Access to innovative medicines in a middle-income country
Moye Holz, Daniela Denisse

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2019

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.
Discussion and Conclusions

Chapter 7
New and better medicines are coming into the market improving health outcomes and the quality of life of patients. In recent years, the World Health Organization (WHO) has designated many of these new and innovative medicines, including several for cancer, as essential medicines. In some middle-income countries (MIC), cancer care has been included in the service package of their health systems to achieve Universal Health Coverage (UHC). If high-cost innovative essential medicines can considerably improve cancer care, then these health systems face considerable challenges to ensure widespread access to these medicines.

The general aim of this thesis was to study how a MIC addresses the problem of guaranteeing access to high-cost innovative essential medicines. Our research used Mexico as an example of a MIC, and cancer medicines as an example of innovative essential medicines. Thus, the main research question of this thesis was: *How does a middle-income country such as Mexico promote access to innovative and essential cancer medicines, as part of universal health coverage?*

This final chapter summarizes and discusses the main findings of this thesis, and expands on the methodological considerations and implications for policy makers and future research.

### 7.1. Main findings

**Which policy strategies and approaches has the Mexican government taken to improve access to (innovative) medicines, within the National Pharmaceutical Policy (NPP) context?**

Mexico has taken a series of independent measures without developing one single and comprehensive national pharmaceutical policy (NPP). The government has implemented the following measures: pooled procurement of (mainly generic) medicines for public health institutions; the creation of the coordinating commission (Comisión Coordinadora para la Negociación de Precios de Medicamentos y otros Insumos para la Salud - CCNPMS) to negotiate single public procurement prices of patented (single-source) medicines; and the creation of the “CesMed” platform for sharing information between public health institutions on medicine prices and best procurement practices. These measures intended to improve access to medicines, generate savings on the pharmaceutical expenditure and promote the efficient use of resources.
Discussion and Conclusions

What is the effect of a price negotiating commission on public procurement prices and the accessibility of innovative cancer medicines?
The prices of eight innovative cancer medicines (bevacizumab, dasatinib, imatinib, nilotinib, rituximab, sorafenib, sunitinib, and trastuzumab) decreased during the period of study (2010 to 2016) when expressed in US dollars (considering inflation). Price differences between and within health institutions showed that the CCNPUMIS has failed to monitor institutions’ adherence to the negotiated prices. We also found that the quantities of products procured in the public sector increased over the study years, suggesting improved availability of medicines.

What is the utilization rate and access to innovative cancer medicines in the public sector in Mexico?
Over a period of six years, the use of selected innovative cancer medicines increased in the public sector, particularly for rituximab, imatinib, and trastuzumab. Overall, the use of the selected cancer medicines was lower in the Mexican Social Security Institute (IMSS) and the Ministry of Health (MoH) facilities than in other social health insurance (SHI) institutions. There were also geographical differences, with an increased use of these medicines in the central region of the country. Use was lower in the other parts of the country and did not increase much in those areas.

What is the actual availability, price, and affordability of essential cancer medicines in Mexico?
Availability of a range of selected cancer medicines (n=49) for the treatment of breast cancer, colorectal cancer, leukemia, and renal cancer did not reach the WHO’s target of 80%, neither in the public nor in the private sector, and with little difference between them. Prices in the public and private sectors were lower than in other Latin American (LATAM) countries and were largely comparable with international reference prices. Yet, most essential cancer medicines were unaffordable to patients in both sectors. Innovative (patented) cancer medicines (n=19) were less available and less affordable than other essential cancer medicines (n=30).

How do health professionals perceive the accessibility of cancer medicines in the public sector in Mexico?
The selection of cancer medicines for public procurement followed the public insurance treatment protocols, yet most clinicians considered these protocols to be outdated and the range of cancer medicines procured to be too limited. Public
hospitals that outsource pharmaceutical services seem to have achieved better availability and more efficient use of resources than those that were supplied through central procurement carried out by the MoH. Informants perceived the availability of cancer medicines as sufficient; however, for certain types of cancer, health professionals encountered barriers such as shortages, and poor coverage and hospital accreditation by the public health insurance “Seguro Popular” (People’s Health Insurance – SPS). Informants reported that in response to such barriers, the hospitals used several ad-hoc actions to mitigate their effect on individual patients.

7.2. Reflections on main findings

We will reflect on the main findings using the WHO Access Framework,¹ which distinguishes four main components of access to essential medicines: selection, affordability, sustainable financing, and reliable health systems.

Selection and availability of essential cancer medicines – the case of innovative essential medicines

We found that cancer medicines covered by SPS were more available than other cancer medicines, and particularly for priority diseases where government action plans exist, such as leukemia and breast cancer.²,³ In Chapter 5, we considered essential medicines for two diseases covered by SPS for children only and two diseases covered by SPS for adults and children. We included in our sample medicines that were not covered by SPS but were included in the national clinical guidelines (NCG) and the clinical guidelines of the National Institute of Oncology (INCAN). However, we believe that SPS covers a comprehensive amount of essential cancer medicines. In 2015, approximately 80% of cancer medicines listed in the WHO model of Essential Medicines List (WHO-EML) were covered by SPS.⁴,⁵ As our results show, the selection of medicines by the SPS had a direct effect on their availability to patients.

