

Trends in treatments for erectile dysfunction in Chile between 2010 and 2020 with special focus on penile prostheses

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Summary Objectives: Evidence regarding demand trends for erectile dysfunction (ED) treatments are scarce in South America. This study aims to evaluate trends in ED treatments in Chile over a 10-year period (2010-2020) and estimate the potential number of candidates for penile prosthesis.

Materials and methods: Sales trends of pharmacological treatments and penile prosthesis were obtained from market studies. The potential number of candidates for penile prosthesis implantation was calculated by crossing epidemiological data with previously reported ED prevalence, proportion of sexually active men, percentage of men seeking medical assistance for ED, and the proportion of patients who are non-responders to ED oral drug therapies

Results: In the 10-year studied period, the Chilean male population older than 50 years increased 34.7%, with an average annual variation (AAV) of 3.4%. For the same period, the sales of oral drug therapies for ED increased by 71.3% (AAV 6.2%), the sales of intracavernosal vasoactive agents (ICVA) decreased by 0.4% (AAV -0.2%), and penile prosthesis sales increased by 113% (AAV 6.7%). We estimated that only 0.05% of sexually active men older than 50 years old with ED who sought medical assistance finally had a penile prosthesis implanted to manage their condition.

Conclusions: Demand for ED oral drug therapies significantly increased in Chile during the last decade, while ICVA remained stable. The annual rate of penile prosthesis implantation increased. However, the gap between the potential penile prosthesis candidates and the actual number of devices implanted is suspected to remain extremely high.

KEY WORDS: Erectile dysfunction treatment; Pharma-trends; Penile prosthesis.

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INTRODUCTION

Worldwide, penile prosthesis (PP) implantation has increased annually by an average of 8.1% in the period 2006-2011 and is expected to have a compound annual growth rate (CAGR) of 2.1% in the period 2017-2023 (1, 2). Despite this constant increase, the annual number of devices sold is still considered extremely low compared to the number of

potential candidates. In the most important PP market, the USA, it is estimated that no more than 3% of the patients with erectile dysfunction (ED) will finally undergo PP surgery to treat the condition (3).

There is a lack of information about PP implantation trends in South American countries. The main reason is that the number of devices sold annually is extremely low compared with bigger markets such as the USA.

Particularly in Chile, the trends in PP implantation and other available treatments for ED are unknown. Chile has a population of 18.7 million people as of 2019 (4) and the second highest growth domestic product per capita (GDPPC) of South America (US \$16,280 US) after Uruguay (US \$17,870) (for reference, GDPPC is US \$62,794 in the USA) (5). According to the World Health Organization (WHO), male life expectancy in Chile is 76.5 years (6).

Among Chilean men over 50 years old, the prevalence of any degree of ED is 58% (7-9). During the last decade, the available treatments for ED in Chile have been phosphodiesterase 5 inhibitors (PDE5is) (sildenafil, vardenafil, tadalafil), intracavernosal vaso-active agents, and PP (malleable and 3-piece inflatable). Neither public nor private insurance covers any pharmacological treatment for ED. Some health insurances partially cover hospital stay and operation costs including surgeon's fee for PP. However, the device must always be paid by the patient, with prices ranging from US \$1,000 for a malleable PP to US \$10,000 for a 3-piece inflatable PP.

The aim of this study is to evaluate the trends in Chile over a 10-year period in regard to the available treatments for ED with special focus on PP. It also estimates the potential number of candidates for PP according to population demographics, sexually active men, and ED prevalence.

MATERIALS AND METHODS

For our analysis we considered Chilean ED patients over 50 years old. We estimated the total number of this group by crossing demographic and clinical data. Demographic information was obtained from the Chilean National Institute of Statistics (4). Annually, male populations older than 50 years old examined from January 1, 2010 to

January 1, 2020 were considered for analysis. The proportion of sexually active men and the ED prevalence were obtained from previous Chilean surveys (7-10).

