pharmacies	Public, Private	City/large town
Medical stores and hospitals	Public	District
Private prescribers	Public, Private	District
Health center	Public	Small town/ rural community
Second-tier pharmacies and chemical sellers	Public, Private	Small town/ rural community
Community health worker	Public	Small town/ rural community
NGO clinics	NGO	Small town/ rural community
Independent Delivery Networks (IDN)	Not specified	Not specified
Fiscal Intermediaries		
Insurers	Public, Private	National
Payers		
Government	Public, Private	National
Employers or employer coalitions	Public, Private	National, Regional, District
Patients/Individuals	Public, Private	National
Healthcare purchasing groups	Not specified	Not specified
Third-party payers	Not specified	Not specified
Others		
Third-party logistics (3PLs)	Public, Private	All

Note. Adapted from "The World Medicines Situation 2011 — Storage and Supply Chain Management," by Yadav, P., Tata, H. L., & Babaley, M., 2011, The World Medicines Situation 2011 3rd Edition, p. 4.; "The health care value chain: Producers, purchasers, and providers (1st ed.)," by Burns, L. R. (2002), and "Value chains in health care," by Pitta, D. A., & Laric, M. V., 2004, The Journal of Consumer Marketing, 21(7), 451–464. (https://doi.org/10.1108/07363760410568671).

Additionally, Figure 5, developed by Pitta and Laric (2004), describes a segment of the healthcare supply chain, highlighting the complex interconnections among various stakeholders. However, this study is based on the U.S. healthcare supply chain, and it is not tailored to LMICs.

Figure 5

Participants and relationships in the healthcare supply chain



Note. From "Value chains in health care," by Pitta, D. A., & Laric, M. V., 2004, *The Journal of Consumer Marketing,* 21(7), 451–464. (https://doi.org/10.1108/07363760410568671).

The healthcare supply chain starts with the patient and the healthcare provider, where accurate communication is essential for diagnosis and treatment. Pharmacists join the chain, adding complexity due to drug interactions and dosing information. Hospitals create a supply chain around the patient, where the patient's response to treatment has a significant impact on outcomes. Insurance companies play a critical role in the healthcare supply chain, as they can affect access to services and influence the choice of providers and treatments. Employers also contribute to this chain by negotiating health benefits and insurance policies, which can impact employees' choices and coverage. The healthcare

supply chain is increasingly complex due to factors such as privacy concerns, insurance interventions, and tax regulations (Pitta & Laric, 2004).

2.3.3 Pharmaceutical Price Components

To properly study pharmaceutical pricing, it is crucial to understand the various components that contribute to the overall cost. While there are numerous studies on developing national policies to regulate drug prices, the actual mechanisms behind pricing are often neglected.

The WHO and Health Action International (HAI) Project on Medicine Prices and Availability adopted a comprehensive "five-stage approach" (Table 2) to assess the effect of cost components on drug prices worldwide. It states that the components of medicine prices differ between countries, across different sectors of the healthcare system, and among various medications. Additionally, these components are incurred in varying sequences. (World Health Organization [WHO], Health Action International [HAI], 2008).

The five-stage approach outlined in the report will be applied in this project, with a specific focus on costs related to imported medicines.

Table 2

The staged approach to price components for imported medicines

Stage #	Stage Name	Description
Stage 1	MSP/CIF	• Medicine's Base Price (MSP) • Costs for insurance and international freight (CIF)
Stage 2	Landed price	• Total cost at the end of Stage 1 • Finance/banking fees • International inspection paid either by the importer/buyer or be included in the selling price • Import tariff or duty • Importer's mark-up* • Port and clearing charges • Pharmacy board fee or national drug authority fee • Quality control testing cost • Local transport costs to the wholesaler, importer or Central Medical Stores • Other fees and tariffs • National taxes
Stage 3	Wholesale selling price or central medical stores price	• Total cost at the end of Stage 2 • Wholesale mark-up • Regional or state taxes • Transport costs
Stage 4	Retail price (private) or dispensary price (public)	• Total cost at the end of Stage 3 • Retail mark-up • Local or town taxes
Stage 5	Dispensed price	• Total cost at the end of Stage 4 • Value Added Tax (VAT) and Goods and Services Tax (GST) • Dispensing fees

*"A mark-up is a charge added to the purchasing price to cover the costs and margins of the wholesaler or retailer. The mark-up may be a fixed amount or a percentage charge." (World Health Organization (WHO), Health Action International (HAI), 2008, p. 133).

Note. Adapted from "Measuring Medicine Prices, Availability, Affordability and Price Components 2nd Edition," by World Health Organization (WHO), Health Action International (HAI), 2008, (https://asksource.info/resources/measuring-medicine-prices-availability-affordability-and-price-components).

The following price components should not be included in the price components analysis (World Health Organization (WHO), Health Action International (HAI), 2008): registration fees, patient fees for service, co-payments, informal charges, discounts and rebates, manufacturing price components.

Figure 6 illustrates the pricing structure of pharmaceuticals in three LMICs. Mendis (2007) explains that as drugs move through the private sector's distribution network, their prices mainly escalate due to mark-ups at the wholesale and retail levels.

Figure 6

Example of price components for three LMICs

Charge[b]	Malawi		Nepal		Pakistan
	Imported product	Local product	Imported product	Local product	Local product
Import tariff	US$ 8.70 (1200 kwacha)	NA	5%	NA	NA
Port charges	0.5%	NA	Up to 3%	NA	1%
Clearance and freight	Air: 1%; Road or surface: 0.75%	NA	Up to 3%	NA	1%
Pre-shipment inspection	NA	NA	0.125–1%	NA	Quality control testing: US$ 49.00–81.00 (3000–5000 rupees)
Pharmacy board fee	US$ 250/year	US$ 10.90/year (1500 kwacha/year)	NA	NA	US$ 19.00 (1200 rupees)
Importers' margins	Varies	NA	5%	NA	NA
Value-added tax	Exempt	Exempt	Exempt	Exempt	Exempt
Central government tax	Exempt	Exempt	Exempt	Exempt	NA
State government tax	Exempt	Exempt	Exempt	Exempt	NA
Wholesale mark-up	20–30%	20–30%	5–10%	10%	5–10%
Retail mark-up	Not regulated: 35–65% observed	Not regulated	16%	16%	10–15%

NA, not applicable (the charge does not exist).

[a] Complete information on price components and cumulative mark-up could be obtained from only two countries and for Pakistan information was available only for a local product. The imported essential medicine and the locally produced essential medicine in the private sector were selected by the investigators based on the availability of reliable information.

[b] Currency exchange rates used in these calculations were: US$ 1.00 = 136.6 Malawian kwacha, 72.1 Nepalese rupees, and 60.5 Pakistani rupees.

Note. From "*The availability and affordability of selected essential medicines for chronic diseases in six low- and middle-income countries,"* by Mendis, S., 2007, Bulletin of the World Health Organization, 85(4), 279–288, (https://doi.org/10.2471/BLT.06.033647)

The WHO has issued guidance to assist countries in creating pricing policies for pharmaceutical goods. The guidance outlines 10 pricing policies, including mark-up regulation and tax exemptions or reductions. The WHO advises a regressive mark-up system, where the mark-up rate decreases as the price of the product rises. Essential medicines and active pharmaceutical ingredients should be tax-free, according to the WHO. Additionally, the organization proposes tax reductions or exemptions, alongside safeguards to ensure that these reductions lead to lower prices for medications for consumers and purchasers (World Health Organization, 2020). Therefore, when analyzing pharmaceutical prices, it is crucial to understand national pricing policies for pharmaceutical products.

2.4 System Dynamics

2.4.1 System dynamics overview

By recognizing that organizations and their environments are complex, interconnected, and ever-changing systems, “System dynamics (SD) is a perspective and set of conceptual tools that enable us to understand the structure and dynamics of complex systems” (Sterman, 2002). It is a method to break down these systems into their basis elements and reassembles them in a way that is easy to understand and simulate (Tang & Vijay, 2001). The goal of SD is to reveal how an organization’s internal and external structure and policies impact its outcome. Then this knowledge is used to make strategic decisions that drive positive results (Sterman, 2002).

SD models rely on feedback loops to capture the complex interactions within a system. A feedback loop occurs when a change in an element of a system eventually comes back to influence that same element, leading to further change. Positive feedback loops are self-reinforcing, while negative feedback loops are self-correcting. To illustrate these intrinsic feedback relationships, causal loop diagrams (CLD) are often used. CLDs visually represent how a change in one element of the system can trigger a cascading effect, ultimately circling back to influence the original element, creating a feedback loop that perpetuates further change. These diagrams provide a clear and concise way to map out the cause-and-effect relationships between different variables within a system. These diagrams were then converted into stock flow diagrams for the purpose of simulation modelling (Sterman, 2002).

Sterman (2002) defined the modeling process as consisting of five key steps: (1) articulating the problem, which involves selecting the problem theme, identifying key variables, and defining the reference modes; (2) formulating a dynamic hypothesis, which includes generating initial hypotheses and mapping causal structure with tools like causal loop diagrams; (3) developing a simulation model; (4) testing the model; and (5) implementing changes in the real system. In Section 3 we describe this process in more depth as related to our problem context.