Stakeholders (Chapter 6) confirmed that medicines covered by SPS were more regularly available than those without SPS coverage. They reported that the selection of medicines for procurement planning and treatment prescription is largely based on the SPS protocols and coverage. SPS tries to provide access to a comprehensive package of interventions for more prevalent diseases, including
cancer. However, stakeholders perceived that the lack of SPS coverage can set limits to access to medicines in general and in particular be a barrier for access to new innovative essential medicines. SPS does not cover many of the new innovative medicines that have been included in the national formulary. This fact was evidenced in Chapter 4, where medicines covered by SPS for priority diseases (rituximab, trastuzumab, and imatinib) were used more frequently than the other medicines that were either not covered or covered only for children’s cancers (bevacizumab, nilotinib, dasatinib, sorafenib, and sunitinib). The lack of coverage of these medicines by SPS may also explain the low use and access at the MoH facilities in comparison to other SHI institutions.

As explained in Chapter 6, the selection process of cancer medicines for reimbursement in Mexico is largely effective in focusing procurement, supply, and use. For example, imatinib is covered by SPS for leukemia and its availability was better than nilotinib and dasatinib (therapeutic alternatives to imatinib). In 2017, the WHO-EML included nilotinib and dasatinib. The future will tell whether the SPS will include these medicines in its coverage package and if their availability and use will then increase.

**Affordability of innovative essential cancer medicines and other essential cancer medicines**

The government has contained public procurement prices of essential medicines through pooled procurement (mainly for generic medicines and recently also for patented medicines), price negotiations (Chapters 2 and 3), and the use of reference pricing for SPS medicines. Our results in Chapter 5 show that public procurement prices of cancer medicines in Mexico were lower than prices in other LATAM countries and some were comparable to international reference prices. For innovative medicines in the public sector, Mexico has used mainly price negotiations to improve their affordability. Our assessment of public procurement prices (Chapter 3) showed a continuous decrease in the prices of selected innovative (patented) cancer medicines, and the number of medicines and companies participating in the price negotiations has increased every year (Chapter 2). Although a direct causal link is difficult to establish, the CCNPMIS mechanism seems to have decreased the prices of patented medicines when expressed in US dollars, preventing price increases in the public sector despite
inflation and currency devaluation, and therefore generated savings to the public health system (Chapter 2 and 3).

We also found that prices of innovative medicines in the private sector were much higher than the public sector, but were lower than retail prices in some other countries of the region (Chapter 5). In the private sector, high prices of medicines are probably due to a lack of price regulation in Mexico, as only a voluntary pricing mechanism exists for patented medicines in which companies set a maximum retail price (MRP) (Chapter 2). High prices in the private sector usually lead to catastrophic expenditure or to treatment cessation, in particular when low-income patients are unable to get their medicines in the public sector. The government has been able to implement some pricing policies to contain the high prices of medicines in the public sector (e.g. CCNP MIS). The government and other relevant stakeholders should now also develop medicine pricing policies for the private sector to prevent the impoverishing effects of high-cost medicines.

Our results also showed that most cancer medicines in the public and private sectors were unaffordable to patients without SPS coverage (Chapter 5). Of these medicines, innovative (patented) medicines were the least affordable. Our informants also felt strongly that the high prices of medicines were a barrier to better access to these medicines at public health facilities and at private pharmacies (Chapter 6). Medicines can account for about half of cancer treatment costs. Considering that cancer treatments often require more than one type of medicine, treatment as a whole becomes even less affordable than the price of a single medicine would suggest. This often leads to catastrophic expenditures. Despite the government’s efforts, the high prices of these medicines and the lack of sufficient resources to procure these medicines remain important barriers for access. Therefore, additional measures to reduce the prices of medicines and improve their affordability for patients are necessary to further increase access to (innovative) essential cancer medicines.

Access to essential cancer medicines within the health system – procurement and financing of cancer medicines, and other barriers to consider

Chapters 4 and 6 showed inequities in resource allocation to essential cancer medicines. In Chapter 4, the volumes of innovative medicines procured were
unequally distributed across health institutions and geographical regions. Access at IMSS and MoH facilities was lower than in other SHI institutions. IMSS is the largest healthcare provider and medicines purchaser in the country.\textsuperscript{16} Even though IMSS covered all the innovative medicines studied, the institution faces barriers to provide optimum access to these medicines and does not address the needs of all cancer patients. Access at MoH institutions was the lowest in comparison to the other health institutions. MoH facilities are mainly (though not only) financed through reimbursement from SPS. This fact is worrisome as close to 40% of the population, including the most vulnerable sections, receive healthcare through MoH facilities. Stakeholders (Chapter 6) also reported that institutions lack the necessary resources to procure the appropriate amounts of innovative medicines to provide access to the best level of treatment to their patients, forcing institutions and patients to rely on charity.\textsuperscript{20} These findings call for a revision in financing mechanisms and budget allocation per patient per disease. The main healthcare providers (IMSS and MoH) should have the necessary resources to procure and provide access to the innovative medicines that they have decided to cover. Sufficient financial resources should ensure timely and appropriate access to treatment and care, in order to reduce reliance on charity.

