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# A Cost Analysis of Phosphodiesterase Type 5 Inhibitors in the United States



Behnam Nabavizadeh, Amanda Nguyen, Diane Li, Jeroen van Meijgaard, and Benjamin N. Breyer

**OBJECTIVE** 

To perform a cost analysis of generic and brand-name Phosphodiesterase Type 5 (PDE5) in-

hibitors at different dosages and pharmacies across the US.

**METHODS** 

Using an all-payer retail pharmacy-claims database, we analyzed prescription drug data for three generic and six brand-name oral PDE5 inhibitors at different dosages across US chain and

independent pharmacies in 2019.

**RESULTS** 

We obtained cash price data from 60,186 pharmacies (35,976 chain and 24,210 independent). The nationwide mean cash price per unit (PPU) ranged from  $\$8.6 \pm 5.2$  (sildenafil 20 mg at chain pharmacies) to  $\$107.1 \pm 71$  (Adcirca 20 mg at independent pharmacies) equal to 1145.3% difference. Chain pharmacies provided significantly lower average prices for one brandname and six generic PDE5 inhibitors. Tadalafil PPU was cheaper at higher quantities, however, PPU increased with quantity prescribed for sildenafil. Looking at the top 10 metropolitan statistical areas, the highest PPUs were observed for tadalafil (Cialis) 10 mg and sildenafil (Viagra) 50 mg in Atlanta ( $\$67.4 \pm 8.7$ ) and Los Angeles ( $\$50.3 \pm 24.0$ ), while New York ( $\$9.7 \pm 2.6$ ) and Miami ( $\$27.9 \pm 16.4$ ) had the lowest PPUs for tadalafil (Cialis) 5 mg and sildenafil (Viagra) 100 mg, respectively.

CONCLUSION

A substantial variability in PDE5 inhibitor cash prices exists across manufacturer, dosage, quantity, pharmacy type, and location. In addition, the pricing does not necessarily correlate with the regional socioeconomic factors. This highlights the importance of provider awareness and patient counseling on drug price including potentially assisting patients in identifying opportunities for cost savings. UROLOGY 183: 127–133, 2024. © 2023 Elsevier Inc. All rights reserved.

rectile dysfunction (ED) is a common disease among men with an increasing prevalence worldwide. It is estimated that ED affects more than half of men aged 40-70 years and more than 70% of men older than 70 years. ED affects up to 30 million men in the United States (US). Although ED is not a life-threatening condition, it can negatively impact mental health, quality of life, and interpersonal relationships.

Current management options for ED range from lifestyle modifications and noninvasive therapies to invasive options which are generally utilized in a step-wise manner. Oral Phosphodiesterase Type 5 (PDE5) inhibitors currently serve as the mainstay of ED treatment.<sup>8</sup> The efficacy and safety profile of PDE5 inhibitors have been tested in several well-designed randomized clinical trials showing such drugs are effective medical therapy and are generally well tolerated. Begins Despite high efficacy of PDE5 inhibitors, the dropout rate remains high among patients, ranging from 30% to 80% with almost half of the subjects abandoning PDE5 inhibitors within 1 year. While PDE5 inhibitor treatment discontinuation has been shown to be multifactorial, direct patient cost has been a prominent modifiable determinant of treatment discontinuation.

In a cost analysis of PDE5 inhibitors in 2018, Mishra et al investigated the variation in cash prices of PDE5 inhibitors within a 25-mile radius of their institution in Cleveland, Ohio. They found that the largest price difference for 10 tablets of 100 mg sildenafil between all pharmacies was 38,000% and chain pharmacies offer PDE5 inhibitors at a significantly inflated cost (>900%) compared with independent pharmacies. In a more recent study in 2022, Levy et al identified the relationship between pharmacy type and medication price for 14 common medications for ED and benign prostatic

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hyperplasia (BPH) management, as well as how the socioeconomic status of a neighborhood can impact pharmacy pricing. This study was focused specifically on pharmacies in the Upper East Side and East Harlem neighborhoods of New York City representing the upper and lower ends of the socioeconomic spectrum in a major urban city. It demonstrated large variation in the cash prices for common ED medications in these two neighborhoods. Among all 14 medications, the greatest variation among pharmacies was seen for ED medications as compared to BPH medications. Tadalafil 20 mg and sildenafil 100 mg were up to 26.7 and 15.4 times less expensive at independent pharmacies, respectively.