2.4.2 Applicability to this capstone project

Most popular methods for modeling supply chains are based on static, constant conditions. However, supply chains are dynamic systems influenced by factors like costs, lead times, and sales forecasts. The SD approach can be a more suitable modeling technique for capturing these complexities. SD allows for the representation of the intricate interactions between different supply chain variables, providing a more accurate and comprehensive understanding of the system's behavior (Moosivand et al., 2019).

In the health and medicine domain, Darabi and Hosseinichimeh (2020) found that 38% of the reviewed studies were on regional health modeling, 35% of them were on disease-related modeling, and 27% of them were on organizational modeling. 85% of the disease-related SD models focus on population-level analyses, which is aligned with SD's traditional strengths in modeling aggregate phenomena. However, despite cancer being the second-leading cause of death, there are few cancer-related SD models (Darabi & Hosseinichimeh, 2020).

Existing SD models examining health commodity availability often center on upstream pharmaceutical production and supply chain logistics. However, only a few models capture the impact of downstream supply chain problems (Nadkarni et al., 2018). A few studies under the regional health modeling are related to this project, focusing on access to medicines and overall supply chain management of essential medicines (Darabi & Hosseinichimeh, 2020):

Kumar & Kumar (2018) concluded that the factors responsible for stockout of essential medicines in India were 1) environmental factors, population growth, poverty, and the rise of lifestyle diseases leading to sudden demand increase; 2) remote areas facing longer lead times for medicine deliveries; 3) budgetary constraints limiting the funds available for medicine procurement; 4) supply chain operational issues, such as inaccurate demand forecasting, lack of safety stock, long back-end order processing time; and 5) corruption that is a major issue in LMICs. To eliminate stockout problems, they use SD models to simulate and build an optimum medicine stock for essential medicines in India rural areas. However, the affordability impact on patients' access to medicines are not in scope of their analysis.

Nadkarni et al. (2018) used SD modeling to understand and predict access trends of oxytocin in Zanzibar, Tanzania. They developed a conceptual framework to measure a weekly access ratio that is the number of available effective doses (supply) over the number of doses needed until the next deliverable (demand). The model predicted a major gap between therapeutic oxytocin procurement and availability, and an access ratio that over years would be influenced by the population increasing. However, their study did not consider affordability as part of accessibility.

According to Darabi and Hosseinichimeh's (2020) review, the pharmaceutical downstream supply chain's impact on patient access to medicine is a problem that can be analyzed using SD. This problem displays the key features that SD addresses, such as being dynamic, persistent, and complex (Sterman, 2002). Firstly, the supply chain is constantly changing over time due to fluctuations in demand, changes in regulations, and unexpected disruptions. Secondly, the issue of limited patient access remains unresolved, indicating resistance to previous solutions. For instance, when distributors increase their markups, medicine sales decrease, making it unaffordable for more patients, which counteracts the

intended effect. Thirdly, the involvement of multiple stakeholders, including manufacturers, distributors, wholesalers, pharmacies, insurers, and patients themselves, creates complex interactions that lead to unpredictable outcomes.

3 Data and Methodology

After defining our research problem and reviewing the current state-of-practice, we determined that system dynamics modeling was the optimal method to understand the complex pharmaceutical downstream supply chain and its impact on patients' access to medicines. We collected mainly qualitative data for our analysis due to the unavailability of quantitative data. Following the system dynamics process, we developed a comprehensive Causal Loop Diagram to understand the dynamic system structure.

3.1 Data sources

3.1.1 Quantitative data collection and unexpected results

The study aimed to understand how the downstream supply chain of pharmaceuticals impacts patient access to medicine, requiring historical data on pricing and inventory that influence affordability and availability, respectively. The pricing data refers to the markups of each intermediary (e.g., wholesalers, distributors, pharmacies, or hospitals) or transaction prices between them. The inventory data refers to stock events at the point of administration or inventory levels of each intermediary.

The focus was on obtaining oncology-related data from one of the seven LMICs – Indonesia, Vietnam, India, Morocco, Egypt, Nigeria, and Ivory Coast – as proposed by PharmaCo.

However, the level of price transparency is very low. One of the major third-party data providers in the healthcare industry did not have the required data set for the target countries. Another data provider specializing in African countries did not have existing data channels for the selected countries but expressed the potential to collect such data if funded.

We then approached the Access to Oncology Medicines Coalition (ATOM Coalition), a global initiative led by the Union for International Cancer Control (UICC) in collaboration with over 40 partners across the private and civil society sectors. The ATOM Coalition aims to address barriers to the availability, affordability, and appropriate use of oncology medicines in LMICs. However, they do not have the required data either.

It highlights the challenges in obtaining historical pricing and inventory data related to oncology medicines especially in LMICs.

3.1.2 Qualitative data sources

Given the challenges in obtaining quantitative historical data, qualitative data gained from interviews and literature reviews provided major inputs for our analysis. We conducted interviews with various relevant functions from PharmaCo, including Supply Chain, Sales, Access, Demand Forecasting,

and representatives from regional countries. These interviews provided valuable insights into the downstream supply chain flows, stakeholders involved, and patient and product journeys related to oncology medicines in two of the targeted LMICs.

To validate the analysis and findings, the study utilized the *Technical Report on Pricing of Cancer Medicines and Its Impacts* published by the World Health Organization (WHO) in 2018. The document describes pricing approaches and their impacts on availability and affordability of medicines for the prevention and treatment of cancer. This report clarifies questions about optimal pricing policy, approaches for pricing cancer medicines, and impacts of these pricing approaches on the affordability and availability of cancer medicines. It also discussed what are the potential unintended consequences of pricing policies or their lack, and what are the potential options that might enhance the affordability and accessibility of cancer medicines.

In WHO's report, availability was defined as "Presence of medicines in national formulary available to patients for free or for a fixed fee," and affordability for the health system was defined as "Proportion of spending on cancer medicines compared to existing expenditure on medicines or other health products and services; for individual patients – The number of days' wages needed to pay for the cost of treatment." Our study adopted the definition of availability and affordability from WHO's technical report.

The qualitative data obtained from interviews and WHO reports, together with the limited quantitative data available, formed the major inputs for the development of a Causal Loop Diagram (CLD).

3.2 Methodology

The system dynamics methodology, as described by John Sterman in 2002, provides a structured approach to understanding and modeling complex systems using causal loop diagrams (CLDs) and simulation models. The process begins with problem formulation, where the primary task is to define the system under study, identify the key variables that influence the system, and establish reference modes that describe expected behavior or trends over time. This fundamental step ensures that the model accurately represents the real-world scenario and addresses the right questions.

In the next phase, dynamic hypothesis formulation, initial assumptions are made about how variables interact. These interactions are mapped using causal loop diagrams, which visually represent the relationships and feedback loops within the system. Each variable is connected by arrows indicating positive or negative influences, helping to identify reinforcing or balancing loops that drive system behavior. This qualitative tool lays the basis for converting the diagram into a quantitative simulation model, where mathematical equations define the relationships. However, translating these qualitative

relationships into a quantitative simulation model, which involves defining mathematical equations for each connection, requires a significant amount of data that may not be currently available. Consequently, this step, though critical for deeper analysis and simulation, falls outside the scope of immediate study and can be pursued later when adequate data is accessible.

The development of a qualitative analysis and quantitative simulation model, rigorous testing against real-world data or established reference modes, and continuous refinement based on feedback are essential phases that build upon the initial qualitative analysis provided by the CLD. These steps ensure the model's assumptions are valid and accurately reflect the system's dynamics.

3.2.1 Problem Definition

The problem we are trying to address in our work is defined by the limited patient access to cancer medicines in LMICs. It focuses on downstream supply chain impact on medicines affordability and availability. The downstream supply chain entities contribute to the final treatment price at the point of administration, which is directly linked to affordability for the patient and related to drugs' availability as covered by the Causal Loop Diagram in Section 4.

We started with experts interview to map the downstream supply chain of a low-income African country of PharmaCo (

Figure **7**) to understand the medicines' physical flow.

