https://doi.org/10.35839/repis.5.3.938

Opportunity cost of high-cost medicines and health decisions in times of pandemic

Costo de oportunidad de medicamentos de alto costo y decisiones sanitarias en tiempos de pandemia

Santiago Hasdeu[1,2,a], **Laura Lamfre**[1,2,b], **Andrés Freiberg**[1,3,c]

Abstract

Introduction: Making fair coverage decisions by allocating limited resources implies prioritization. Given the pandemic, this is even more difficult, given the economic recession and the need to cope with new demands for health technologies, in addition to the rest of the needs of the health system. Health Technology Assessment and the regulation of drug prices are two strategies recommended by WHO-PAHO to increase the efficiency and equity of health systems. We analize the budget impact and opportunity cost of spinraza, a high-cost drug that would be effective in increasing the survival of patients with a rare disease named Type I Spinal Muscular Atrophy. In Argentina, it is covered without price regulation, paying three times more expensive than in Brazil, although a National Health Technology Assessment did not recommend this. Methods: The opportunity cost of spinraza for Spinal Muscular Atrophy is expressed as the possibility of purchasing mechanical respiratory assistance equipment, which has become a universal priority in the pandemic context. At the current sale price, and for 100 estimated patients with Type I Spinal Muscular Atrophy under treatment, Argentina invests in spinraza funds equivalent to those needed to buy 2 417 respirators, with which it could have increased its installed equipment capacity by 35% at the beginning of the pandemic. Acceptability curves for coverage of these technologies and scenarios of potential lives saved in the face of different types of drug price reduction were analyzed. Discussion: Argentina, like other countries in the region, must redesign decision-making processes on high-cost drug coverage to ensure the efficiency, equity, and sustainability of the health system. The pandemic context can be an opportunity to base decisions on tools such as prioritization based on health technology assessment with binding recommendations, estimating the opportunity cost of interventions, and regulating the prices of high-cost drugs.

Keyword: pain, neurosurgery, hospitalization, visual analog scale, clinical protocols.

Resumen

Introducción: Tomar decisiones justas de cobertura asignando recursos limitados, implica realizar una priorización. Ante la pandemia esto es aún más difícil, dada la recesión económica y la necesidad de hacer frente a nuevas demandas tecnologías sanitarias, además del resto de necesidades del sistema de salud. La evaluación de tecnologías sanitarias y la regulación de precios de medicamentos son dos estrategias recomendadas por la OMS-OPS para incrementar la eficiencia y la equidad de los sistemas de salud. Se analiza el impacto presupuestario y costo de oportunidad de spinraza, un medicamento de alto costo que sería eficaz para incrementar la sobrevida de pacientes con una enfermedad poco frecuente denominada Atrofia Musculo Espinal tipo I. En Argentina se cubre, sin regulación de precios, pagando un precio tres veces más alto que en Brasil, pese a que esto no fue recomendado por una evaluación de tecnología sanitaria nacional. Métodos: Se expresa el costo de oportunidad de spinraza en AME tipo I en posibilidad de compra de equipos de asistencia respiratoria mecánica, los cuales han pasado a representar una prioridad universal en el contexto de pandemia. Al precio de venta actual, y para 100 pacientes estimados con Atrofia Musculo Espinal tipo I en tratamiento, Argentina invierte en spinraza fondos equivalentes a los necesarios para comprar 2 417 respiradores, con los que podría haber incrementado su capacidad instalada de equipos en un 35% al inicio de la pandemia. Se analizan las curvas de aceptabilidad para cobertura de estas tecnologías y escenarios de potenciales vidas salvadas ante distintos tipos de reducción de precio del medicamento. Discusión: Argentina, como otros países de la región, debe rediseñar procesos de toma de decisión sobre cobertura de medicamentos de alto costo para asegurar la eficiencia, equidad y sustentabilidad del sistema de salud. El contexto de pandemia puede ser una oportunidad para basar las decisiones en herramientas como la priorización basada en evaluación de tecnologías sanitarias con recomendaciones vinculantes, la estimación del costo de oportunidad de las intervenciones y la regulación de precios de medicamentos de alto costo.

Palabras clave: dolor, neurocirugía, hospitalización, escala visual analógica, protocolos clínicos.