To calculate the number of Chilean men who could be potential candidates to receive a PP to treat their ED, we estimated the proportion of men who would suffer severe ED, defined as patients who are PD5is non-responders. This population was calculated by crossing the number of sexually active Chilean ED patients and the internationally reported percentage of men with ED who seek medical assistance (11, 12) and the estimated proportion of men with ED who are PD5is non-responders (13, 14). Finally, we compared the estimated number of potential candidates for PP implantation to the actual number of Chilean men who finally had a PP implanted in the same period. For the period of 2010-2020, the sales trends of pharmacological ED treatments were obtained from pharmaceutical studies performed annually (15). This information includes the sales of the generic and labeled drugs per unit of sildenafil, vardenafil, tadalafil, and intracavernosal vasoactive agents. For PP, six companies represented 100% of the Chilean market: *Boston Scientific*[®], (*Marlborough, Massachusetts, USA*), previously named *American Medical System*[®] (*Minnetonka, Minneapolis, USA*), *Coloplast*[®] (*Humblebaek, Denmark*), *Promedon*[®] (*Cordoba, Argentina*), *Zephyr*[®] (*Geneva, Switzerland*), and *Rigicon*[®] (*Ronkonkoma, New York, USA*). All companies shared their unit sales data for the study period. With this information we calculated average annual variations (AAV) of ED drugs and PP, and modeled growth trends for the study period. Data were analyzed using the statistical software *GraphPad*[®] *Prism 8.0* (*GraphPad Software, San Diego, California, USA*).

Descriptive statistics are reported as percentages and frequencies for categorical variables. Ethical and regulatory approvals were obtained from the *Ethical Committee of the Faculty of Medicine of Pontificia Universidad Católica de Chile*.

RESULTS

In the 10-year period (January 1, 2010, to January 1, 2020) the Chilean male population older than 50 years old increased by 34.7% (Figure 1) with an AAV of 3.4%. The total sales of PD5is (sildenafil, vardenafil, tadalafil) in the same period increased by 71.3% with an AAV of 6.2% (Figure 1). For the study period the mean market shares for each drug were: Sildenafil 71,9%, Tadalafil 28%, Vardenafil 0,1%. The sales trends of intracavernosal vasoactive agents for the same period time were negative (-0.4%) with an AAV of -0.2% (Figure 1).

During the study period, a total of 1087 PP were implanted, 68% were malleable, while 32% were 3-piece inflatable PP (Figure 1). The 10-year increase was 113% (year 2010: 59 implants; year 2019: 126 implants) with an AAV of 6.7% per year.

For the study period, we estimated the annual number of men affected with severe ED by crossing the demographic data with the percentage of sexually active men older than 50 years old and the ED prevalence, reported in Chile (7,8,9). In 2019, Chile had 2,569,856 men older than 50 years old, of which 77% declared being sexually active (n = 1,978,789), and 58% of these men report some degree of ED (n = 1,147,698). According to international data (11, 12), 22.5% of such men would seek medical assistance or treatment (n = 258.232).

Figure 1.

- a) Annual growth of men older than 50 years old in Chile. Ten-year variation 34.7%; average annual variation (AAV) 3.4%.
- b) Annual growth sales of PD5is in units of sildenafil, vardenafil, tadalafil. Ten-year variation 71.3%; AAV 6.2%.
- c) Annual sales growth of intracavernosal prostaglandin (units). Ten-year variation -0.4%, AAV -0.2%.
- d) Annual growth of PP implantation (units). Ten-year variation 113%, AAV 6.7%.