We also found differences in procurement and supply systems between hospitals, which influence the availability of medicines (Chapter 6). Facilities using outsourced pharmacy services reported more timely and better access to cancer medicines than hospitals supplied by the state’s MoH through centralized procurement, which reported more problems with the timely availability of medicines. Thus, the government and health institutions should review the centralized procurement procedures in order to improve access to all essential cancer medicines. In general, there should be stronger efforts from each institution – in collaboration with state and federal MoHs – to move towards more efficient and reliable supply and procurement mechanisms.

Additionally, the geographical differences in access at MoH facilities (Chapter 4) highlight the lack of investment of the federal and state governments in the equal provision of access to cancer care and innovative (and other essential) cancer medicines, particularly in regions where the cancer burden is higher (e.g. the northern and western regions in Mexico).\textsuperscript{17,18} In Chapter 6, stakeholders reported that geographical barriers (e.g. long distance to health facilities) contribute to late
diagnosis when patients do not seek healthcare and/or to disease progression when patients do not get treatment in a timely manner or decide to stop treatment due to traveling costs. Health facilities suffer from the lack of capacity to expand accreditation by SPS to treat more cancers in addition to a lack of budget allocation from the state government for cancer and/or late or limited reimbursement by SPS. This lack of capacity and limited financial resources for cancer medicines can leave patients untreated or with the need to pay for their treatment out-of-pocket in the private sector. The regional allocation of resources should consider the health needs and priorities of each state and each institution, and the number of patients they treat, in order to bring care closer to patients.

The government has reported that the price reductions achieved by the CCNPMIS have led to increased savings in the public sector (Chapter 2). However, the government has not reported how these savings are being used. The government should consider reinvesting such savings in the pharmaceutical expenditure. The government could also invest such savings in the health system to allow an increase in health financing, the procurement of more medicines and for building procurement capacity in institutions with procurement and supply inefficiencies.

**Government actions towards improved access to innovative and essential cancer medicines**

Mexico has implemented several measures to improve access to medicines without developing a single and comprehensive NPP that presents a coherent action plan addressing all aspects of access to medicines (Chapter 2). Mexico has adopted mechanisms in isolation to ensure the safety and quality of medicines, the rational use of medicines using the national formulary, and the implementation of pooled procurement and price negotiations to improve the efficiency of pharmaceutical expenditure and access to medicines. These strategies may have contributed, to some extent, to the stabilization of pharmaceutical expenditure in Mexico. Pharmaceutical spending decreased from 287 US dollars (USD) per capita in 2010 to 282.2 USD per capita in 2015. Our data showed that the government has reported on savings achieved, but has failed to monitor the implementation and compliance of these measures and their final impact on access to medicines.

As described above, the government implemented price negotiations through the CCNPMIS but this has not resulted in the improved access that is needed.
Although each negotiation round has included more medicines and has achieved more savings, the impact of these negotiations and the actual access to these medicines in the public sector has neither been measured nor reported (Chapter 2). Based on our assessment of eight innovative essential cancer medicines (Chapter 3), we noted that the prices of most patented medicines did decrease. However, we did not find evidence of a single procurement price as we expected (based on the price negotiation process) because, in practice, many hospitals procured innovative medicines at different prices. Thus, the CCNPMS has not been able to fully implement and enforce the negotiated price of patented medicines, which seriously weakens the real effect of the negotiations. Strict enforcement of the negotiated price will promote transparency and will improve the impact of the CCNPMS on prices of medicines in the public sector and ultimately access to medicines by patients.

Extrapolating main findings to other innovative essential medicines in Mexico and other middle-income countries

Our findings are consistent with those of previous research conducted in Mexico about access to medicines, particularly at the MoH level for SPS patients. Studies focusing on access to medicines in general for SPS patients, including ours, reports that availability remains below WHO’s 80% availability target. It is very likely that the barriers we found to access to cancer medicines, such as geographic differences, distance to health facilities, differences in the type of coverage, unreliable supply, and lack of affordability, are equally valid for other NCD medicines. For hospitals providing cancer care in addition to other treatments, lessons from resolving the barriers to access to cancer medicines could be extrapolated to other medicines for NCDs. Other NCDs also require care and treatment in secondary and tertiary level health facilities that may not be close to patients; treatment for some NCDs also require several medicines and access can be dependent on coverage, affordability, and their timely procurement and availability. Therefore, strengthening the healthcare system to address barriers to optimum cancer care and access to cancer medicines, could ultimately improve access to treatment for all NCDs.

Innovative cancer medicines are among the most expensive new medicines in the pharmaceutical market. It is very likely that the price differences we found between and within institutions are true for other innovative medicines beyond
cancer. It may be – but more research is necessary – that the prices of other innovative medicines for NCDs have followed a similar pattern: no price increases in the public sector despite price increases in the private sector (when expressed in local currency), and price decreases in the public sector when expressed in US dollars.

7.3. Methodological considerations

The main strength of our study is the combination of various quantitative and qualitative methods to analyze pharmaceutical policies and to measure access to innovative medicines. We first summarize the various methods that we use and then discuss their strengths and limitations.