[1]Argentine Public Network for Health Technology Assessment (RedArets)
[2]National University of Comahue, Argentina
[3]Sevilla University, España

ORCID:
[a]https://orcid.org/0000-0002-1405-0303
[b]https://orcid.org/0000-0003-2457-0254
[c]https://orcid.org/0000-0001-6814-2476

Corresponding author:
Santiago Hasdeu

Address: National University of Comahue, Argentina

Email: hasdeusanti@gmail.com

Reception date: february 04, 2021

Approval date: may 23, 2021

Quote as: Hasdeu S, Lamfre L, Freiberg A. Costo de oportunidad de medicamentos de alto costo y decisiones sanitarias en tiempos de pandemia. Rev. Peru. Investig. Salud. [Internet]; 5(3): 181-188. Available from: http://revistas.unheval.edu.pe/index.php/repis/article/view/938

Introduction

Making fair coverage decisions, allocating limited resources, implies prioritizing, and is a great challenge that attempts to address from philosophy, ethics and economics (1-4). Faced with this COVID pandemic, this may be even more difficult, since it is not only a health crisis, but a “total social fact, which convulses all social relations, and shocks all the actors, the institutions and values ”(5). With a forecast of large economic losses (6), governments finance interventions designed to contain the pandemic, and try to slow the spread of the virus, avoid hospital overflow, and protect lives. This strategy seeks to buy time (7) for governments to urgently expand their capacities for intensive therapy, especially respiratory support for severe pneumonia, the only thing that has saved seriously ill patients from COVID-19 (8) while waiting for the vaccination of the population, which has little chance of reaching the entire population before the end of 2021 (9). Up to 20% of those over 80 years of age would progress seriously and end up requiring mechanical ventilation (MRA) (10). Approximately 12% of those hospitalized for COVID-19 require ARM (8). In Argentina and in most of the countries of the region, COVID-19 cases continue to increase (11), while respirators are in deficit globally (12). Respirators are considered so important that the president of the United States invoked the Defense Production Act so that local companies increase their production for that country (13), and in Argentina similar measures were taken by Presidential decree so that all production local was bought by the state (14).

Economic context and decision-making on health technologies

Like many countries in the region, Argentina combines pre-existing difficulties with new challenges related to the pandemic. With a fragmented and segmented health system, the costs of new technologies are steadily increasing, where judicialization for coverage is increasingly frequent, finding a fragile balance between demand and coverage (15). Given the pandemic, a drop in GDP of 11.8% is anticipated for Argentina with a rebound of 4.9% in 2021 and for Peru a fall of 13.9% in 2020 with a recovery of 7.3% for 2021 (16). While urgent needs appear to face COVID, while continuing to meet all other health needs not related to COVID.

Argentina uses an explicit list of benefits, the Obligatory Medical Plan (PMO), as a formal reference for the subsector of national social security and prepaid medicine companies (41% of the population) but which is also referenced by other funders such as provincial social works, pensioners and retirees social work, and, to a certain extent, the public subsector (17). Two thirds of the population have formal coverage and the remaining third is served exclusively in the public subsector. Total investment in health is close to 10% of its GDP (18), despite which allocative inefficiencies persist with consequences for the overall equity of the system (19).

High-cost drugs take a growing percentage of the health budget in Argentina as in other countries in the region. In Argentina they represent 34% of the PMO's total drug spending while in Chile, only three orphan drugs prosecuted in 2018 represented 28 times the annual per-capita budget of the Ricarte Soto Law for high-cost diseases (20), and in Colombia the coverage of high-cost drugs is indicated as one of the causes of the financial health crisis (21). In Peru, the Ministry of Health has had the Intangible Solidarity Health Fund (FISSAL) since 2002, which finances a series of high-cost diseases (seven types of most frequent cancers, the comprehensive treatment of chronic kidney failure and rare and orphan diseases) in people in poverty (22,23).

Central strategies to improve efficiency and equity in relation to the use of medicines are the evaluation of health technologies (HTS) (24) and the regulation of medicine prices (25). The countries of the region are trying to advance towards the consolidation of HTA processes that include evaluations of the economic impact and equity (26). The drug price regulation strategy, which has not been implemented in Argentina, unlike other countries in the region, such as Brazil, Colombia and Uruguay (27), which have various experiences that have made it possible to improve the efficiency of their drug purchases. WHO-PAHO also recommends other strategies, including promoting competition either through biosimilars, parallel imports, and even incentives for import substitution, modification of procurement mechanisms including risk-sharing mechanisms, and aggregation of demand to through joint negotiation mechanisms and consolidated purchases (28).

While in Argentina a National Agency of HTAs still awaits to be law (29), the official coverage recommendations emanate from an interim official commission, the National Commission for Health Technology Assessment (CONETEC), created in 2018, with the aim of "issuing recommendations on the incorporation, form of use, financing and / or policies for the coverage of health technologies […] of a public nature and free consultation for all actors in the health system, including judicial processes "(30). Its reports are not binding and its recommendations are not fully complied with, weakening the potential impact of this strategy (31).