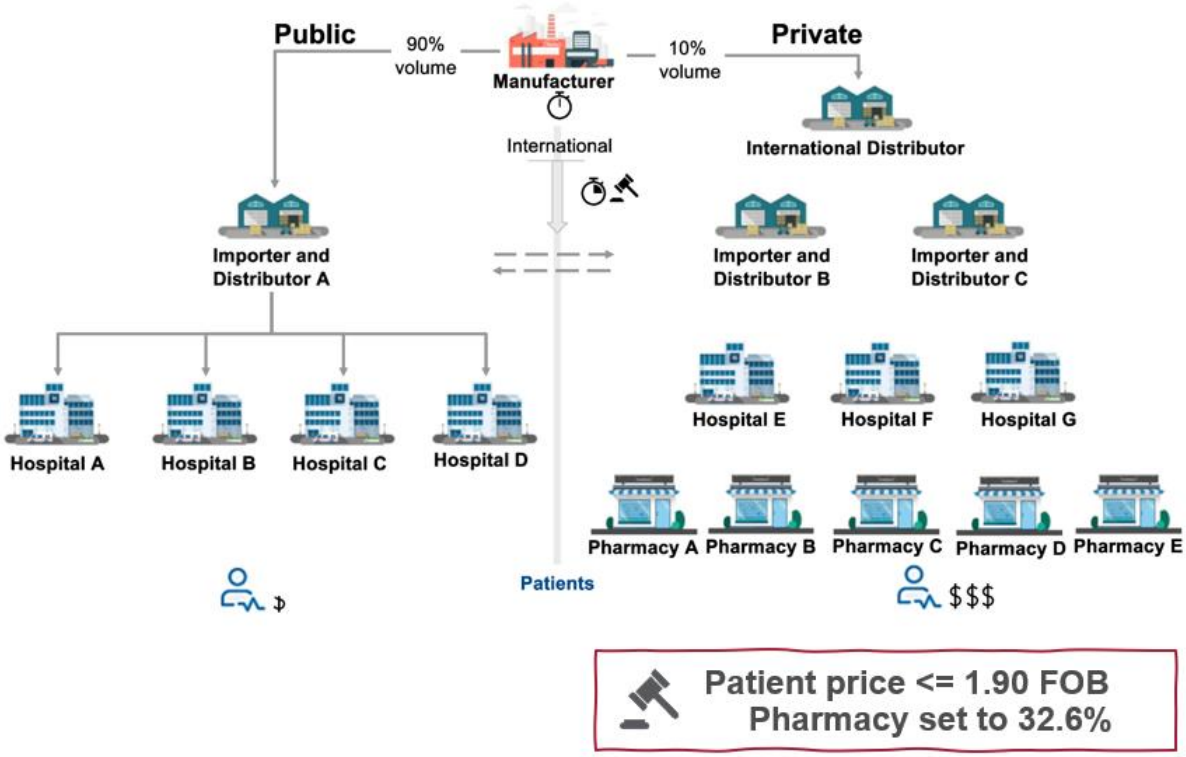
The flow of medicines goes from the international level, through the national and regional levels, and finally reaches the patients at the local level (city/large town, small town, and rural community), with both public and private sector involvement. However, the distribution channels differ in their volume and structure. Approximately 90% of the medicines are distributed through public channels, while only 10% go through private channels. Interestingly, there is a possibility for stock to be shared between the public and private sectors. The public sector has a more streamlined distribution structure with fewer intermediaries compared to the private sector. Access to cancer treatment facilities is a significant challenge in this country, as there are limited hospitals capable of treating cancer, and the majority of these hospitals are located in the most developed city of the country. This poses difficulties for rural populations in terms of accessing diagnosis, treatment, and obtaining necessary medicines.

To regulate the pharmaceutical supply chain, the government has implemented certain policies aimed at controlling pricing and ensuring product quality. Firstly, there is a minimum shelf-life requirement for imported medicines to maintain their efficacy and safety. Secondly, the government has implemented pricing regulations to enhance affordability. Price controls are often in place, and in the specific case explored, the patient price cannot exceed 1.9% of the free-on-board (FOB) pricing, which is

the cost of the goods at the point of origin. Additionally, private pharmacies' markups are set to a maximum of 32.6% to limit excessive profit margins (Cisse, 2020).

Figure 7

Illustrative Downstream Supply Chain for Oncology Medicines in a LMIC



3.2.2 Variables

In the context of system dynamics, variables are specific elements within a system that can influence the behavior of the system as a whole. These variables are used to explain the dynamics of complex system and how they interact with each other and respond to various inputs or changes. The variables are interconnected through causal relationships that can form feedback loops, either reinforcing or balancing the system's behavior. Their relationship is detailed in Section 4. These variables are important to understand the system response to different scenarios.

The Table 3 lists the variables considered to create the System Dynamics Causal Loop Diagram.

Table 3

List of variables and feedback loops

Variables Name	Description
Patient under treatment	number of individuals currently receiving oncology medication as part of their treatment regimen
Economies of scale	saving in costs gained by an increased level of volume of medicines distributed
Treatment price at administration point	cost to the patient or the healthcare system for oncology medicines at the point where they are administered
Ability to pay	capacity of patients or healthcare systems to afford oncology treatments without causing financial hardship
Patient's household income	total earnings of a patient's household
Insurance coverage	extent to which a health insurance policy covers oncology treatment
Patient out-of-pocket treatment price	the amount patients must pay themselves for their cancer treatment after any insurance coverage.
Private cancer budget	funds allocated by private sectors, such as non-governmental organizations or private insurance, for cancer treatment and medication
Government cancer expenditure	the amount of public funds spent by government agencies on cancer treatment, including medicines
Number of registered alternatives medicines	variety of oncology medicines approved to be available in the local market
Attractiveness to competition	the degree to which the oncology drug market attracts new competitors, influenced by potential profits and market size
Intellectual property (IP) effect	patent laws and IP rights affect the market competition by delaying the entry of generic or alternative drugs
Cost of holding inventory in the channel	cost associated with storing inventory that remains unsold
Willingness of local entities to hold inventory	the desire of downstream supply chain chain to stock, which is influenced by shelf life
Probability of stock-outs	likelihood of inventory depletion leading to an inability to meet patient demand for oncology medicines
Availability of medicines	presence of required oncology medicines in the supply chain ready to be distributed to patients
Total lead time	duration from ordering the medicine to its delivery and availability for patient use
Number of touches	number of times a medicine is handled or transferred between different entities in the supply chain
Number of entities in the channel	organizations involved in the downstream supply chain, such as manufacturers, distributors, and pharmacies
Shelf life	the period during which a medicine remains effective and can be used safely

Variables Name	Description
Average margin in the channel	typical profit percentage added to the cost of oncology medicines by each entity in the supply chain
Total markup from downstream entities	the cumulative increase in medicine prices due to markups applied by each entity in the supply chain
Tariffs and taxes	tariffs assigned by a government on imported oncology medicines based on their assessed value, including associated freight and insurance costs; while taxes refer to the compulsory financial charges levied by local, state, or national governments on the distribution of these medicines within the country

Note: In the causal loop diagram, variables are used to describe the system dynamics.

3.2.3 Formulation of Dynamic Hypotheses

Within the five dimensions of accessibility outlined in Figure 3 (section 2.1.2), this study proposes that the downstream supply chain influences the most significantly on affordability, corresponding to ability to pay, and availability, corresponding to ability to reach.

Based on the definition of affordability in Section 2.1.2, this study hypothesizes that the key factors influencing affordability are patient out-of-pocket expenses and patients' income. Insurance coverage is complex and varies from country to country. To simplify the analysis, this study assumes that the medicine price at the administration point positively impacts patient out-of-pocket expenses, meaning that as the price increases, the out-of-pocket expenses for patients also increase, regardless of the specific insurance scheme in place.

In turn, higher out-of-pocket expenses negatively impact affordability, making treatments less accessible to patients. Therefore, this study proposes that affordability is a function of the medicine price at the administration point, with higher prices having a negative impact on affordability. As the price of medicine increases, it becomes less affordable for patients, particularly those with limited income, thus reducing their access to necessary treatments.

For the purpose of this analysis, patient income is considered a controlled variable, allowing the study to focus on the relationship between medicine prices and out-of-pocket expenses. The following formulations are developed based on this assumption:

Notations:

- i: Entity in the channel
- n: Total number of entities in the channel
- m_i: Markup for entity i [%]
- p_i: Selling price for entity i [$]

- p_0: Ex-factory price for the manufacture [$]
- p_n: Medicine price at administration point [$]
- c_i: Operational cost for entity i [$]
- C_i: Total cost for entity i [$]
- C_n: Total cost for the last entity [$]
- c_{s_i}: Shortage Cost when understock for entity i ($/unit/time)
- c_{e_i}: Excess Holding Cost when overstock for entity i ($/unit/time)
- B_i: Penalty for not satisfying demand (beyond lost profit) ($/unit)
- g_i: salvage value ($/unit)
- CR_i: Critical Ratio, Cycle Service Level (CSL), willingness of entity i to hold inventory (%)

Markup is "the difference between the cost price and the selling price, computed as a percentage of either the selling price or the cost price (*Dictionary.Com | Meanings & Definitions of English Words*, 2024)." This study adopts the definition of markup as the difference between the cost price and the selling price, computed as a percentage of the cost price (see Equation 1):

$$m_i = \frac{p_i - C_i}{C_i} \times 100\% \tag{1}$$

The selling price of a specific entity can be expressed as shown in Equation 2:

$$p_i = C_i \times (m_i + 1) \tag{2}$$

The total cost for entity (i) is composed of the selling price of the upstream entity ($i-1$) and the entity's (i) total operational costs (see Equation 3).

$$C_i = p_{i-1} + c_i \tag{3}$$

The medicine price at the administration point can be formulated as in Equation 4.

$$\begin{aligned} p_{n=} C_n \times (m_n + 1) \\ = p_o \times \prod_{i=1}^{n}(m_i + 1) + c_1 \times \prod_{i=1}^{n}(m_i + 1) \\ + c_2 \times \prod_{i=2}^{n}(m_i + 1) + \ldots + c_n \times \prod_{i=n}^{n}(m_i + 1) \end{aligned} \tag{4}$$