Data sources
To answer the research questions we used the following data sources:

- **Literature and document review**
  We used government reports, policies and official documents, and peer-reviewed and grey literature. These publicly available sources allowed us to collect data on strategies and policies on access to medicines as reported by the government and other relevant stakeholders. We gathered this information from government and international organizations’ official websites and using search engines such as Google Scholar, PubMed, Scielo, and others.

- **Trends in use and prices of medicines**
  We used public procurement data that consisted of the amounts of medicines procured, the actual price paid per medicine per institution, and expenditure. We collected these data individually from each public health institution in the country providing cancer care through the national transparency platform, which allows the public to request information directly from any public or governmental institution.

- **Adapted WHO/HAI Methodology**
  We used the standard WHO/Health Action International (HAI) survey methodology, which collects data on the actual availability of a standard basket of essential
medicines at the time of data collection, public procurement prices, and prices paid by patients. These data allow the calculation of medicines’ availability and affordability. We adapted the standard WHO/HAI methodology to meet our research requirements (see below).

- **Qualitative methods using stakeholder’s interviews**
  We collected information on opinions and insights from stakeholders through semi-structured interviews to collect experiences, opinions, insights and other information provided by stakeholders on access to cancer medicines. The interviews followed an interview guide that considered different aspects that influence access to medicines in a hospital setting, including the selection of medicines and procurement planning, the procurement procedures, the actual availability of medicines, the barriers that hinder access to cancer medicines, and the actions taken to counter these barriers.

**Methodological strengths**

- **Literature and document review**
  In Chapter 2, we carried out a systematic review of publicly available literature. In particular, the strength of using government documents and reports was that it allowed some accountability from the government’s side as the main source of information and on the progress made on its policies. By using peer-reviewed and grey literature, we could contrast the government’s reports on the effects and outcomes of policies with third-party reports from experts. This approach ultimately offered the most holistic view possible to the government’s progress towards access to medicines and the development and implementations of its policies.

- **Trends in use and prices of medicines**
  We used public procurement data as reported by public health institutions. The main strength of using procurement data is that it allows price and procurement transparency to document and analyze trends in use and prices. In Chapter 3, we used procurement data to identify price trends of innovative medicines throughout a six-year period. The main strength of the methodology and data used in this chapter was that we were able to obtain information on the price changes in time, and between and within health institutions. This approach yielded new evidence of the effect of the negotiating commission on price uniformity across the country.
In Chapter 4, we used drug utilization research methods to measure the use of innovative cancer medicines as a proxy of access. The main strength of using drug utilization research methods is that these methods offer information on trends in use and allow for comparison of use and access between different insurance schemes and geographical regions. We believe that the methods we used provided valuable information on use and price trends that policymakers and relevant stakeholders should consider to work towards more equitable access to medicines and improve the role of the negotiating commission.

- **Adapted WHO/HAI Methodology**

In Chapter 5, we developed and used a specific adaptation of the WHO/HAI methodology for assessing access to cancer medicines in the Mexican context. The main strength of our adapted methodology was the development of a new sampling framework for public health facilities and the selection of cancer medicines. This new sampling framework considered regions and hospitals according to the marginalization levels, the OECD (Organization for Economic Co-operation and Development) health indicator, the number of hospitals at each state, and the cancer incidence. The number of facilities we surveyed exceeded the minimum number of facilities recommended by the WHO/HAI methodology, leading to representative and valid results. We also changed the standard WHO/HAI list of essential medicines to survey a list of cancer medicines only, enabling us to obtain all relevant information. Thus, we selected four cancers that were responsive to pharmacological treatment: breast cancer, colorectal cancer, leukemia, and renal cancer. From these diseases, we selected medicines that were included in the national formulary and included in clinical guidelines, resulting in a list of 49 essential cancer medicines (both generic and patented). This number was sufficient to give a clear picture of the access to medicines for these diseases. We developed this adapted methodology in close collaboration with experts from HAI.

- **Qualitative methods using stakeholder's interviews**

In Chapter 6, we used qualitative methods to collect information on experiences and barriers to access to cancer medicines from stakeholders working at cancer hospitals. The main strength of our methodology is the detailed and in-depth information we gathered from stakeholders in the field about how health facilities experience access to cancer medicines. Using the sampling of hospitals for
Chapter 5 we identified and interviewed 67 informants, including oncologists, pharmacists, procurement officers, social services personnel, SPS managers and hospital directors. The sample was sufficient to reach saturation and find differences and similarities about aspects that influence access to cancer medicines in public hospitals. The information provided by stakeholders allows for a more comprehensive assessment on access to medicines as it considers the insights and experiences of stakeholders in the field to improve the quality of healthcare, procurement efficiency and access to medicines.

Methodological limitations

The methods that we used also have some limitations, in particular regarding data collection and data processing.