This article analyzes the opportunity cost of covering sprinaza for Type I Muscular Atrophy (SMA) in Argentina. SMA is a hereditary neuromuscular disease characterized by the involvement of the cells of the anterior horn of the spinal cord (motor neurons), which presents with symmetric proximal weakness and progressive atrophy of the muscle groups. It is a rare disease, highly disabling and with high mortality in its most serious forms. It has an approximate incidence of 1 in 6,000 / 10,000 live births, and is the main cause of infant mortality due to a genetic disease (32). Four forms of presentation of SMA are known, and there is evidence that in SMA type I, spinraza reduces mortality and the requirement for mechanical ventilatory assistance, as well as improves motor function, allowing the development and acquisition of certain skills (for example sitting, standing, or walking) until at least 13 months of observation. It is estimated that approximately 100 patients with SMA type I receive spinraza in Argentina (32).

Spinraza was not included in the WHO Essential Medicines List (33), and despite having a negative recommendation by CONETEC (31), it was included in the PMO for one year (34,35). Its opportunity cost is related to the purchase of mechanical ventilation equipment, which has become one of the highest priorities in effective and safe health technologies to face the pandemic. The objective of this study is to illustrate, in this way, the impact of high-cost drugs such as spinraza (Nusinersen®), and the urgent need to adopt strategies to improve efficiency and equity; Among them, base decisions on ETES and implement price regulation schemes. The context of a pandemic can become an opportunity to re-discuss health policies related to high-cost drugs, which put the sustainability of health systems at risk.

Methodology

The budgetary impact and opportunity cost of

spinraza for SMA type I expressed in prospective purchase capacity of MRA equipment for critical care in severe pneumonia caused by COVID-19 was represented. It was chosen to exemplify with spinraza due to its high budgetary impact, having been recently evaluated by CONETEC, making recommendations against its coverage at current prices, and because these recommendations were not taken into account. The comparison with the ability to purchase respirators is based on the fact that this has been one of the main technologies that health systems went out to buy immediately in the face of the pandemic, exceeding the available supply (12) 12, thus making explicit a homogeneous preference for all health decision-makers. This comparison is arbitrary, since there are other high-cost drugs that impact health systems, as well as other technologies necessary to cope with the pandemic. Those mentioned are selected to show theoretical alternatives in a budget line from the point of view of an impartial decision-maker who must prioritize public resources with a fixed budget. Although budgets, by their nature, must be flexible, and in the face of the pandemic, most countries authorized an increase in the budget for Health, they work with a fixed budget based on various considerations, which include economic contraction, inflation and the devaluation of the peso-dollar exchange rate (37), as well as advantages given by the greater simplicity for the analysis.

Spinraza for Spinal Muscular Atrophy

In 2019, 259 patients with different disease subtypes and under the responsibility of various funders were under treatment with spinraza (32). An estimated 100 patients / year with SMA type I under treatment with spinraza in Argentina.

In the context of a pandemic where the need for respirators becomes a priority for all health systems, indifference curves are plotted to illustrate the possible decisions when prioritizing between respirators and spinraza.

In this exercise, an annual budget set by the cost of spinraza -tax-free- is assumed to treat 100 patients / year with SMA type 1. Only SMA type 1 is considered, because the contrast with severe patients with COVID-19 implies units It requires equally disappointing forecasts, the interventions of which carry a certain likelihood of saving lives in the short term. Spinraza would improve MRA-free survival or death at 13 months with a Hazard Ratio = 0.53, suggesting a Number Needed to Treat (NNT) of 3.38 patients / year (38). This survival would be maintained until at least 32 months of life (39). Based on information provided by consultation with various funders who are covering treatments in Argentina, the tax-free price of spinraza is $ 80,580 per dose. Six doses are required in the first year, at a cost per patient / year of $ 483,448 and $ 48,348,000 for the estimated 100 patients.

Respirators

In many regions of the United States, Brazil, Chile and Peru, the installed capacity of respirators was exceeded in the scenario of a COVID-19 pandemic (40). In Argentina, estimates of total respirators have been reported at 8,560 at the beginning of the pandemic, leading to a ratio of 25.5 respirators per 100,000 inhabitants (41.42). Despite the fact that it was later significantly increased, the available respirators could be insufficient according to different scenarios of the evolution of the pandemic (43). Mortality of patients requiring a respirator due to COVID ranges from 30 to 80% (44.45). Assuming that all serious cases that do not access ARM die, and that access to critical care in Argentina reduces mortality to 40%, the ventilator would have an NNT of 1.72; In other words, for every 1.72 people with severe COVID-19 pneumonia who access ARM, one life would be saved. The median duration of mechanical assistance in the ICU is estimated at 10 days (10) and, therefore, a ventilator could be used in 3 patients per month. For simplicity, in this analysis we will consider a single annual peak, where each ventilator would be used in only three patients. This simplification is conservative, since most predictive models show that a single short peak is unlikely to occur, and a second peak is already underway in Argentina and other countries in the region. The price of standard respirators available in the Argentine market and in the region is USD 20,000 per unit (46). Costs of human resources, inputs and indirect costs are not included in the analysis.