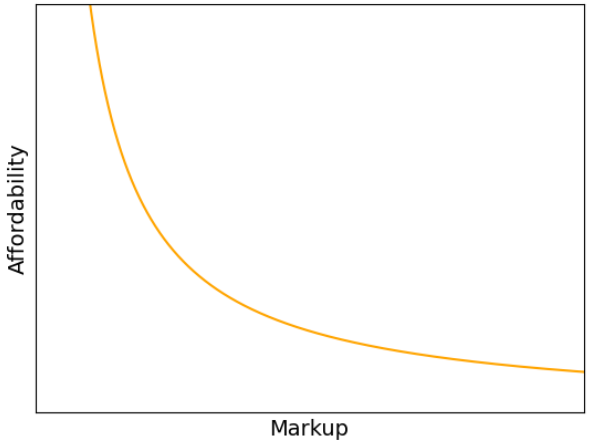
Therefore, affordability can be formulated as a function of markup (see Equation 5).

$$\begin{aligned} Affordability = f\left(\frac{1}{p_n}\right) = \\ = f\left(\frac{1}{p_o \times \prod_{i=1}^{n}(m_i + 1) + c_1 \times \prod_{i=1}^{n}(m_i + 1) + c_2 \times \prod_{i=2}^{n}(m_i + 1) + \ldots + c_n \times \prod_{i=n}^{n}(m_i + 1)}\right) \end{aligned} \tag{5}$$

Based on Equation 5, we can see that as the markup increases, it becomes less affordable for patients. The costs of the entities in the upper stream have a more significant impact on the price at the administration point compared to the costs of the entities closer to patients. Figure 8 demonstrates the relationship between markup and affordability.

Figure 8

Affordability vs. Markups



Based on Equation 1, the equation of total cost for entity i can be expressed as Equation 6:

$$C_i = \frac{p_i}{m_i + 1} \tag{6}$$

Assuming the penalty for not satisfying demand of zero ($B_i = 0$), the shortage cost for entity i, as expressed in Equation 7, indicates a direct relationship between markup and shortage cost. As markup increases, the shortage cost also increases, incentivizing the entity to take proactive measures to prevent shortages.

$$c_{s\_i} = p_i - C_i + B_i = p_i - C_i = p_i \times (1 - \frac{1}{m_i + 1}) \tag{7}$$

Assuming salvage value of zero ($g_i = 0$), the excess holding cost for entity i, as expressed in Equation 8, indicates an inverse relationship between markup and excess holding cost. As markup increases, the excess holding cost decreases. While this might suggest a greater willingness to accept overstock, it's important for an entity to consider the overall cost balance between excess holding and shortage costs to determine the optimal inventory level.

$$c_{e\_i} = C_i - g_i = C_i = \frac{p_i}{m_i + 1} \tag{8}$$

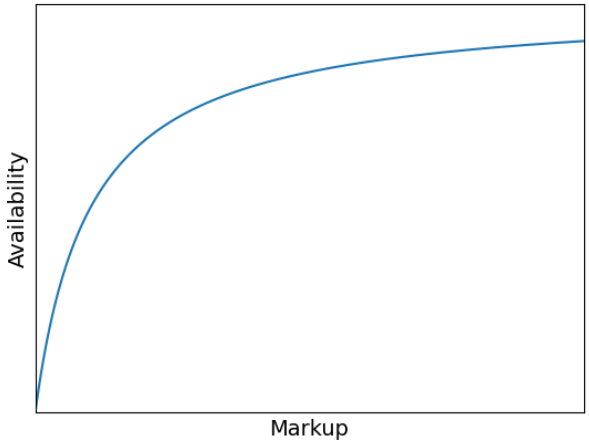
This study assume the Cycle Service Level can represent availability that represent the entity's willingness to hold the inventory for a medicine. Equation 9 indicates that as the markup increases, the CSL increases, the medicine becomes more available as the entity is more willing to hold the inventory.

$$Availability = CR_i = \frac{c_{s\_i}}{c_{e\_i}+c_{s\_i}} = 1 - \frac{1}{m_i+1} \quad (9)$$

Figure 9 demonstrates the relationship between markup and affordability.

Figure 9

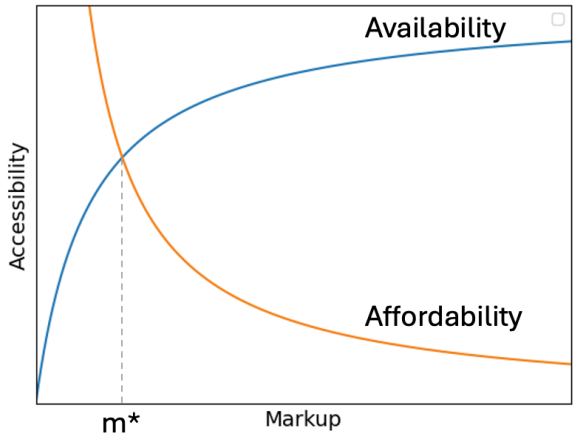
Availability vs. Markups



The dynamic hypotheses that explain the dynamics of patient accessibility to oncology medicines considered both affordability and availability (Figure 10). The key relationship to be analyzed is the trade-off between affordability and availability, which is influenced by the markup strategies employed by the various entities in the supply chain. The reference mode, which estimates the behavioral relationship between affordability, availability, and markup evolution, is described in Figure 10.

Figure 10

Reference Mode of Affordability and Availability vs. Markups



The green curve represents Affordability. As the Markup increases, the Affordability decreases, meaning that higher markups make the product less affordable for patients or consumers. This is because a higher markup translates into a higher final price for the end-user, reducing their ability to afford the treatment.

The blue curve represents Availability. As the Markup increases the Availability also increases. This suggests that higher markups increase suppliers and distributors' willingness to make the product more widely available in the market, as they can earn higher profits from selling the product.

The intersection point of the two curves represents a balance or optimal point (m^*) where both Affordability and Availability are relatively high. At this markup level, the product is reasonably affordable for patients while also being sufficiently available in the market, ensuring adequate access.

3.2.4 Definition of boundaries

In a system dynamics causal loop diagram, defining system boundaries is crucial to understand the scope and scale of the analysis. System boundaries determine what is included in the model and what is considered external to it. Setting the boundaries involves making decisions about what is critical to the problem at hand and what level of complexity is manageable for the model. This ensures that the model remains focused and relevant while also acknowledging that no system operates in complete isolation.

System boundaries define the limits of the system being modeled. They include all elements that are dynamically connected within the system and directly relate to the behavior or issue being studied, such as patients diagnosed with breast cancer, patients' deaths, medicines manufactured, medicines registered for supply in a given country, and medicines expired.

These elements are considered internal to the system, meaning their interactions and the feedback among them are of interest and are dynamically modeled. They influence and are influenced by each other within the confines of the model.

While several factors influence the pharmaceutical downstream supply chain and patient access to oncology medicines, some elements are considered out of scope for this study. These factors either do not significantly affect the system's behavior for the purpose of the analysis or would make the model overly complex and beyond the available resources to develop it.

Out-of-scope factors include aspects related to the disease itself, such as breast cancer burden, diagnosis, staging, survival rates, and incidence rates. Additionally, other treatments like surgery and radiation therapy, as well as the nuances of private and public healthcare systems, are not considered. The study also excludes factors related to the upstream supply chain, such as the medicine registration process, manufacturing process, differences in processes for essential versus non-essential medicines, production cycles, and country distribution infrastructure and reliability. Furthermore, the model does not incorporate certain operational aspects, including ordering frequencies, inventory management policies, and sales and operations planning and demand forecasting. While these out-of-scope elements may influence the system, they are not actively modeled to maintain the model's focus and manageable complexity.

3.2.5 Developing the Causal Loop Diagram

The causal loop diagram (CLD) describes the complex system dynamics related to the impact of downstream supply chain on pricing and availability of cancer medicines. This tool helps in understanding how different variables in a system interact with one another over time. In this model, the nodes (or variables) and the links (or connections) between them illustrate how changes in one aspect of the system can influence others, often in non-linear ways. The "+" and "-" signs indicate the direction of the relationship (positive or negative). A positive relationship means that if one variable increases, the other also increases (and vice versa for decreases), whereas a negative relationship means that if one variable increases, the other decreases (and vice versa). We will present and explain the CLD in the next section.

4 Results

Section 4 presents the results of our system dynamics analysis of the pharmaceutical downstream supply chain and its impact on patient access to oncology medicines in LMICs. The centerpiece is a comprehensive Causal Loop Diagram (CLD) that captures the complex interactions and feedback loops among key variables in the system. We walk through each of the major feedback loops in the CLD - Market Scale (R1), Competition (B1), Insurance Support (R2), and Inventory Management (R3) - explaining the dynamics and insights from each loop. Additional variables outside the main loops are also discussed in terms of their influence on treatment price and medicine availability. A stakeholder analysis is presented to highlight the level of interest and influence of various entities in the supply chain. Finally, we identify and discuss some of the key levers in the system that could potentially be adjusted to improve patient access. Throughout the discussion, we reference insights from a World Health Organization technical report to provide context and validation for the CLD.

4.1 Causal Loop Diagram (CLD)

Developing a causal loop diagram (CLD) involves a structured process to visually map the relationships between variables in a system, illustrating how different elements dynamically interact.