- **Literature and document review**
  Regarding the use of literature and document review, in Chapter 2, we were unable to obtain some government documentation that would have allowed for a complete assessment of the impact of the policies we analyzed. Our assessment explained the policies implemented and their results as reported by the government and in the literature. However, these reports lacked details on the resulting impact and effect of these policies on access to medicines. Moreover, we could not obtain information from relevant stakeholders. The information provided by stakeholders could have provided a more in-depth description of the policies and their effects, impact, and results, and even detailed information missing from public documents.

- **Trends in use and prices of medicines**
  In Chapters 3 and 4, the main limitation was the inability to verify the quality and completeness of the procurement data reported by health institutions. In addition, gathering data had its challenges as some states and institutions were reluctant to provide the information we requested in full (i.e. by providing partial data for only some years of study or not providing any data). Some states (Hidalgo and Michoacan) did not provide any data at all. We had data limitations particularly in the northern, western and eastern regions, and for the years 2010 and 2011. This is another example of the inefficiency caused by the fragmentation of the system: a single procurement data reporting and sharing system that would allow timely and efficient data sharing does not exist, neither for external researchers nor for the management unit of the central government itself. Being unable to verify the
quality of procurement data and the underreporting from states and institutions could have biased our results and may have led to an underestimation of the use of medicines in those regions of the country where data was scarce.

Furthermore, in Chapter 3 we used the maximum retail price (MRP) (as reported by the Ministry of Economics) as a proxy of prices in the private sector. However, a real comparison between the public and private prices of innovative medicines was not possible as we were unable to obtain information on real patient prices in the private sector. We requested these data from IMS Health, but the information provided did not include actual prices of medicines. In addition, it would have been preferable to make a complete assessment of the CCNPMMIS using actual negotiated prices, but we could not retrieve data on the actual negotiated price, as these data are confidential. We were therefore not able to assess whether the prices actually paid by the hospitals were above or below the negotiated price, which may have led to some inaccuracy of the estimated prices. However, we believe that using median prices provided a close assumption of the actual negotiated prices and at least provided information on the most commonly paid prices of the selected medicines.

When using drug utilization research methods (Chapter 4), we compared the volume of medicines used against the whole population as a denominator, rather than the number of patients with cancer, which may have added some inaccuracy to our estimate. At the time of data collection, the cancer patient registration system in Mexico had not been implemented yet. Once this repository with actual data on cancer patients (incidence, diagnosis, morbidity, progression, cured, diseased, etc.) is available, further research should compare the volume of medicines procured against the number of patients with the disease to better measure use and consider targeted measures where needed. Using actual patient data should increase the accuracy of the estimates of use and access to medicines.

- Adapted WHO/HAI Methodology

In Chapter 5, our adaptation of the WHO/HAI methodology used a convenience sample of private pharmacies instead of a systematic sample as suggested by the original WHO/HAI methodology. This was done because cancer medicines are not marketed in standard private pharmacies in the country. Instead, cancer medicines are only available in selected pharmacy chains. We were also unable to
survey private hospitals providing cancer care (chemotherapy and some pharmacy services). The private sector in Mexico is private-for-profit, and private hospitals and their pharmacies are private companies that do not allow transparency of their data. Therefore, the limitation of this study resulted in the private sector being understudied. However, the effect of this lack of representation in our study is probably limited since only around 20\%\(^1\) of the population (mostly in the upper economic quintiles) get cancer care in the private-for-profit sector; our results, therefore, remain relevant for the other segments of the population.

- **Qualitative methods using stakeholder’s interviews**

In Chapter 6, a limitation may have been that we did not interview one key group of stakeholders: the patients. We acknowledge that patient experiences and opinions are important to understanding gaps that need to be addressed to improve the quality of cancer care and access to treatment. It was not possible within the limited scope of this research project to get the necessary ethical clearance for such patient interviews within our timeline, both in Groningen and in Mexico. Comprehensive qualitative health research on access to medicines and the quality of healthcare requires patients’ experiences to provide a full assessment and further improve access to care and medicines.

### 7.4. Policy implications

In this section, we will discuss the implications of the findings as presented in this thesis. As in the introduction, we will use the WHO Access Framework\(^1\) to guide our policy recommendations in the four main components of access to essential medicines: selection, affordability, sustainable financing, and reliable health systems.

**Selection of cancer medicines**

We found that SPS has become a strong instrument to improve the accessibility of medicines and guarantee access to cancer care to the population. The SPS needs to have plans in place for the expansion of its coverage, based on the regular update of treatment protocols and thus the selection of essential medicines. This expansion should also consider including innovative medicines through transparent mechanisms with consideration of pharmacoeconomic principles, safety, efficacy,
health outcomes and the right to health to guarantee access to the most cost-effective interventions. When updating treatment protocols, these should be aligned with the latest objective medical evidence, national clinical guidelines and specialists’ expertise (e.g. considering the INCAN’s clinical guidelines). The implementation plan should be realized in full, to guarantee treatment harmonization across regions, SHI and health institutions, guaranteeing an equal level of quality and health service for all citizens. Facilities accredited by SPS should guarantee access to medicines covered by SPS. Similar to WHO’s concept of essential medicines, inclusion of medicines into SPS coverage requires that they become equally accessible to all who need them.