Results

Under a fixed budget, the choice to cover spinraza for the entire estimated population implies losing the opportunity to have funds to buy 2 417 extra respirators and thus increase Argentina's initial installed capacity by 35%.

Given that both technologies would have a potential impact on lives saved, the analysis is deepened by comparing spinraza and respirators, assuming a fixed budget and a scenario in which only these two technologies could be financed. In this hypothetical situation, if the impartial decision maker had the sole objective of maximizing lives saved, he could save more than 99% of the lives at stake by spending his entire budget on purchasing only respirators. This occurs even assuming that each respirator was used in only three patients, in a single epidemic peak, ignoring that its amortization allows it to be used for several years for the benefit of other patients with other diseases.

Neoclassical economic theory describes that a financier with a fixed budget, when faced with the possibility of incorporating different goods, will buy those that provide the greatest utility, until reaching a point where the marginal profits per monetary unit spent on each of the goods are equal. This funder

will break even when, given your budget and pricing constraints, you maximize the profit you make from your expenses. Graphically speaking, it will be in equilibrium when, given its budget line, it reaches the highest indifference curve. The indifference curves represent possible combinations preferred by a theoretical decision-maker interested in equity, not in maximizing lives saved.

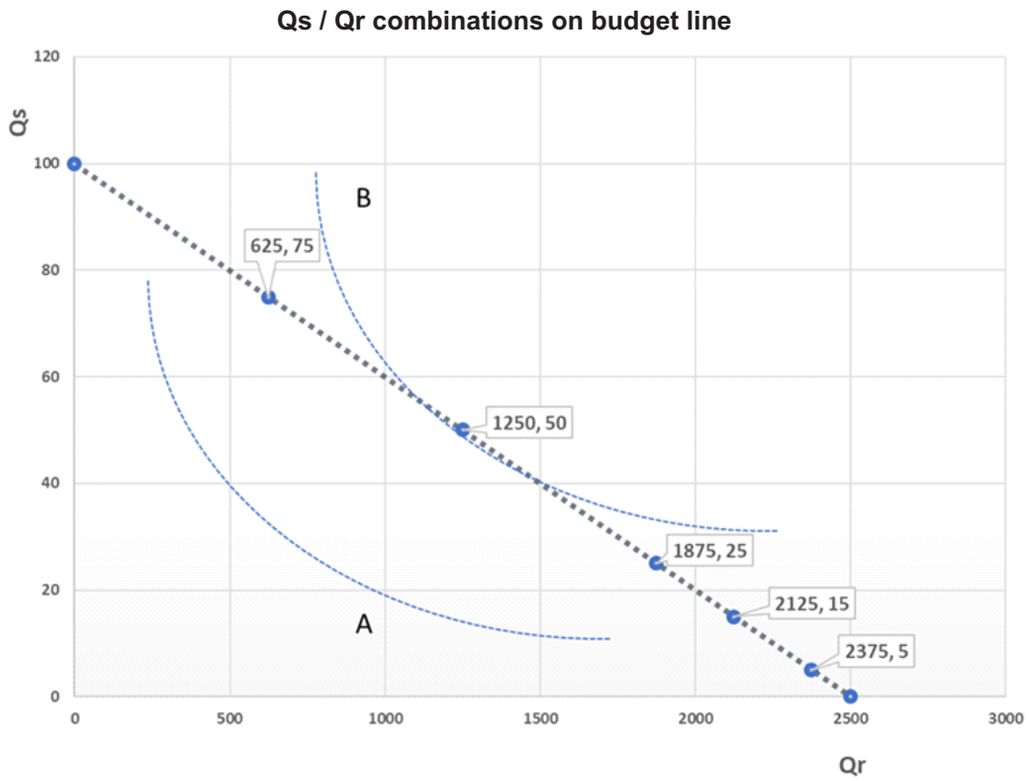

Figure 1: budget line and indifference curves: spinraza versus respirators.

In figure 1, the points (Qs and Qr) represent interchangeable quantities (patients / year of treatment with spinraza and respirators) under a fixed budget of slightly less than USD 50 million. Indifference curves A and B represent possible "preferred" combinations for a decision maker interested in equity, not in maximizing lives saved. Curve A is inefficient. In B, the decision maker interested in maximizing absolute equity "prefers" to cover progressively more spinraza or respirators as the marginal benefit of an extra unit is relatively smaller.

The impact of the cost of spinraza stands out even more when the benefit in lives saved is measured. Indeed, if a decision-maker with an equity mandate wanted to apply 50% of the total budget to each technology and health problem, they would buy 1,209 respirators and cover 50 patients / year with spinraza. At this "fair" point, it would stop saving 15 lives of SMA type 1 patients and 2 108 lives of critically ill COVID-19 patients. Most of the economic evaluations carried out in other countries considered spinraza cost-effective only based on discounts greater than 90% (27) 27. As can be seen in the following figure, at the current sale price in Argentina, even obtaining discounts of up to 95%, investing the entire hypothetical budget in spinraza would give the opportunity to save 30 lives of SMA patients, losing the opportunity to save 211 lives that they could potentially be saved by incorporating more respirators. In this scenario, made possible by discounts, no patient with SMA type 1 would be left out of treatment.