In this study, we aim to build upon previous studies by assessing a much larger sample size at the national level. We conducted a cost analysis of generic and brand-name PDE5 inhibitors at varying dosages and pharmacies across the US. We aim to identify different factors associated with the cash price of PDE5 inhibitors to inform prescribers and patients in order to increase affordability. We hypothesized that a large variability exists by the type of retail pharmacy, dosage, quantity, and location. Moreover, generic medications are expected to have larger variations as compared to their brand-name counterparts.

#### **METHODS**

#### Database

We analyzed a representative sample of prescription drug data from an all-payer retail pharmacy-claims database, reflecting 846,703 deidentified pharmacy claims across chain and independent pharmacies in 52 states and U.S. territories. <sup>13</sup> Data includes the drug and quantity that was dispensed, the location and date of the transaction, and the usual and customary cost (U&C) of the product that was dispensed. These data do not include any personal identifiers, and do not include information on what was paid for the medication. This dataset has been used in prior literature to evaluate prescription drug pricing. $^{14,15}$  We analyzed all prescriptions dispensed for both generic and brand-name oral PDE5 inhibitors in 2019. We only included oral PDE5 inhibitors at different dosages with at least 10 pharmacies contributing data to the price calculations. The study protocol was reviewed and was deemed exempt from obtaining institutional review board approval. The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement was followed for the design and reporting of this study. 16

#### Statistical Analysis

We calculated cash price per unit (PPU) and accounted for the quantity filled for each claim, using all claims for PDE5

inhibitors at independent and chain retail pharmacies. For each claim, we calculated PPU by dividing the reported cash price, also known as the U&C amount, divided by the quantity filled. Cash price is defined as the price charged by a pharmacy to dispense a prescription drug to a cash-paying customer. To aggregate the data from the claim to the pharmacy-quantity level, we took the average cash price across all claims in a pharmacy-quantity group for a drug. To aggregate the data from a claim to pharmacy level, we took the average PPU across all claims in a pharmacy for a drug, weighted by the quantity filled on that claim. We calculated the average PPU for the top 10 most populated metropolitan statistical areas (MSAs). We also obtained socioeconomic factors (from US Census Bureau and US Bureau of Economic Analysis) for the top 10 most populated MSAs to investigate their association with cash PPU for different PDE5 inhibitors. These factors included median household income, share uninsured, and regional price parity. The U.S. Office of Management and Budget defines an MSA as an area that consists of at least a city with a population of at least 50,000 inhabitants.<sup>17</sup>

Mean price differences between chain and independent pharmacies were tested using unpaired Welch two-sample t test with a level of significance set at an alpha of 0.05. Mean price differences across dosage and across quantity group were tested using a one-way ANOVA test. Analyses were performed using R software version 4.1.2.

#### **RESULTS**

Average cash prices from a sample of 60,186 pharmacies (35,976 chain and 24,210 independent) were obtained (Table 1). The mean PPU for six brand-name and three generic oral PDE5 inhibitors at different dosages are presented in Table 2. The nationwide mean PPU varied from  $\$8.6 \pm 5.2$  (corresponding to sildenafil 20 mg at chain pharmacies) to \$107.1 ± 71 (corresponding to Adcirca 20 mg at independent pharmacies), which is equal to 1145.3% difference. Chain pharmacies provided significantly lower average prices for one brand name and six generic PDE5 inhibitors. There was a significant association between PPU and pharmacy type for Viagra 100 mg (P = .0033), tadalafil (Adcirca) 20 mg (P = .0129), tadalafil (Cialis) 5 mg (P < .0001), tadalafil (Cialis) 10 mg (P = .0005), tadalafil (Cialis) 20 mg (P = .0002), vardenafil 20 mg (P = .0001), and sildenafil (Revatio) 20 mg (P < .0001). The price difference in average U&C price at independent pharmacies relative to chain pharmacies ranged from - 10.8% (Levitra 10 mg) to 7.5% (Adcirca 20 mg) for brand-name, and from - 6.8% (sildenafil 25 mg) to 83.7% (sildenafil 20 mg) for generic drugs. Additionally, significant associations between PPU and dosage were found for Cialis (P < .0001), tadalafil (P < .0001), sildenafil (P < .0001), and vardenafil (P < .0001). Interestingly, PPU for Levitra (P = .1426), Viagra (P = .5291), and Stendra (P = .9459) were not associated with the dosage prescribed.