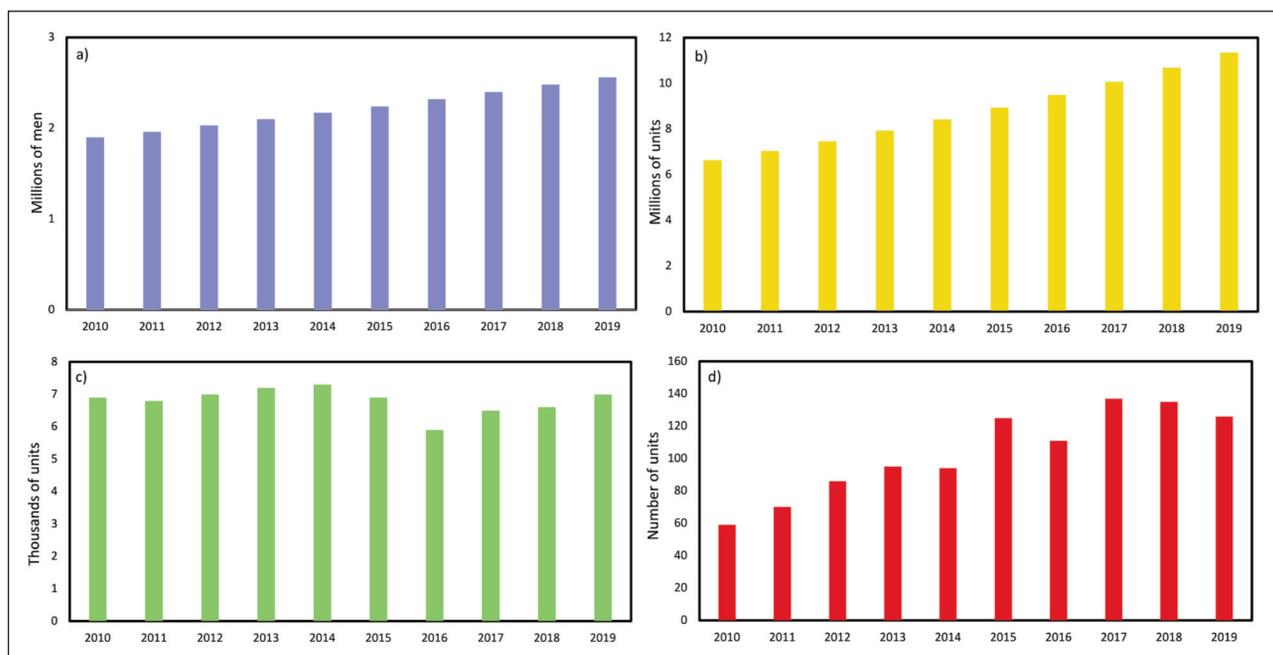


Figure 2.
Estimation of net PP candidates in Chile according to demographic data, percentage of sexually active men, ED prevalence, ED patients who seek medical assistance, and estimated proportion of patients who are PD5is non-responders.

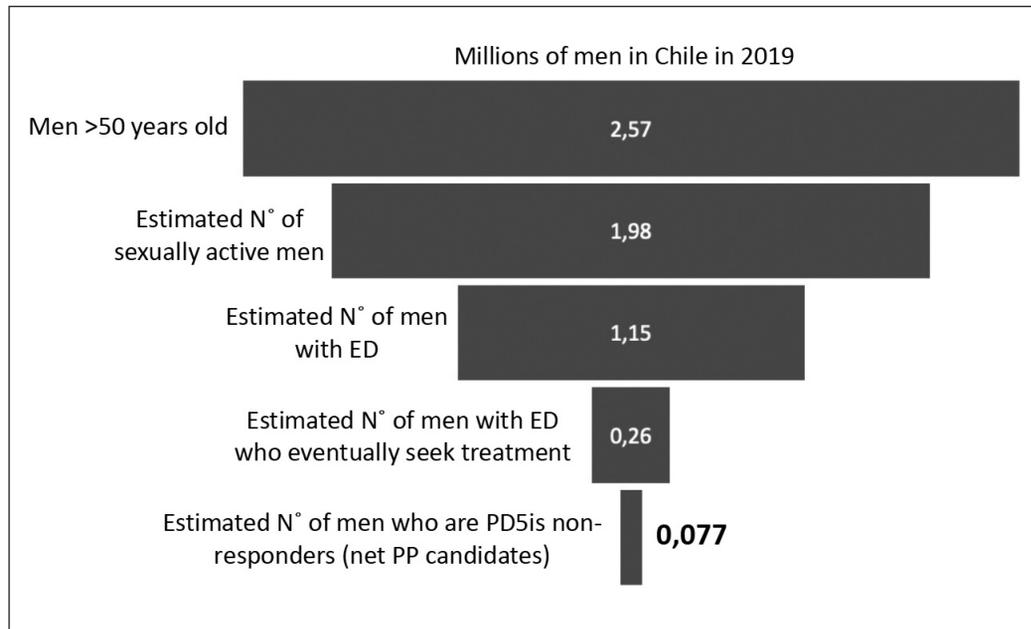
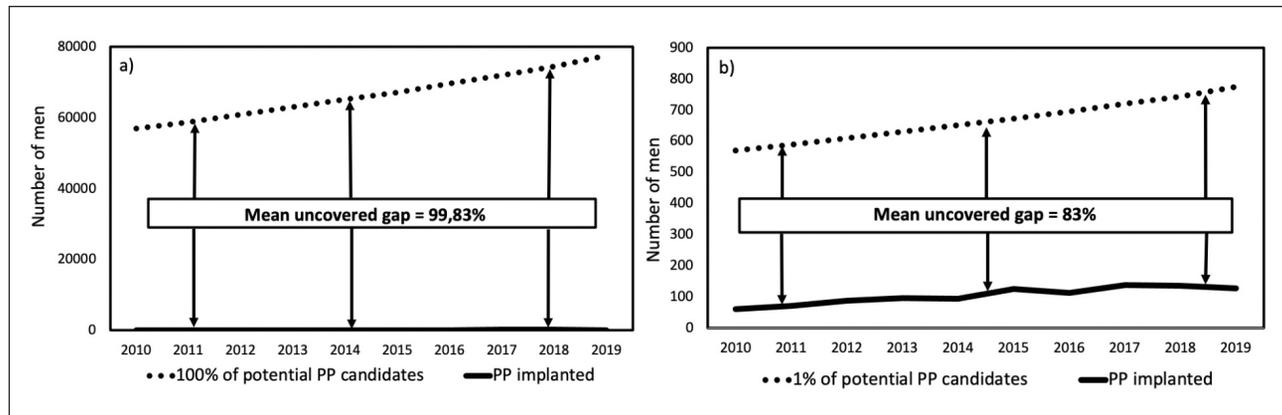