Connect the variables with arrows to show the relationship between variables and determines how it is related to others.

This diagram presents a simplified model designed to capture specific dynamics within complex systems that have numerous interacting feedback loops. Feedback loops are processes where changes in one aspect of the system influence it again after passing through other system components—like how changes in the price of treatment can affect the availability of medicine, which in turn influences the price again.

The purpose of the model is to serve as a tool for systems thinking, aiding in structuring, and guiding managerial discussions. The diagram is a simplified version targeting specific dynamics to represent very complex systems with numerous feedback loops that can amplify or dilute the effects of changes in the system.

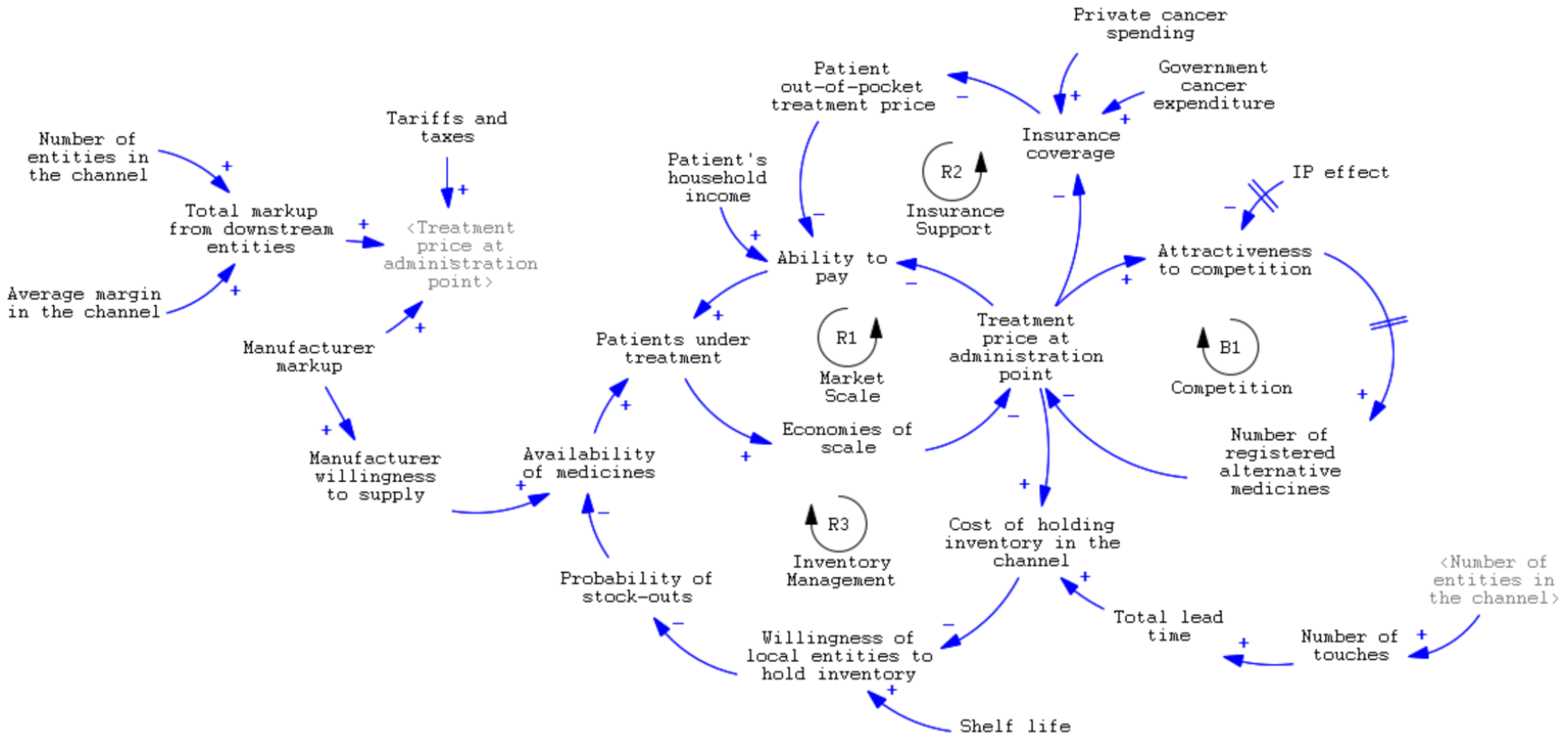
Figure 11 illustrates these feedback loops and In the context of system dynamics, variables are specific elements within a system that can influence the behavior of the system as a whole. These variables are used to explain the dynamics of complex system and how they interact with each other and respond to various inputs or changes. The variables are interconnected through causal relationships that can form feedback loops, either reinforcing or balancing the system's behavior. Their relationship is

detailed in Section 4. These variables are important to understand the system response to different scenarios.

The Table 3 lists the variables considered to create the System Dynamics Causal Loop Diagram.

Figure 11

Causal loop diagram



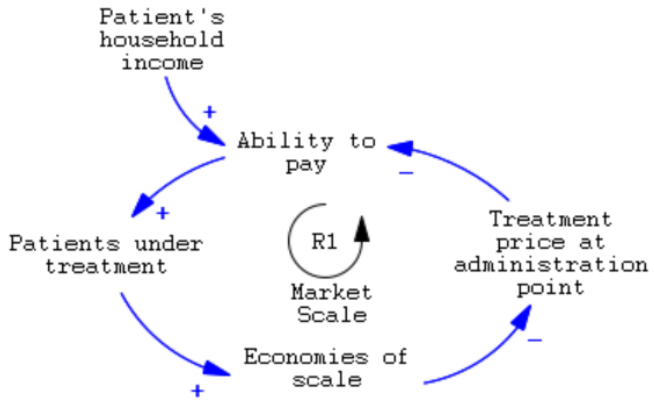
Created with Vensim PLE Version

4.2 Market Scale (R1)

The reinforcing loop Market Scale R1 seen in Figure 12 is a feedback loop that tends to amplify the size of the market or the volume of sales for cancer medicines. A larger market scale can often lead to lower unit costs due to economies of scale, meaning the cost per unit of medicine decreases as the quantity distributed increases.

Figure 12

Reinforcing loop 1 – Market Scale



The basic mechanism described by the reinforcing loop R1 Market Scale highlights the role of medicine treatment price at the administration point. This variable is the most significant factor negatively impacting patient ability to pay, which in turn reduces the number of patients receiving cancer treatment. Consequently, this decrease leads to reduced economies of scale, resulting in a higher treatment price at the administration point. The patient's ability to pay is directly related to the patient's household income when public or private insurance is not taken into account.

As market size increases, economies of scale typically improve. This can occur because fixed costs are spread over a larger number of units, operational efficiencies improve with larger production runs, and bulk purchasing and distribution of materials can reduce costs. When economies of scale are achieved, this often results in a reduction in the price of treatment at the point of administration. Essentially, the cost savings from producing more units of the drug can be passed on to healthcare providers and ultimately to patients. As more patients are treated (due to lower prices and increased ability to pay), the size of the market continues to grow, which can further increase economies of scale. This brings us back to the beginning of our reinforcing loop.

The R1 loop indicates limited economies of scale due to market size restrictions caused by lower ability to pay compared to higher treatment price.

WHO insights:

The reinforcing loop R1 suggests that as economies of scale increase, treatment prices may decrease, enhancing patients' ability to pay, leading to more patients being able to afford treatment and potentially further increasing market scale. The market scale loop explains the interactions for the downstream supply chain; however, this dynamic may be limited to downstream entities.

The WHO report points out that despite the potential for economies of scale, the prices of cancer drugs have often been set high, affecting patient access and ability to pay. This suggests that the potential benefits of economies of scale may not be fully realized in practice due to manufacturers' pricing strategies that do not necessarily reflect production costs.

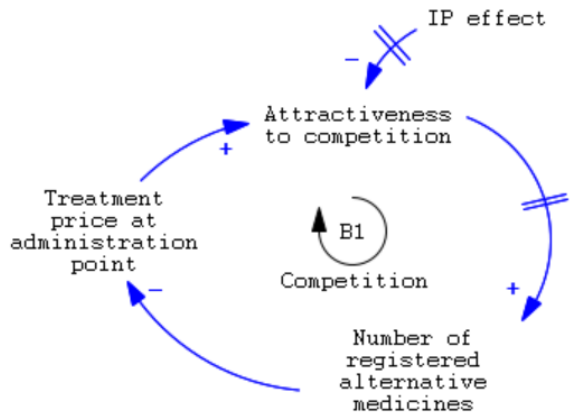
The WHO report notes that the marginal costs of producing medicines are relatively low compared to their prices and are likely to remain low over a wide range of quantities produced, suggesting potential economies of scale. It is generally accepted that long-term marginal costs of production tend to decrease over a wide range of outputs before increasing due to diseconomies of scale.

4.3 Competition (B1)

The Competition B1 feedback loop shown in Figure 13 acts as a regulatory mechanism within the cancer medicines market. It serves to adjust market dynamics by increasing the entry of competitors when treatment prices are high, which should theoretically lead to lower prices due to increased competition. This feedback loop is inherently designed to stabilize the market by ensuring that prices do not escalate to the point of limiting access. However, it is subject to delays as indicated in Figure 13.