Table 1. Breakdown of pharmacies that contributed data on PDE5 inhibitors to the study.

Pharmacy Type	Pharmacy Stores, n (%)	Pharmacy Stores With Observed Cash Price for Brand-Name, $n\ (\%)$	Pharmacy Stores With Observed Cash Price for Generic, <i>n</i> (%)
Chain	35,976 (59.8)	1118 (3.1)	26,222 (72.9)
Independent	24,210 (40.2)	303 (1.3)	1882 (7.8)
All pharmacies	60,186	1421 (2.4)	28,103 (46.7)

**128** UROLOGY 183, 2024

**Table 2.** Mean (SD) cash PPU for PDE5 inhibitors (brand-name and generic) at different dosages stratified by the pharmacy type.

Brand Generic	Comerie	D	Ві	rand, mean (SD)	)	Generic, mean (SD)			
	Generic	Dosage	Chain Independent		P Value	Chain	Independent	P Value	
Adcirca	Tadalafil	20mg tablet	99.6 (30.2)	107.1 (71.0)	0.6720	63.9 (19.7)	84.3 (54.9)	0.0129	
Cialis	Tadalafil	2.5mg tablet	-	-	-	10.6 (2.4)	12.7 (6.4)	0.1123	
Cialis	Tadalafil	5mg tablet	15.4 (1.4)	15.5 (4.7)	0.8870	10.2 (2.0)	12.9 (4.1)	<0.0001	
Cialis	Tadalafil	10mg tablet	86.9 (4.0)	82.9 (21.3)	0.4173	60.2 (13.9)	71.3 (27.3)	0.0005	
Cialis	Tadalafil	20mg tablet	86.3 (4.1)	91.0 (27.0)	0.2477	58.9 (14.0)	84.4 (113.2)	0.0002	
Levitra	Vardenafil	10mg tablet	62.1 (3.6)	55.4 (37.6)	0.4905	49.7 (8.1)	-	-	
Levitra	Vardenafil	20mg tablet	62.7 (3.1)	62.3 (18.6)	0.8891	47.8 (7.8)	60.6 (16.7)	0.0001	
Revatio	Sildenafil	20mg tablet	-	-	-	8.6 (5.2)	15.8 (10.8)	<0.0001	
Stendra	-	100mg tablet	74.8 (3.0)	-	-	-	-	-	
Stendra	-	200mg tablet	75.1 (3.7)	-	-	-	-	-	
Viagra	Sildenafil	25mg tablet	-	-	-	44.3 (17.0)	41.3 (28.8)	0.3571	
Viagra	Sildenafil	50mg tablet	89.1 (5.5)	86.6 (27.0)	0.5166	43.7 (16.6)	41.7 (33.8)	0.3183	
Viagra	Sildenafil	100mg tablet	86.3 (7.0)	91.7 (23.2)	0.0033	42.2 (17.1)	43.2 (31.2)	0.2978	

PDE5, Phosphodiesterase Type 5; PPU, price per unit; SD, standard deviation. As color goes from blue to red PPU increases. PPU is expressed in US dollar. Significant P values are presented in bold typefaces.

Table 3. Average cash PPU by quantity group.

Drug Name	Quantity Group	Average Cash PPU	P Value*
Sildenafil (Revatio) 20 mg tablet	≤10	\$8.01	<.0001
	11-30	\$8.61	
	> 30	\$9.01	
Sildenafil (Viagra) 50 mg tablet	≤10	\$41.96	<.0001
, , , ,	11-30	\$45.63	
	> 30	\$52.35	
Sildenafil (Viagra) 100 mg tablet	≤10	\$42.97	<.0001
	11-30	\$46.48	
	> 30	\$52.29	
Tadalafil (Cialis) 5 mg tablet	≤10	\$10.75	<.0001
	11-30	\$10.38	
	> 30	\$10.52	
Tadalafil (Cialis) 10 mg tablet	≤10	\$63.09	<.0001
	11-30	\$57.99	
	> 30	\$46.90	
Tadalafil (Cialis) 20 mg tablet	≤10	\$62.06	<.0001
	11-30	\$58.19	
	> 30	\$46.68	

<sup>\*</sup> Significant P values are presented in bold typefaces.