In our exercise, the scenario of only treating 100 carefully selected SMA patients at a 50% discount equates to a cost of 2,018 lives of people with COVID-19, and each percentage point off the price of spinraza would save 44 lives of people with COVID-19. In other words, a decision maker who agrees to pay for spinraza at a discount of only 50%, under the fixed budget of our scenario, is effectively valuing each life of a patient with SMA, 70 times more than each life of a serious patient with COVID-19.

Discussion

Pharmaceutical innovation is very important, but the cost of new products with proven benefits limits access to drugs and other technologies in resource-limited settings (22). In the case of spinraza for patients with SMA type I there would be a potential benefit, but the balance between benefits, cost and opportunity cost for society must be analyzed in depth. The possibility of an improvement in survival is something promising that will need to be confirmed with new studies and long-term follow-

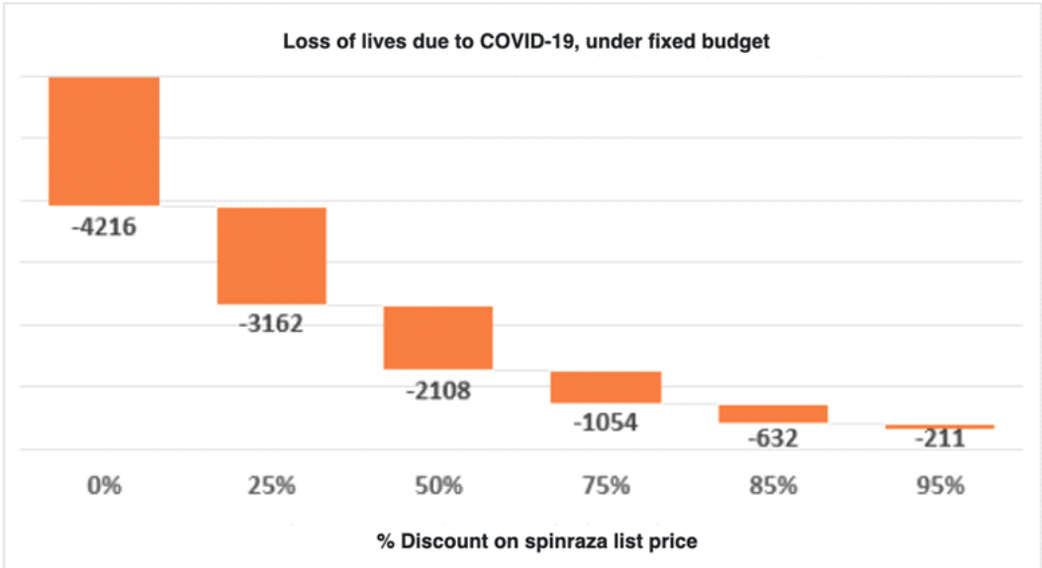

Figure 2: Potential loss of life of seriously ill patients by COVID-19 after the maximum capacity of respirators is saturated, according to% discount to the spinraza list price In this simulation, the treatment of all patients with SMA type 1 is covered and the remainder of the fixed budget for the purchase of respirators is used.

up, but in the meantime, the main problem seems to be the price. It is suggested that the price we pay is a manifestation of our relative valuation of some diseases over others, by will or by judicialization, which in the end ends up pointing a market to a seller. A society expresses its preferences by selecting the interventions it pays, and its possibilities in the prices it pays. Various publications about the opacity of the drug industry value chain (47), as well as the aforementioned successful experiences in price regulation, suggest that this is a strategy that allows improving access, without putting sustainability at risk. of the industry. Investment in marketing would double investment in research and development, and profit margins are higher than in most industries (48). In the region, large international differences in the prices of other high-cost drugs such as Trastuzumab have already been published (49). The difference found between the price of spinraza in Argentina and that of Brazil (50) is 200%, which confirms that a price regulation policy and strategy is necessary to reduce this discretion. Brazil used a scheme where the regulation of the price of new drugs was related to the results of the ETES carried out (27).