Figure 13

Balancing loop 1 – Competition



The Competition balancing loop describes how a higher treatment price at the administration point increases attractiveness to competitors. This increase potentially leads to a higher number of registered alternative medicines, which in turn reduces the treatment price. This loop is affected by two delays: one caused by intellectual property rights that limit the attractiveness of competition (IP effect), and another caused by the time required to register a new medicine in the country once it is legally possible to apply for it.

WHO Insights:

Intellectual property rights and market exclusivity periods, while briefly mentioned as the "IP effect" in the causal loop diagram, have broader implications, including promoting or discouraging competition, affecting the number of alternative medicines available, and influencing market size and economies of scale. The WHO report discusses how intellectual property rights and market exclusivity contribute to high medicine prices and may limit market competition. The number of registered alternative medicines is limited by intellectual property laws that grant market exclusivity to patent holders. Market dynamics extend the period during which original manufacturers can maintain higher prices without facing competition. The WHO report also states that market exclusivity is a key factor in incentivizing innovation and research by ensuring that companies can recoup their investment in research and development, but it must be carefully considered, as high financial returns and market dominance can lead to excessive risk-taking in R&D, which may not always be aligned with the most pressing public health needs. The report notes that while it is expected that prices for cancer medicines would fall after the end of market exclusivity, many biologics continue to generate high sales revenues even after patent

expiration, suggesting that the effects of market exclusivity may extend beyond the patent period due to factors such as the complexity of manufacturing biosimilars.

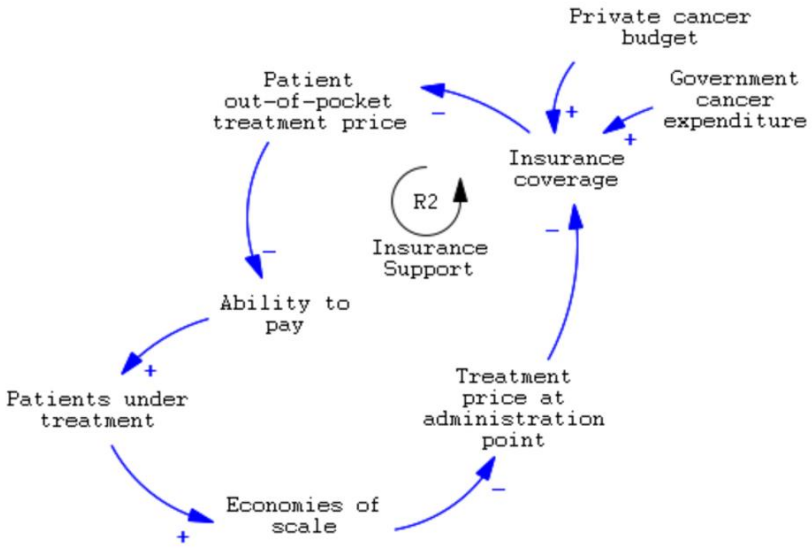
In summary, the document emphasizes that patent law and market exclusivity play a multifaceted role in shaping the market for cancer medicines, influencing not only the availability and pricing of these medicines, but also the broader dynamics of innovation and access within the healthcare system, which is beyond the scope of this work.

4.4 Insurance Support (R2)

The reinforcing loop R2 presents an overview of insurance support to improve patients' ability to pay by providing financial assistance to reduce patients' out-of-pocket treatment costs. Figure 14 illustrates the causal relationship between private and public cancer spending and its influence on patient access to treatment.

Figure 14

Reinforcing loop R2 – Insurance Support



As the price of treatment at the point of administration decreases, public and private insurance coverage can be expanded within the same budget constraints. This expansion leads to a reduction in out-of-pocket costs for patients. As a result, lower out-of-pocket costs improve patients' ability to pay, which ultimately increases the number of people treated. This sequence of effects demonstrates the significant impact of insurance coverage on patient access and affordability.

WHO insights:

The report describes how global spending on cancer medicines has grown faster than the number of cancer patients. Global spending on cancer medicines has outpaced the growth of overall healthcare spending, particularly in low-income countries.

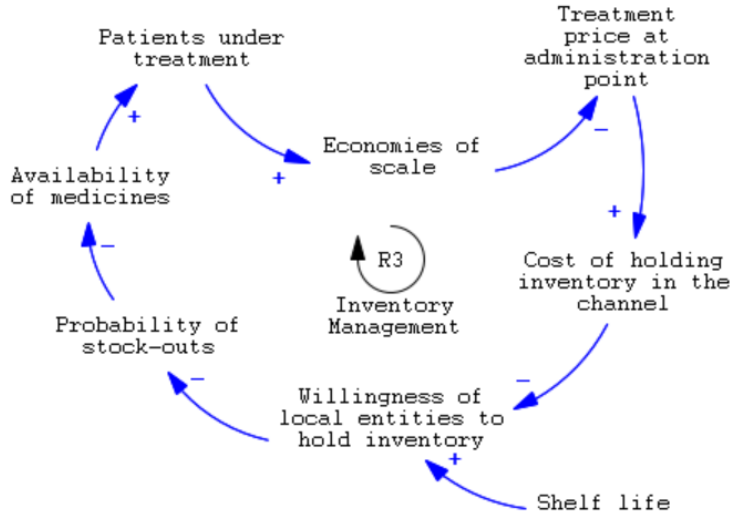
Insurance programs play a critical role in mitigating out-of-pocket costs for patients. According to the report, the cost of cancer treatment for individuals in countries such as India and South Africa could be as high as 10 years of wages, and even in the U.S., the cost could be as high as 1.7 years of average annual wages. Without insurance, cancer treatment is unaffordable for many, underscoring the importance of insurance support in enabling access to care. However, the report suggests that even with insurance coverage, the high cost of cancer treatment can lead to financial hardship for patients, indicating that insurance coverage may not be comprehensive. Patients facing financial hardship due to the cost of cancer treatment often compromise on care, reducing doses or skipping treatment altogether to save money.

4.5 Inventory Management (R3)

Inventory costs are not merely storage expenses but also include costs associated with handling the medicines. When these costs are substantial, local entities might opt for smaller inventories, which can compromise medicine availability. Figure 15 shows the impact of the impact of treatment price on cost of holding inventory in the channel.

Figure 15

Reinforcing loop R3 – Inventory Management



The inventory management loop R3 suggests that a higher treatment price causes a lower availability of medicines.

Figure 15 demonstrates how the treatment price influences inventory costs, affecting how much stock local entities are willing to hold. High treatment prices can discourage these entities from maintaining large inventories, thereby increasing the likelihood of stock-outs. The occurrence of stock-outs at the point of administration results in a reduction in the availability of medicines, thereby limiting the number of patients that can be treated.

Meanwhile, the shelf life of medicines plays a critical role in inventory decisions. A medicine with a longer shelf life allows entities to hold stock for extended periods, decreasing the chances of stock-outs and ensuring better availability of medicines to patients.

WHO insights:

The availability of oncology medicines must be understood within the context of the healthcare system, as the system capacity and the population served differ. The efficiency of the health system, including expenditures on cancer medicines and the overall functioning of healthcare, impacts the availability of these medicines.

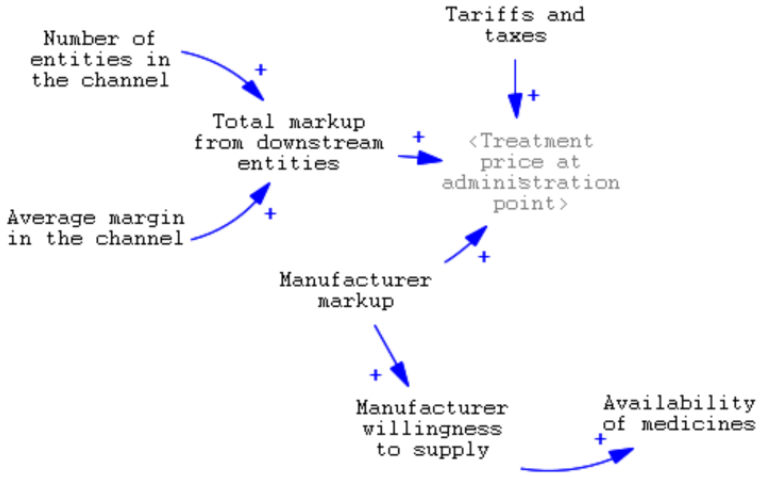
The WHO reports mention that patients in countries with lower income had lower access to cancer medicines, with availability often subject to higher out-of-pocket payments by patients. Despite the increase in spending on cancer medicines mentioned in Insurance Support (R2), the availability of cancer medicines remains low in many countries. Regulatory environments, including approval processes and inclusion in the emergency medicines list, can affect the availability of cancer treatments. Effective inventory management is crucial in the pharmaceutical supply chain to ensure that medicines are available when needed without incurring excessive costs, such as expending fees.

4.6 Additional Variables

Figure 16 illustrates other key variables to be considered when assessing the downstream impact on treatment price and availability of medicines at the administration point.