Figure 3.

a) Estimated uncovered gap between all (100%) potential PP candidates and devices actually implanted in the 10-year study period.
b) Estimated uncovered gap considering a scenario where only 1% of potential PP candidates would be willing to undergo surgery versus the devices actually implanted.



Finally, according to previous reports (13, 14), 30% of these patients would not respond to PD5is and become potential candidates for PP implantation ($n = 77.470$). In Figure 2, the estimated prevalence of ED and potential PP candidates are presented for each year of the study.

If we consider that all potential PP candidates were willing to receive an implant during the study period, the estimated gap between this number (net PP candidates) and the actual number of implanted units is 99.83% (Figure 3).

In order to perform a more realistic analysis, we considered an alternative scenario where only 1% of the PP potential candidates would be willing to undergo surgery. Even in this theoretical setting, the gap between the number of PP actually implanted and the potential demand was 83% (Figure 3).

Finally, using the same methodology, we estimated that only 0.05% of sexually active men older than 50 years old

with ED who sought medical assistance finally had a PP procedure to manage the ED.

DISCUSSION

According to the *Organization for Economic Cooperation and Development*, Chile is an aging country in *South America*, and it is expected that age-related conditions such as ED will significantly increase in the next decades (16). This epidemiological data is consistent with the observed 10-year growth in the number of men older than 50 years old (34.7%). The combination of this fact with the proportion of them who declare being sexually active (77%) and the high prevalence of ED (58%), we believe explains the constant annual rate of increase in the sales of PD5is.

Interestingly, the 10-year growth observed in the sales of

PD5is (71.3%) and its AAV (6.2%) almost doubled the growth rates observed for the population of men older than 50 in the same period (10-year variation 34.7%; AAV 3.4%). This difference may be explained by three reasons. First, a significant number of PD5i consumers might be men under 50 years old (11, 12). Second, in Chile, PD5is are over-the-counter medicines (no prescription needed), with multiple new generic low-price drugs, which facilitates its access. Finally, as recently reported by *Dogan and Madendere* (17), Chile is in the top five worldwide for PD5is search trends on the internet, specifically for Sildenafil, which confirms the fact that these drugs are extremely well known in this country. In the last two decades, similar annual growth rates of PD5is sales have also been reported in other countries, and the worldwide market is expected to grow 6.5% annually by 2023 (7, 11), being Sildenafil the most prescribed drug by physicians, particularly among andrologists (18).

For clinicians who treat ED patients regularly, it is not surprising to observe that the annual sales trends of intracavernosal vasoactive agents have remained stable or were even slightly negative in the study period (AAV -0.2%).

A lack of spontaneity, pain, and risk of priapism, among others, may explain why the demand for intracavernosal vasoactive agents has remained unchanged in the last 10 years in Chile. Combining our clinical experience and results, we believe that intracavernosal vasoactive agents still have a role in the management of moderate/severe ED. However, in the whole spectrum of ED treatments available, it seems to occupy a specific niche without potential for growth. Penile prosthesis have been an option to treat ED for the last 40 years and are available in almost all countries around the world. Recently, in the period 2006-2010, Bass et al. reported an AAV of 8.1% in PP sales worldwide, which was based on information given by two companies: *American Medical System*® (Minnetonka, Minneapolis, USA) and *Coloplast*® (Humblebaek, Denmark) (1). In this study, the USA represented 85.9% of the worldwide market, followed by *Germany* (2.3%), the *United Kingdom* (2.1%), and *Italy* (2.0%). In the last two decades, other countries such as *France* and *Saudi Arabia* have reported AAVs of 4.9% and 31.3% respectively (19, 20). Compared to the global tendencies, our study shows a similar trend in the last decade (6.7%). Regarding the type of implant, we observed that 68% were malleable and 32% were 3-piece inflatable implants, which are similar to other countries where PP are not covered by either public or private insurance (20). On the other hand, in the USA, where most PP devices are covered by insurance, 90% of implanted PP were inflatable, and only 10% were malleable (21).