Argentina, like other countries in the region, has committed itself through international pacts to protect the right to health "in accordance with the possibilities, organization and resources of the State" (51) "... as far as public and community resources allow ... ”(52) for the“ ... enjoyment of the highest possible level of health ... ”where the highest is“ ... according to biological, socio-economic preconditions and the resources available by the State ... ”(53). The right to health and life of everyone is equally protected, but the appearance of innovative technologies that could save lives but have prices such as spinrasa, or even higher prices such as zolgensma, which, also for the treatment of SMA, it is sold at 2.1 million dollars per patient (54), it is evident that it is necessary to have binding ETES processes and price regulation, as well as a broad social debate. Most of the countries in the region show incipient progress in HTA but still have significant opportunities for improvement (22) 22. Despite the negative recommendation of the CONETEC ETES, the Argentine Ministry of Health included spinraza in the PMO in 2019. A voluntary agreement with the seller provided a discount, in exchange for funders to cover all forms of SMA. The majority did not adhere, calculating an even greater budget impact. Recently, the Ministry of Health of Argentina terminated this Resolution, incorporating a spinraza protected coverage scheme for SMA. In January 2021, a new drug for the treatment of SMA was registered and approved for commercialization in Argentina, it is Onasemnogene abeparvovec (Zolgensma®) (55), which at a cost of 2.1 million dollars per patient comes to confirm the need for National States to raise the need for evaluation, regulation and price negotiation.

This research presents among its limitations the assumption of the fixed budget and analyze the comparison between only two technologies, both decisions made for educational purposes. Another limitation is having taken the cost of the respirator without considering the costs related to supplies and human resources. This underestimation is probably offset by the conservative assumption that a ventilator would be used by only three patients. Regarding the comparison of spinraza prices between countries, although both are expressed in dollars, it may be necessary to adjust these data for inflation and purchasing power parity (25).

Argentina, like other countries in the region, must

redesign decision-making processes on coverage, using the ETES as an input for prioritization with binding recommendations, for which it must guarantee the competence of the institutions that already exist and develop them. The pandemic context may be an opportunity to revalue the importance of estimating the opportunity cost of interventions, especially in the case of high-cost drugs. Implementing price negotiation policies, which may include risk-sharing agreements or discounts ordered from the State, are some of the urgent strategies that can help to face the costs of the pandemic and continue to cover other health needs.

Funding Source

The present research was funded by the authors.

Authors' contributions

All authors participated in the entire research process.

Conflicts of interests

The authors report having no conflicts of interest.

Referencias

1. N. Daniels, Just health: meeting health needs fairly, Cambridge: Cambridge University Press, 2007.
2. WHO, «Making fair choices on the path to universal health coverage,» WHO , Geneva, 2014
3. Rawls, John. A Theory of Justice, Oxford University Press, Oxford, 1971
4. Fischer K. A systematic review of coverage decision-making on health technologies - Evidence from the real world. Health Policy. 2012. 107 (3): 218-230.
5. Ignacio R. La pandemia y el Sistema-Mundo. Le Monde Diplomatique. 25 April 2020. [En línea]. Disponible en: https://mondiplo.com/la-pandemia-y-el-sistema-mundo. [Último acceso: 12 Mayo 2020].
6. CEPAL 21 de abril 2020. Dimensionar los efectos del COVID-19 para pensar en la reactivación. Informe especial N°2. Disponible en https://repositorio.cepal.org/bitstream/handle/11362/45445/4/S2000286_es.pdf
7. OMS. ACTUALIZACIÓN DE LA ESTRATEGIA FRENTE A LA COVID-19. 14 de abril de 2020 Disponible en https://www.who.int/docs/default-source/coronaviruse/covid-strategy-update-14april2020_es.pdf?sfvrsn=86c0929d_10
8. Richardson S. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City Area. JAMA,2020: 323 (20); 2052-2059.
9. OMS. Conferencia de prensa Jefa de Científicos de OMS Soumya Swaminathan. WHO on a COVID-19 vaccine and treatment. 20 junio 2020. Disponible en https://youtu.be/vquaknWJVvA
10. N. Ferguson et. al., «Report 9: Impact of non-pharmaceutical interventions to reduce COVID-19 mortality and healthcare demand,» WHO Collaborating Centre for Infectious Disease Modelling, London, 2020.
11. Gobierno - Ministerio de Salud Argentina, «Informe Diario COVID-19,» Ministerio de Salud, 4 June 2020. [En línea]. Available: https://www.argentina.gob.ar/coronavirus/informe-diario. [Último acceso: 5 June 2020].
12. Megan L. Ranney, Valerie Griffeth, Ashish K. Jha. Critical Supply Shortages — The Need for Ventilators and Personal Protective Equipment during the Covid-19 Pandemic. N Engl J Med 2020; 382:e41 April 30, 2020. DOI: 10.1056/NEJMp2006141
13. CNN. Trump invokes Defense Production Act for ventilator equipment and N95 masks. By Maegan Vazquez, CNN April 3, 2020. Disponible en https://edition.cnn.com/2020/04/02/politics/defense-production-act-ventilator-supplies/index.html
14. Decreto 260/2020. DECNU-2020-260-APN-PTE - de Emergencia Sanitaria Coronavirus (COVID-19). Disposiciones. Disponible en http://servicios.infoleg.gob.ar/infolegInternet/anexos/335000-339999/335423/norma.htm
15. Cetrángolo O. Financiamiento fragmentado, cobertura desigual y falta de equidad en el sistema de salud argentino. Revista de Economía Política de Buenos Aires, 2015: 13 (22) 38-47.
16. WORLD ECONOMIC OUTLOOK UPDATE. June 2020. A Crisis Like No Other, An Uncertain Recovery. Disponible en https://www.imf.org/en/Publications/WEO/Issues/2020/06/24/WEOUpdateJune2020 (Ultimo acceso 24/6/2020)
17. Prosanity Consulting-Universidad ISALUD, «actualización de la estimación del gasto necesario para garantizar la cobertura asistencial contenida en el pmo,» Universidad Isalud, Buenos Aires, octubre 2019. Disponible en http://www.consensosalud.com.ar/isalud-prosanity-consulting-presentaron-la-actualizacion-del-pmo-2019/
18. OPS, «Cuánto gasta Argentina en Salud: un análisis de las cuentas en el sector público, privado y de la seguridad social,» OPS y MINSAL, 12 Diciembre 2019. [En línea]. Available: https://www.paho.org/arg/index.php?option=com_content&view=article&id=10420:cuanto-gasta-argentina-en-salud-un-analisis-de-las-cuentas-en-el-sector-publico-privado-y-de-la-seguridad-social&Itemid=225. [Último acceso: 15 Abril 2020].
19. Maceira, Daniel. Caracterización del Sistema de Salud Argentino. Debate en el contexto Latinoamericano. Revista Estado y Políticas Públicas Nº 14. mayo de 2020 - septiembre de