Table 3 demonstrates cash price of PDE5 inhibitors at different quantities for the six most commonly filled oral PDE5 inhibitors. For sildenafil (Revatio) 20 mg (P < .0001), and sildenafil (Viagra) 50 mg (P < .0001) and 100 mg (P < .0001), average PPU increases as the quantity increases. However, tadalafil (Cialis) 10 mg (P < .0001) and 20 mg (P < .0001) were cheaper at higher quantities.

We observed a large variation in the mean PPU across the country. Table 4 demonstrates variability in cash PPU for different PDE5 inhibitors in the top 10 most populated MSAs, which include more than 85 million of the US population. The highest PPUs were observed for tadalafil (Cialis) 10 mg and sildenafil (Viagra) 50 mg in Atlanta ( $$67.4 \pm 8.7$ ) and Los Angeles ( $$50.3 \pm 24.0$ ), while New York ( $$9.7 \pm 2.6$ ) and Miami ( $$27.9 \pm 16.4$ ) had the lowest observed PPUs for tadalafil (Cialis) 5 mg and sildenafil (Viagra) 100 mg, respectively. We also observed several disparities between PDE5 inhibitor pricing and the regional

socioeconomic factors. For example, while the Atlanta MSA has the highest prices for tadalafil (Cialis) at different dosages, it has the lowest regional price parity among other MSAs. The New York and Los Angeles MSAs, the two most populated MSAs with highest regional price parities, have the lowest PPUs for tadalafil (Cialis) 5 mg and tadalafil (Cialis) 10 mg, respectively. The Houston MSA has the highest share of uninsured population (18.05%) and average PPU above the national average for 4 of the 6 PDE5 inhibitors. The lowest PPUs for sildenafil (Viagra) 50 mg and 100 mg can be found in the Miami MSA while it has the lowest median household income among all top 10 MSAs.

#### DISCUSSION

To the best of our knowledge, this study is the first to investigate the variability in cash price of different generic

UROLOGY 183, 2024 129

Table 4. Cash PPU of PDE5 inhibitors by the top 10 metropolitan statistical areas.