We also recommend that experts and representatives of all SHI institutions and the SPS be involved in updating the national formulary. This could promote the quality, equality, and equity of healthcare delivery. The ultimate goal should be that all medicines listed in the national formulary are available in all SHI institutions and health facilities, and covered by SPS. The update of the cancer medicines list in the national formulary should also be included in the National Cancer Control Program, in an effort to harmonize cancer treatment across the country and provide equal access to all patients. This move would be a key step in reducing health inequities in Mexico.

**Affordability of cancer medicines**

Prices in the public and private sectors in Mexico are unaffordable for patients despite being lower than international prices. The government should further strengthen the functioning of the CCNPMIS to guarantee its sustainability, and improve its impact and performance by developing indicators and monitoring mechanisms to guarantee that health facilities respect the negotiated prices and do not undercut them through separate arrangements with suppliers.

Besides the existing negotiating process, the government should include other pricing policies recommended by the Lancet Commission, the WHO, and other actors. For example, additional pricing measures such as compulsory licensing and price transparency for single-source products should be considered as it will be difficult to achieve UHC without them.
In the private sector, the government should move towards pharmaceutical pricing regulation. Medicines in the private sector continue to be more expensive than in the public sector, especially for (patented) innovative medicines. The voluntary pricing mechanism by the pharmaceutical industry does not take into consideration the country’s income level and patients’ ability to pay. The government should play a more active role in price setting for patented medicines entering the Mexican market, using all well-known effective measures.

All these policies and strategies should be included in a comprehensive NPP. This policy should consider the selection, affordability, financing, and quality use of essential medicines as part of fully achieving UHC. The required components and checklist of essential human rights and health system components for NPP, as recently listed by Perehudoff, could serve as a basis for the development and implementation of the Mexican NPP.

**Sustainable financing and sustainable health system**

The government (through the national and state MoHs) should increase the health budget to further strengthen and improve the functioning of health facilities and SPS. Continuous actions to strengthen the SPS should include: revising its coverage, financing, and reimbursement procedures; expanding coverage to other prevalent cancers for adults (e.g. stomach cancer, lymphomas in young adults, etc.); and expanding the accreditation of health facilities throughout the country to bring healthcare closer to the patients. This investment should include building infrastructure and capacity of health facilities to provide adequate and quality cancer care. These actions should aim at strengthening the financing and care system to expand and guarantee access to medicines and furthermore reduce the current reliance on charity.

To maintain the financial sustainability of SPS, the health system should implement price and procurement monitoring systems to increase transparency and analyze the healthcare delivery at accredited health institutions. This approach can assist SPS to identify where resources are being spent and where inefficiencies are occurring. These actions should be part of an integrated effort between SPS, the MoH and all health institutions to find the gaps and barriers that prevent effective access to medicines.
When addressing cancer coverage in particular, the National Cancer Control Plan should complement efforts to strengthen the health system overall as a core element. This plan should integrate SPS and the other SHI institutions under the same programs and strategies. More support and collaboration within institutions can help to reduce the fragmentation of the health system, and thus inequalities and inequities in access to healthcare towards better control of NCDs, including cancer.

The government needs to be more transparent about how it uses the savings from price negotiations and pooled procurement. We recommend re-investing these savings in expanding the quantities or the range of innovative essential medicines covered by the system, in strengthening the health system, and in building health capacity.

**Lessons for other low- and middle-income countries**

As the cancer burden of disease continues to increase, it is necessary that low- and middle-income countries (LMIC) consider including cancer coverage into their health coverage schemes to reach UHC. Cancer care is complex because a full range of preventive, diagnostic, treatment, and palliation services are required. LMICs should, therefore, develop cancer control plans as part of their health system reform. The experiences from how a MIC such as Mexico has taken important steps towards UHC and is now expanding its cancer coverage may provide some lessons for other LMICs.

To provide cancer coverage and access to cancer care and medicines, Mexico implemented the Fund against Catastrophic Expenditure (FPGC) as part of the SPS to have the necessary resources to finance high-cost diseases. SPS has continuously expanded coverage since its implementation. Currently, Mexico provides complete cancer coverage to children and adolescents, and comprehensive cancer care for a number of prevalent cancers in adults. An insurance scheme usually reimburses healthcare based on its treatment protocols and list of interventions. SPS provides treatment guidelines and reimburses therapies accordingly. It also provides reference prices for institutions/hospitals as a maximum for reimbursement. Accreditation of health facilities by SPS attempts to achieve an equal and harmonized level of care across the country, reducing healthcare disparities and inequalities. Implementing similar public health
schemes, with similar measures to harmonize treatment and expand coverage, could improve health systems in LMICs to reach UHC.

The price negotiating commission in Mexico has achieved lower prices of innovative medicines in the public sector. Other MICs could also use such negotiating strategy together with other pricing policies to prevent price increases, promote price transparency, and reduce prices of innovative medicines, thereby increasing their accessibility and protecting the financing sustainability of the health system.

A common barrier to access to medicines in LMICs is unreliable supply and procurement systems. We believe that outsourcing services to guarantee the availability of medicines at hospitals could assist in the efficient use of resources and management of hospital pharmacies. If the private sector has the infrastructure in place to provide efficient and good quality pharmacy services, the public sector should use and collaborate with the private sector rather than creating or maintaining its own system in parallel.