2020. ISSN 2310-550X, pp. 155-179. Disponible en http://repositorio.cedes.org/handle/123456789/4536
20. Juan Cruz para Observatorio Judicial - informe 15, «Corte Suprema versus Ricarte Soto - Una aproximación a la judicialización de remedios de alto costo,» 13 2 2019. [En línea]. Available: http://www.observatoriojudicial.org/corte-suprema-versus-ricarte-soto/. [Último acceso: 24 3 2020].
21. Andia OI. Las causas de la crisis financiera del sistema de salud colombiano desde los medicamentos. Revista Salud UIS 2019: 4(51); 277-281.
22. Ministerio de Salud del Perú. Informe anual 2013. Fondo Intangible Solidario de Salud. Lima: MINSA; 2013.
23. Parra-Baltazar I, Pinto-Dongo C, Quispe-Iporra S. Ley de cobertura universal de enfermedades de alto costo. Revista Peruana de Medicina Experimental y Salud Pública 33.2 (2016): 379-380. http://dx.doi.org/10.17843/rpmesp.2016.332.2191
24. OPS-CSP. RESOLUCIÓN CSP28.R9 EVALUACIÓN E INCORPORACIÓN DE TECNOLOGÍAS SANITARIAS EN LOS SISTEMAS DE SALUD. Washington DC. Septiembre 2012
25. OMS. Medir precios, disponibilidad, asequibilidad y componentes de los precios de los medicamentos. SEGUNDA EDICIÓN. WHO/PSM/PAR/2008.3
26. Lessa F, Caccavo F, Curtis S, Ouimet-Rathé S, Lemgruber A. Strengthening and implementing health technology assessment and the decision-making process in the Region of the Americas. Rev Panam Salud Publica. 2017;41:e165. https://doi.org/10.26633/RPSP.2017.165
27. Leticia Lucia dos Santos Dias, Maria Angelica Borges dos Santos, Cláudia Du Bocage Santos Pinto. Contemporary regulation of drug prices in Brazil – a critical analysis. Saúde Debate | Rio de Janeiro.2019: 43(121); 543-558. DOI: 10.1590/0103-1104201912120
28. WHO guideline on country pharmaceutical pricing policies, second edition. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO.
29. Lafferriere L, Zambrano M. Proyecto de Agencia Nacional de Evaluación de Tecnologías Sanitarias 'AGNET': inquietudes en su implementación e incidencia en los amparos de salud. Revista DFyP, 2016: 142-158.
30. MINISTERIO DE SALUD , «Resolución 623/2018.,» Boletin Oficial de la República Argentina, Ciudad de Buenos Aires, 27/03/2018.
31. Lifschitz, Esteban et al. Agencia de evaluación de tecnologías sanitarias en Argentina. 1° edición adaptada. CABA, Argentina. Fundación Sanatorio Güemes, 2018.
32. CONETEC Argentina, «Nusinersen en atrofia muscular espinal. Informe tecnico 01,» 18 November 2019. [En línea]. Available: www.argentina.gob.ar/. [Último acceso: 30 5 2020].
33. World Health Organization. (2019). World Health Organization model list of essential medicines: 21st list 2019. World Health Organization. https://apps.who.int/iris/handle/10665/325771 . License: CC BY-NC-SA 3.0 IGO
34. MINISTERIO DE SALUD Y DESARROLLO SOCIAL SECRETARÍA DE GOBIERNO DE SALUD Resolución 1452/2019 RESOL-2019-1452-APN-SGS#MSYDS. Ciudad de Buenos Aires, 09/08/2019
35. Poder Ejecutivo Nacional. Resolución 2020-115 AP- MS 26 de Junio de 2020.
36. Araújo M, González A, Fariñas A. Tendencia del presupuesto cubano en salud en el periodo 2004-2010. Revista Cubana de Salud Pública, 39(2), 219-228.
37. Instituto Nacional de Estadística y Censo (INDEC) Argentina. Informes técnicos. Vol 5, n°34 Estimador mensual de actividad económica. Estimación preliminar a diciembre 2020. ISSN 2545-6695
38. Finkel R, Kuntz N, Mercuri F, Chiriboga C, Darras B, Topaloglu H, Montes S, Zhong Z, Gheuens S, Bennett C. Efficacy and safety of nusinersen in infants with spinal muscular atrophy (SMA): final results from the phase 3 ENDEAR study. European Journal of Paediatric Neurology, 2017: 21,e14-e15.
39. Gerrity M, Prasad V, Obley A. Concerns about the approval of nusinersen sodium by the US Food and Drug Administration. JAMA internal medicine, 2018: 6(178); 743-744.
40. Nichols M, Kim R, Jerome K, Nalla A, Greninger A. Covid-19 in critically ill patients in the Seattle region—case series. New England Journal of Medicine, 2020: 45; e35-e41.
41. N. Bar, «Coronavirus en la Argentina: afirman que el 50% de las camas de terapia intensiva están disponibles,» La Nacion , 26 abril 2020. [En línea]. Available: https://www.lanacion.com.ar/salud/coronavirus-en-la-argentina-afirman-que-el-50-de-las-camas-de-terapia-intensiva-estan-disponibles-nid2358354. [Último acceso: 22 mayo 2020].
42. Chequeado. Qué pasa con los respiradores: quiénes los fabrican y cuántos se calcula que harían falta. Disponible en https://chequeado.com/el-explicador/que-pasa-con-los-respiradores-cuantos-hay-en-la-argentina-quienes-los-fabrican-y-cuantos-se-calcula-que-harian-falta/
43. Centro de Estudios sobre Salud, Economía y Bienestar (CUESEB) Universidad Nacional del Comahue. Modelo de proyección de casos COVID-19. Disponible en www.cueseb.org
44. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. JAMA, 2020: 16(323); 1574-1581.
45. Scottish Intensive Care Society Audit Group