Figure 16

Downstream contribution to treatment price and medicine availability



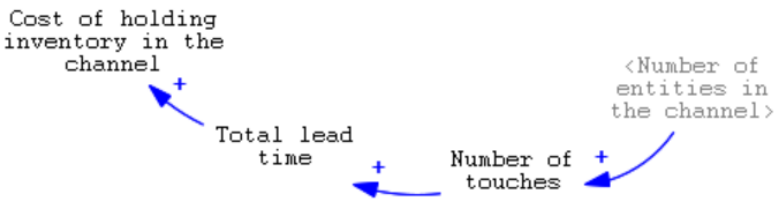
The higher the number of entities in the distribution channel and the average margin maintained by these entities, the greater the cumulative markup from downstream entities, leading to an elevated treatment price at the administration point. Markups and fees, which are applied at various stages of the supply chain, vary considerably across countries and healthcare systems.

Increases in tariffs, taxes, and manufacturer markups also contribute to a higher treatment price at the administration point. Elevated tariffs and taxes can significantly raise cost barriers to accessing cancer medicines. Conversely, a lower manufacturer markup tends to decrease the manufacturer's willingness to supply, resulting in a reduction of their contribution to the availability of medicines.

In Figure 17, the relationship between the supply chain's complexity and inventory costs is illustrated.

Figure 17

Number of downstream entities and cost of holding inventory in the channel



As the number of entities within the distribution channel rises, so does the number of touches—each point in the channel where the product is handled or processed. This increase in touches contributes to a lengthier total lead time. The extended lead time, in turn, results in higher costs associated with holding inventory in the channel. These interconnected factors, which illustrates how the supply chain structure influences overall inventory expenses, are a part of the Inventory Management R3 reinforcing loop.

Figure 16 and Figure 17 illustrate the dynamics between cumulative markups in the supply chain and the downstream entities' willingness to hold inventory. As markups increase, the cost burden shifts downstream, leading to a decreased willingness among these entities to hold inventory. This reluctance, in turn, impacts the accessibility of medicines by reducing their availability and affordability. To mitigate these issues, fostering collaborative relationships and sharing benefits across the supply chain is crucial. Such collaboration could yield more substantial long-term outcomes, although it necessitates frequent feedback and an increased willingness to share risks among all parties involved.

4.7 Key Stakeholders

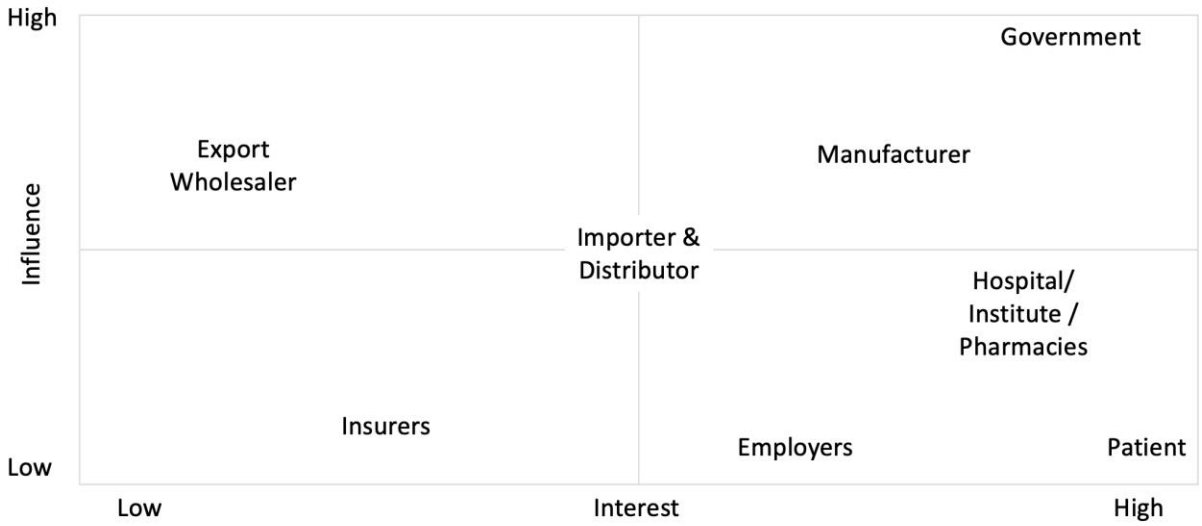
In Section 2, we examined the identity of stakeholders in the context of medicine availability. We identified the stakeholders and their basic attributes. In this section, we dive deeper into their respective roles. Our focus will be on understanding the unique functions and influences each stakeholder has on the availability and accessibility of medicines.

Figure 18 Stakeholder Analysis Matrix — Availability of Medicine presents a framework for assessing the varying levels of interest and influence among different stakeholders in the healthcare and pharmaceutical sectors regarding the availability of medicine.

The vertical axis represents the degree of influence each stakeholder has, ranging from low to high. Influence here means the power or capacity to effect changes in medicine availability, whether through policy, market control, or other means. The horizontal axis measures the level of interest of each stakeholder in the availability of medicine, from low to high. Interest is indicative of the degree to which the availability of medicine affects the stakeholder or the extent to which the stakeholder cares about this issue.

Figure 18

Stakeholder Analysis Matrix – Availability to Medicine



In the stakeholder analysis matrix of medicine availability, entities are plotted based on two dimensions: influence and interest. Those in the upper-right quadrant, such as Governments and Manufacturers, are critical actors with high influence on, and high interest in, the pharmaceutical market. They are instrumental in shaping policies and have considerable stakes in the economic and health outcomes of their actions.

The upper-left quadrant includes entities like Export Wholesalers, who possess substantial influence in the global distribution of medicines, yet their direct stake in patient access is relatively low. Their role is crucial in the international logistics of the pharmaceutical supply chain, but they are more removed from the end-user impact.

On the other hand, the lower-right quadrant features stakeholders such as Patients and Healthcare Providers, who have a strong vested interest in the availability and affordability of medicines, but their ability to influence market dynamics is limited. Their perspective is critical for understanding patient needs and demand-side challenges in healthcare. Employers also belong to this quadrant; they show practical concern for the health of their workforce through health benefits but exert limited influence beyond their organizational boundaries.

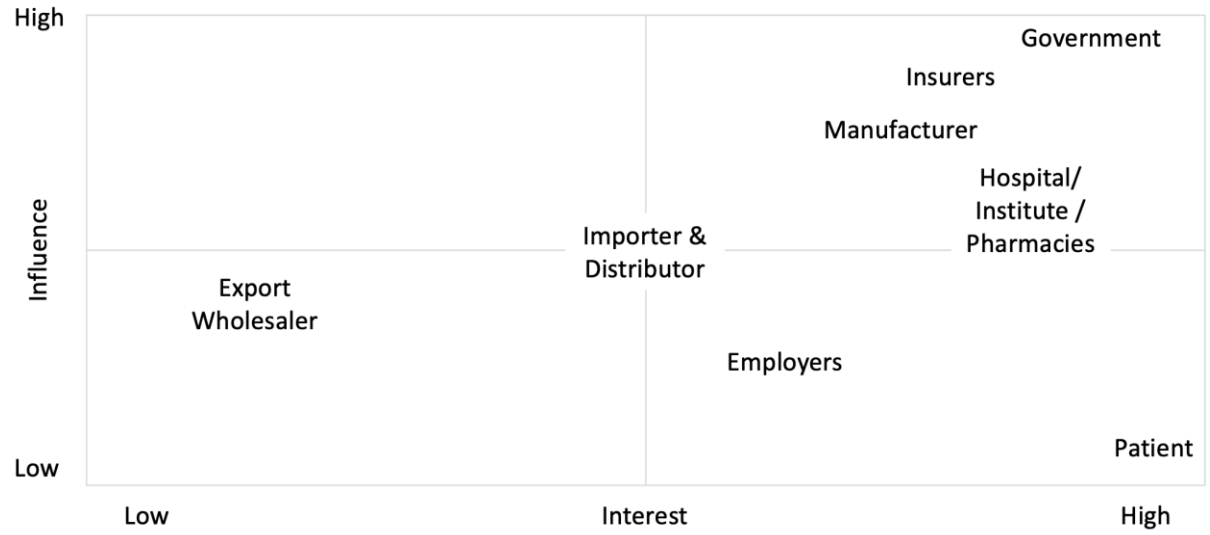
Lastly, the lower-left quadrant sees stakeholders like Insurers. They engage with the system primarily through financial transactions and have a monetary interest in the cost and supply of medicines. However, their direct influence on supply chain mechanics and policymaking is less pronounced compared to more dominant players like governments.

Understanding where each stakeholder falls on the matrix is vital for formulating engagement strategies and policy interventions. It assists in identifying which relationships to prioritize and how to approach each stakeholder, ultimately aiming to optimize medicine availability and public health outcomes.

Figure 19 showcases the Stakeholder Analysis Matrix with a focus on the affordability of oncology medicines. Stakeholders are plotted against two axes: influence and interest, providing insights into their potential to affect and their concern about drug pricing.

Figure 19

Stakeholder Analysis Matrix – Affordability to Oncology Medicines



In the top-right quadrant are stakeholders with both high influence and interest. The Government stands out as a major player, with the power to shape healthcare affordability through policymaking, potential subsidies, and price controls. Insurers also occupy this space, having the authority to determine coverage levels that influence out-of-pocket expenses for patients. Manufacturers, with their pricing decisions, directly control the affordability of their products. Hospitals, Institutes, and Pharmacies are also here, as their markups and pricing strategies within the healthcare system can significantly impact the cost to the patient.