This reveals that when it comes to choosing the type of PP, costs and insurance coverage play an important role.

High satisfaction rates have been reported for PP (90%) (22), and the number of candidates for this treatment are presumed to have significantly increased in the last two decades. Nevertheless, the gap between the number of PP implanted annually and the net number of potential candidates remains extremely high. Only around 3% of ED patients finally undergo surgery in the USA, the country with the highest number of PP implanted and with a high percentage of patients who have insurance coverage (3). According to our data, this proportion in Chile would be

0.05%, and the potential uncovered gap between the net PP candidates and the actual number of implanted devices ranges from 99.83% (considering 100% of the net potential demand) to an extremely conservative 83% (considering 1% of the net potential demand). It is a fact that the number of ED patients has constantly increased worldwide in the last 40 years, the GDPPCs of developed and emerging economies have also increased constantly, the PP satisfaction rates are extremely high, and the costs have decreased. Thus, considering our results and the available information in peer-reviewed journals, it is worth examining why the implantation of PP has not increased substantially, as well as why the gap between potential candidates and actual PP implanted remains extremely high worldwide. We believe that the answers to this question are beyond the scope of this paper. However, considering our results, it is worth proposing some possible explanations.

First, it may be that the number of men with severe ED who are sexually active and seek treatment is overestimated, which would make the estimated number of potential candidates for PP wrong. However, the rising demand for PD5is is evidence against this argument because even if we consider that a high proportion of men who consume PD5is do not suffer from ED, the remaining proportion still represents a high volume of men worldwide (11, 12). Second, it may be that the calculated proportion of ED patients who do not respond to PD5is might be overestimated (30%), meaning that there would be much fewer net PP candidates. However, our own clinical experience and the published evidence consistently indicate that 30% of men with ED will not experience clinical significant improvements in their erections (13, 14). Considering this analysis, it seems that our estimation of the net PP candidates comes from robust data. Third, as demonstrated by *Pescatori et al.* (23), oral drugs (PD5is) are extensively known in the general population as a treatment alternative for ED; however, second and third line treatments, such as PP are known by a minority of men (22.2-27.9%) and women (19.2-20.2%).

The same study evaluated the attitude towards PP revealing that 50,7% of men and 48,4% of women would be willing to choose (men) or support (women) PP as a treatment option for severe ED. This evidence supports the idea that the low awareness that the general population and particularly men have about PP, may be one of most important facts behind the huge uncovered demand.

If we consider the gap between the potential and the actual demand to be real (83 to 99.83%), we believe there is an important issue to address: how PP technology can be more efficiently provided to men who do not have other suitable treatment options? Strategies to improve transfer from manufacturers to the community could be, among others; increasing access through insurance coverage for devices in countries that still do not have them, such as Chile; lower device prices and finally, educating urologists and patients about the benefits of PP in order to increase awareness about this treatment option for patients with ED.

Our study has several limitations. First, it is a retrospective study; second, the number of men with ED and severe ED (PP candidates) were estimated from previous reports that may not strictly represent all Chilean men;

third, the proportion of men that consume PD5is and do not have ED is unknown, which may have impacted the annual sales trend results significantly; fourth, the number of PP that were re-operations is unknown, meaning that the number of men who actually received a PP as treatment for severe ED could be lower; finally, as mentioned, the actual proportion of men who are PP candidates but would be really willing to undergo the procedure is unknown; for the aim of the research, this number was estimated by crossing the available data.

CONCLUSIONS

In the 10-year period (2010-2020), PD5is significantly increased in demand, while intracavernosal injections of vasoactive agents remained stable. The average annual variation of PP in Chile is comparable to the rest of the world. However, the gap between potential PP candidates and the actual number of devices implanted is suspected to be extremely high. This phenomenon seems to be present worldwide, even in countries where the device is covered by insurance. The reasons behind this gap may be addressed by taking actions to increase the access to PP to treat patients with ED worldwide.

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