report on COVID-19, «2 May 2020 Management Information Statistics,» SIGN, Edinburgh, 13 May 2020.
46. Infobae. Respiradores y China. Disponible en https://www.infobae.com/politica/2020/04/26/china-no-enviara-1500-respiradores-y-el-gobierno-apuesta-a-la-industria-local-para-la-lucha-contra-el-coronavirus/
47. Marcia Angell. La verdad acerca de la industria farmacéutica. Editorial Norma, 2006
48. Goldacre Ben. Bad Pharma: How Drug Companies Mislead Doctors and Harm Patients. Faber and Faber 2011.
49. Pichon-Riviere A, Garay OU, Augustovski F. Implications of global pricing policies on access to innovative drugs: the case of trastuzumab in seven latin american countries. Int J Technol Assess Health Care. 2015;31(1-2):2-11. doi: 10.1017/S0266462315000094
50. ANVISA. Câmara de Regulação – CMED Secretaria Executiva PREÇOS MÁXIMOS DE MEDICAMENTOS POR PRINCÍPIO ATIVO, PARA COMPRAS PÚBLICAS PREÇO FÁBRICA (PF) E PREÇO MÁXIMO DE VENDA AO GOVERNO (PMVG). Publicada em 09/06/2020, atualizada 18/06/2020
51. Declaración Universal de Derechos Humanos, 1948, Res. A-217, art. 22; 25
52. Declaración Americana de Derechos y Deberes del Hombre; art XI
53. Pacto Internacional de Derechos Económicos, Sociales y Culturales 1966, art.12; y obs. 9; 14; 19
54. Riera R, Bagattini A, Pachito D. Eficácia, segurança e aspectos regulatórios dos medicamentos órfãos para doenças raras: o caso Zolgensma. CADERNOS IBERO-AMERICANOS DE DIREITO SANITÁRIO,2019: 8(3); 48-59.
55. CONETEC INFORME RÁPIDO DE EVALUACIÓN DE TECNOLOGÍAS SANITARIAS N° 1 2021. Onasemnogene abeparvovec (Zolgensma®) en atrofia muscular espinal. Ministerio de Salud Argentina. Disponible en https://www.argentina.gob.ar/sites/default/files/conectec-informe-zolgensma.pdf