Implications for future research
Following the WHO Access Framework,\(^1\) we propose several future research questions arising from our results and their implications.

- **Selection, availability, and rational use of medicines**

  *Which innovative (cancer) medicines in Mexico are widely used and by which health institutions?*

  Future research should expand on measuring access to other innovative medicines besides those for cancer. It is important to know about the situation behind high-cost medicines for other therapeutic groups such as medicines for Hepatitis C. Furthermore, more research should focus on access to comprehensive treatment schemes of other common types of cancer\(^3^1\) by measuring utilization according to geographic areas, by insurance scheme and at a national level (including the private sector). Public health institutions and the government need to reflect on how to allocate resources more equally and efficiently to ensure universal access to the most cost-effective level of care.

  SPS does not cover some innovative medicines and this might be true for other institutions (e.g. IMSS, ISSSTE). Further research should analyze the actual
utilization of medicines – particularly high-cost innovative medicines. Using (innovative) cancer medicines as an example should provide information about prescription preferences, which in turn should expand on the harmonization of treatment in the country. The health system should strive towards the harmonization between the national formulary and clinical guidelines. The excessive number of medicines in the national formulary has been reported elsewhere. Thus, this research question could provide information on medicines that could be removed from the national formulary in an attempt to harmonize coverage and treatment across the country, and promote the rational use of medicines and the efficient use of resources.

- **Affordability**

  What is the effect of the CCNPMIS on access to all innovative (patented) medicines negotiated since 2008?

  Our findings showed that all medicines had different prices between and within institutions. It is likely that other negotiated medicines may show similar price variations, which might be consistent with other research that has reported on great price variability between institutions accredited by SPS. Furthermore, it is necessary to assess whether other negotiated medicines have achieved further discounts after each negotiation round and the reasons behind this. Price transparency from the CCNPMIS is desirable and further research should focus on how transparency could benefit the impact of the commission.

The CCNPMIS has achieved savings in pharmaceutical expenditure and has increased the number of participating companies and negotiated medicines. However, further research on the CCNPMIS should fully assess the negotiating process and its impact on access and find the gaps that have prevented its institutionalization and its strengthening. Research on access to other innovative medicines could compare negotiated and actual procurement prices with prices in other upper-middle-income countries. This comparison should highlight the strengths and limitations of the CCNPMIS regarding pricing of innovative medicines in Mexico and the areas of opportunity to improve affordability. The prices negotiated should consider the level of income and the health system’s ability to pay.
Are cancer medicines affordable from the health system perspective?
We reported affordability of essential cancer medicines from the patient’s perspective. Further research should assess the affordability of medicines from the health system’s perspective. Continuous monitoring of prices and availability of cancer medicines is necessary to assess their impact on health expenditure and access to cancer care. This assessment is necessary to realize the amount of health financing needed per disease (considering its burden) and to inform policymakers about improving affordability and further expand cancer coverage.

Furthermore, other LMICs should also explore the accessibility of essential cancer medicines and particularly the prices and affordability of these medicines within their own context. We believe that other LMICs could use our adaptation of the WHO/HAI methodology as a standard to analyze the price and availability of essential cancer medicines. Data gathered through this methodology should expand on our knowledge on prices and affordability of cancer medicines in addition to their actual availability.

- Sustainable financing and sustainable health system
Is the resource pooling mechanism used by SPS guaranteeing the timely financing of cancer treatment and expanding coverage (e.g. more diseases (more cancers), other innovative medicines, harmonization of healthcare across the country, accreditation of facilities, etc.)?

The SPS has been a strong mechanism to provide access to healthcare to populations that otherwise would have had to pay out-of-pocket and suffer catastrophic expenditure, or might have not received healthcare at all.38,39 However, to improve access and SPS’s functioning, the challenges that institutions face directly related to the SPS resources and timely reimbursement need to be considered. Operational research should take a closer look at the use of resources, timelines, and schedules for reimbursement, and implementation and harmonization of SPS treatment protocols. This future research should provide insight into the SPS financing system, the possibilities for expanding coverage, and problems that affect timely reimbursement and its sustainability.
Are cancer medicines available and affordable (from the system perspective) in IMSS and ISSSTE?

Methods used to measure access (drug utilization research methods and the WHO/HAI methodology) should be applied to assess the availability and prices of cancer medicines provided by IMSS and ISSSTE – the other main healthcare providers in Mexico. These studies could identify the challenges that these institutions face, and identify some good practices that these institutions follow to guarantee access to medicines. These ‘best practices’ could be introduced into MoH facilities that need to improve the accessibility of medicines. These data and results will help to bridge some of the fragmentation in the health system, the inequalities, and inequities in healthcare and medicines’ access.

What is the effect of other mechanisms used to improve availability and affordability of medicines (e.g. pooled procurement)?