In the bottom-right quadrant, we see stakeholders like patients, who are deeply concerned about the affordability of medicines but often lack the power to influence pricing. Employers are also positioned here; while they can affect affordability through the health benefits they offer, their influence on pharmaceutical pricing is indirect and limited.

Moving to the bottom-left quadrant, Importers and Distributors are featured. They play a role in the supply chain and thus have some impact on pricing and end-user affordability, particularly through the volumes they distribute. Export Wholesalers also fall into this quadrant; they are involved in the supply chain, yet their control over the pricing strategies or policies affecting affordability is not as pronounced.

An integrated approach that acknowledges the varying levels of influence and interest of these stakeholders is essential to optimize patients' access to medicine. Collaborating with high-influence groups could drive systemic changes that improve affordability in the healthcare sector.

5 Discussion

The Causal Loop Diagram (CLD) seen in Figure 11 demonstrates the interconnections of variables affecting the accessibility of cancer medications. The feedback loops Market Scale, Competition, Insurance Support, and Inventory Management highlight the dynamic factors influencing the price and availability of cancer treatments.

In this chapter, we identified key system levers such as private and government spending, insurance coverage, tariffs, and manufacturer markups. Each lever offers a point of intervention to potentially lower treatment price and improve medicine availability. These elements are connected to specific mechanisms that stakeholders can adjust to influence outcomes, helping to guide the system toward improved patient access to essential cancer treatments.

In addition, this chapter provides targeted recommendations for making effective use of these findings. We advocate for systematic data collection to monitor key patterns such as stock-out events, treatment costs, and patient income levels, which are critical to assessing affordability and availability. In addition, understanding the structure of the system through detailed metrics such as treatment prices, cancer budgets, insurance effects, and more will inform targeted policy reforms. These data-driven insights will help stakeholders regulate mark-ups, restructure fees, and prioritize access to improve overall system performance in cancer care.

5.1 System Levers

System levers refer to mechanisms within a system that can be adjusted to influence outcomes. System levers can be policies, practices, or other controllable factors that stakeholders can manipulate to affect the treatment price at the point of administration. Leveraging these factors allows policymakers, healthcare providers, insurers, and other stakeholders to guide the system toward desired goals, such as improved patient accessibility to cancer medicines. Effective use of system levers requires understanding both the direct consequences of adjustments and the indirect effects that may propagate through the system's network of interdependencies.

Based on the causal loop diagram and the stakeholder analysis, the identified levers within the larger healthcare economic system are as follows:

- Private cancer spending and government cancer expenditure: These levers denote the financial resources allocated for cancer within a healthcare budget. Increasing both government and private sector spending creates the potential to enhance access to cancer care by subsidizing treatments and making them more affordable.

- Insurance coverage: The analysis shows that insurance plans have a significant effect on patient access to cancer treatments. The coverage scope, which includes the variety of treatments covered and the degree of coverage, directly influences patients' out-of-pocket costs and overall affordability.
- Tariffs and taxes: According to the diagram, adjusting tariffs and taxes on cancer medicines is a lever that can directly enhance affordability.
- Manufacturer markup: This is a critical factor identified for setting the initial price of new medicines.
- IP effect: The intellectual property regime, including patent laws, can limit competition, thus maintaining higher prices, as indicated by the stakeholders' positions in the analysis.
- Total markup from downstream entities: Markups that occur throughout the supply chain, from manufacturing to the point of sale, are highlighted as a significant factor affecting the final price of cancer medicines.

Additionally, the causal loop diagram highlights the role of supply chain management — how reducing the number of entities involved and efficiently managing the medicine supply chains, streamlining inventory management, can affect the final cost of medicines to patients.

These levers, as described by the causal relationships and stakeholder analysis, are critical to shaping policies and practices that can affect the affordability and availability of cancer care.

5.2 Recommendations

As we navigate through the complexities of the supply chain, we recommend that the pharmaceutical industry prioritize systematic data collection and adopt transparent pricing practices. To address the lack of clear, transparent pricing and decision-making processes that impact the availability and affordability of medicines, we support WHO's recommendation that companies disclose markups, rebates, and inventory levels. This transparency will not only improve patient affordability but also facilitate negotiations and procurement practices.

We recommend a coordinated effort to collect data at every supply chain stage to effectively address these challenges. We believe that such detailed insights are crucial for informing targeted policy reforms, including regulating markups, restructuring fees, and prioritizing accessibility over profit maximization.

5.2.1 Data for Key Patterns

Pharmaceutical companies should prioritize systematic data collection to remove key barriers impacting patient access to cancer medicines.

On availability, companies should track the frequency and duration of stock-out events at the point of care delivery, as well as inventory levels across the supply chain intermediaries. This data is crucial for diagnosing root causes of supply shortages. As defined by WHO (2018), availability represents the "presence of medicines in national formularies available to patients for free or for a fixed fee." Simply having a snapshot of availability at one point in time is insufficient to understand persistent access issues.

Furthermore, countries should monitor cancer medicine expenditures over time, out-of-pocket treatment costs faced by individual patients, and patient income levels. This affordability data, which WHO (2018) defines as "proportion of spending on medicines compared to health expenditures" and "number of days' wages for treatment costs," is critical for assessing affordability.

Lastly, hospitals should record the reasons why patients do not initiate or continue cancer treatment. If affordability is the primary driver, then pricing and markup policies must be reexamined to better align with the realities of consumers' incomes. However, if availability issues like stock-outs are the main reason, then incentives may be needed across the supply chain to increase willingness of the downstream entities to stock and distribute medicines.

5.2.2 Data to Understand System Structure

For a comprehensive understanding of the healthcare system's structure, we recommend collecting, analyzing, and interpreting the variables as outlined in Section 3.2.2. The data include patient demographics and treatment data, financial metrics, supply chain details, and regulatory impacts. By focusing on key areas such as the number of patients under treatment, treatment costs, household incomes, and out-of-pocket expenses, alongside metrics like cancer budgets, IP effects, and supply chain dynamics (including stock levels and lead times), stakeholders can gain essential insights. This information is crucial for identifying potential areas for intervention and designing strategies to improve the overall system's performance in providing cancer treatment.

Additionally, assumptions about the dynamics of LMICs need to be validated against data to understand their magnitude and influence. Some key assumptions directly impacting the downstream supply chain include less competition among manufacturers; poor healthcare infrastructure affecting the delivery of care; low household incomes influencing patients' ability to afford treatments; limited or variable insurance coverage for oncology medicine; and the cost of transportation to treatment centers,

potentially being an additional burden and barrier to access for patients. There are also few institutions capable of treating cancer, which tends to concentrate expertise and resources in more developed cities.

6 Conclusion

The goal of this capstone project is to enhance the understanding of the pharmaceutical downstream supply chain's impact on patient access to oncology medicines LMICs. By employing a system dynamics approach and developing a comprehensive causal loop diagram (CLD), the study identified key stakeholders, their roles, and the complex interactions that influence medicine affordability and availability.

The CLD revealed several critical feedback loops, including market scale, competition, insurance support, and inventory management. These loops highlighted the interconnectedness of various factors in which we identified key levers within the system, such as cancer expenditure, insurance coverage, tariffs and taxes, markups, IP effect, and supply chain management practices, which can be adjusted to improve patient access to medicines.

However, the study faced challenges in obtaining quantitative historical data on pricing and inventory in the LMICs, making it difficult to conduct quantitative analysis on this topic. This lack of transparency in pricing and decision-making processes emphasize the urgent need for systematic data collection and transparent reporting practices across the pharmaceutical supply chain. As defined by the World Health Organization (WHO, 2008), “price transparency refers to disclosure of the net transaction prices of cancer medicines between the sellers (e.g. manufacturers, service providers) and the payers/buyers (governments, consumers).” The key stakeholders should disclose and disseminate information to relevant parties to ensure their accountability.

Despite the complexity of the topic, system dynamics proves to be an effective tool for understanding the interconnections among the various players in pharmaceutical supply chains. However, to dive deeper into the subject, more data is needed for further analysis. This includes data for stakeholder validation of reference models and data to validate simulations.

To address the challenges, this study recommends prioritizing systematic data collection on historical patterns and variables, such as patient numbers under treatment, treatment prices, patient out-of-pocket costs, stock-out events at the point of administration, inventory levels, margins, tariffs, taxes, and lead times. This data can inform targeted policy reforms and supply chain interventions. Additionally, encouraging transparency in pricing practices can facilitate effective negotiations and procurement practices. Engaging high-influence stakeholders, such as governments, manufacturers, and insurers, is crucial to drive systemic changes and align incentives towards efficient distribution and accessibility of medicines.

The next step we recommend would be to build a quantitative system dynamics model using the data collected to validate the reference model. This model can be used to simulate the impact of various policy interventions and supply chain strategies on medicine affordability and availability in LMICs.

By adopting a transparent, data-driven approach and fostering collaboration among stakeholders, the pharmaceutical industry can work towards ensuring equitable access to life-saving oncology medicines for patients in LMICs.

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