Another mechanism implemented by the government to improve procurement efficiency and access to medicines is pooled procurement. Operational research should expand on the effects, strengths, and limitations of the different procurement mechanisms used in the country (e.g. outsourced services vs centralized procurement) including pooled procurement. As institutions continue to face issues with their procurement and supply systems (e.g. stock-outs and late supply by central procurement agencies), more research should find the reasons behind these gaps causing institutions to resort to direct purchases and procure medicines at prices different from those negotiated by the commission or outside the agreed contract conditions. Future research should focus on case studies and carry out observational studies with stakeholder interviews to explore, in-depth, the procurement forecasting and procedures of each facility. Drug utilization research methods should complement this research to provide insights on procurement trends. This research should compare case studies to find good practices, lesson learned and areas of opportunity.

What are the differences between public and private health institutions regarding access to medicines and healthcare delivery for patients with SPS?

SPS procures and reimburses services in the private sector, and this is likely to increase with time. More operational research should look at the experiences in timely access and quality of healthcare and medicines. This operational research should provide information about different healthcare prices between the private
and the public sector, the efficiency in the use of SPS resources, and the actual impact on patient’s healthcare, access to medicines and health outcomes. This information should shed light on the cost-effectiveness of contracting and reimbursing private facilities by SPS to provide healthcare to patients compared to public health facilities.

7.5. Conclusions

Access to innovative essential cancer medicines is incomplete and unequal in Mexico. The availability of essential cancer medicines remains lower than international recommendations, particularly for innovative medicines and for medicines without insurance coverage. Health facilities face barriers related to shortages, procurement issues and mainly a lack of coverage and high prices of cancer medicines, particularly innovative medicines. Although the negotiation of public procurement prices has prevented price increases, and even though prices in the public sector are lower than in the private sector, overall prices remain unaffordable to most patients. Without further government action to increase insurance coverage and reduce prices, universal access to essential cancer care and treatment will not be achieved.

Therefore, in addition to Mexico’s main mechanism to increase access to innovative medicines – price negotiations – the health system needs stronger pricing policies to increase the affordability of medicines in the public and private sectors. These pricing policies, together with all other related pharmaceutical policies and strategies, should be included in one single and comprehensive NPP with a horizontal approach, rather than having individual policies with vertical disease-specific approaches. The NPP should seriously consider international recommendations on pricing policies and other provisions to improve affordability, rational use, and procurement of medicines to guarantee the right to access to medicines in the context of UHC.

The SPS has been a strong mechanism to reach UHC and provide cancer care to all children and adolescents, and to adults for the most prevalent cancers. However, the SPS faces several limitations and challenges, as access to essential cancer medicines continues to be unequal in Mexico, particularly for innovative
essential cancer medicines. SPS coverage needs to expand through several actions: 1) updating treatment protocols and including additional cost-effective medicines, some of which are innovative and still under patent; 2) expanding cancer coverage and including other prevalent adult cancers; 3) expanding the accreditation of facilities to increase healthcare delivery. These actions should take into consideration the financial resources necessary to maintain the financial sustainability of the system. These actions should, in turn, strengthen the health system and advance UHC.

Mexico serves as an example of a MIC that has reformed its health system to reach UHC that includes cancer care. Other MICs on the path to UHC could start by implementing basic essential health coverage packages that include high-cost diseases, such as cancer, with the necessary price controls. These packages should include comprehensive care with the most cost-effective essential medicines. Furthermore, Mexico strives to control pharmaceutical expenditure and increase access to innovative medicines. Price negotiations have proven to prevent price increases of medicines and even decrease the prices of medicines. To provide access to innovative medicines without jeopardizing the financing sustainability of the system, MICs should consider price negotiations together with other pricing policies and price transparency measures to improve the affordability of medicines and guarantee access to innovative medicines as part of a comprehensive NPP.

Improving access to safe, cost-effective, and innovative medicines will provide better quality cancer care, better health outcomes, and fewer deaths due to cancer. In Mexico and other MICs, efforts to improve access to cancer medicines should be coupled with better access to screening, prevention and other types of treatment. All these efforts to expand cancer coverage should be included in the National Cancer Control Plan.
Discussion and Conclusions

References


4. Secretaría de Salud. LINEAMIENTOS para la adquisición de medicamentos asociados al catálogo universal de servicios de salud y al fondo de protección contra gastos catastróficos, por las entidades federativas con recursos transferidos por concepto de cuota social y de la aportación solidaria federal del sistema de protección social en salud [GUIDELINES for the acquisition of medicines associated with the universal catalog of health services and the fund for protection against catastrophic expenses, by the states with resources transferred as a social contribution and the federal solidarity contribution of the social protection system in health]. *Diario Oficial de la Federación.* 2016.


33. Perehudoff K. The right to health as the basis for universal access to essential medicines. A normative framework and practical examples for national law and policy. University of Groningen. 2018.


36. Flores Ramos JM, Murayama Rendon C. Investigación documental a partir de la información publicada por las entidades federativas sobre la situación que guardan los precios de las adquisiciones de los medicamentos asociados al catálogo universal de servicios de salud (CAUSES) e identificación de las variables que permitan explicar el comportamiento de dichos precios en las entidades federativas [Documentary research based on the information published by the states on the situation of the prices of the purchases of medicines associated with the universal catalog of health services (CAUSES) and identification of the variables that explain the behavior of said prices in the federative entities]. *Seguro Popular*. 2009.