Metropolita n	Tada (Cialis tab	) 5mg	Tada (Cia 10mg	alis)	Tada (Cia 20mg	lis)	Silde (Rev 20mg	atio)	Silde (Via 50mg	gra)	Silde (Via 100mg		Total Popul	Media n Hous	Shar e Unin	Region
Statistical Area	Mean (SD)	IQR	Mean (SD)	IQR	Mean (SD)	IQR	Mean (SD)	IQR	Mean (SD)	IQR	Mean (SD)	IQR	ation (N)*	ehold Inco me (\$)†	sure d (%)‡	al Price Parity§
New York- Newark- Jersey City, NY- NJ-PA Metro Area	9.7 (2.6)	8.8– 10.7	57.8 (17.7)	53.0– 66.5	57.2 (18.7)	54.0– 69.2	12.0 (4.6)	12.7– 13.1	43.5 (14.0)	30.5– 46.9	41.8 (16.5)	31.1– 47.6	19,294 ,236	78,773	7.22	114.72
Los Angeles- Long Beach- Anaheim, CA Metro Area	10.1 (2.5)	8.8– 11.0	52.9 (15.7)	43.0– 65.3	58.7 (28.1)	52.5– 66.5	10.4 (5.6)	5.4– 13.1	50.3 (24.0)	37.9– 66.4	47.1 (20.8)	39.3– 59.0	13,249 ,614	72,998	9.15	109.83
Chicago- Naperville- Elgin, IL-IN- WI Metro Area	9.9 (1.9)	9.1– 10.5	56.5 (12.9)	52.6– 65.8	52.8 (14.7)	44.9– 61.3	8.5 (5.0)	3.2– 13.0	44.2 (15.8)	30.5– 58.1	41.3 (15.9)	28.9– 47.6	9,508, 605	71,770	7.6	103.28
Dallas-Fort Worth- Arlington, TX Metro Area	10.3 (1.6)	8.8– 11.0	58.4 (14.7)	50.4– 72.1	57.1 (15.9)	45.4– 72.1	8.1 (5.4)	3.1– 12.9	45.7 (17.1)	30.4– 66.5	44.7 (16.5)	28.9– 58.4	7,320, 663	70,281	16.38	104.24
Houston- The Woodlands -Sugar Land, TX Metro Area	10.3 (1.8)	8.9– 12.3	65.4 (10.7)	62.4– 72.1	61.5 (14.1)	54.3– 72.1	8.5 (6.2)	2.9– 13.0	48.3 (16.3)	30.5– 66.5	49.1 (14.6)	41.3– 66.5	6,884, 138	67,516	18.05	101.69
Washingto n- Arlington- Alexandria, DC-VA-MD- WV Metro Area	10.7 (2.3)	8.9– 12.3	57.0 (14.0)	50.2– 66.0	54.1 (17.7)	43.5– 72.1	10.0 (4.9)	4.6– 13.1	44.3 (15.0)	30.5– 54.9	39.7 (17.6)	28.9– 47.1	6,196, 585	103,75 1	7.57	109.39
Miami-Fort Lauderdale -Pompano Beach, FL Metro Area	10.0 (1.8)	8.8– 10.9	61.0 (12.6)	54.0– 66.8	58.0 (14.9)	54.5– 64.9	9.2 (4.5)	5.3– 13.0	30.1 (14.3)	12.5– 44.9	27.9 (16.4)	11.7– 46.1	6,090, 660	56,775	15.06	108.97
Philadelphi a-Camden- Wilmington , PA-NJ- DE-MD Metro Area	10.2 (2.4)	8.8– 11.0	55.8 (16.7)		57.1 (15.1)		11.2 (4.3)	12.4– 13.1	39.3 (18.1)		39.9 (17.7)	28.9– 55.8	6,079, 130	72,343	5.55	103.72
Atlanta- Sandy Springs- Alpharetta, GA Metro Area	10.8 (1.7)	9.3– 12.3	67.4 (8.7)	65.8– 72.1	64.0 (10.6)	61.1– 72.1	7.5 (4.7)	2.9– 12.9	47.0 (21.2)	29.6– 66.5	42.0 (22.3)	19.7– 66.5	5,862, 424	68,316	12.79	98.32
Boston- Cambridge- Newton, MA-NH	9.9 (2.2)	8.9– 10.5	56.4 (7.7)	53.5– 54.5	56.7 (10.2)	54.5– 54.6	11.7 (3.7)	12.7– 13.1	45.4 (11.1)	46.5– 47.0	43.8 (11.8)	46.5– 47.0	4,832, 346	90,333	2.88	109.54
Metro Area United States	10.3 (2.2)	8.9 - 11.7	60.5 (14.4)	53.2 - 72.1	59.6 (23.6)	54.1 - 72.1	8.8 (5.6)	3.1 - 13.0	43.6 (17.7)	30.3 - 63.3	42.2 (18.4)	28.9 - 53.7	324,69 7,795	\$62,84 3	8.84%	100.00

For PPU, as color goes from blue to red, mean PPU increases. For socioeconomic variables, more intense green color is associated with higher numbers. PPUs are expressed in US dollar.

**130** UROLOGY 183, 2024

<sup>\*</sup>Derived from the US Census Bureau (Table B01003).

<sup>&</sup>lt;sup>†</sup>Derived from the US Census Bureau (Table B19013).

<sup>&</sup>lt;sup>‡</sup>Derived from the US Census Bureau (Table B27010).

<sup>§</sup>Derived from the US Bureau of Economic Analysis (Regional Price Parities by State and Metro Area, released on December 14, 2021).

and brand-name PDE5 inhibitors prescribed for ED across the US. Using a large sample of pharmacies, we found that considerable price variability exists across all PDE5 inhibitors in the US, with 1145.3% difference between the lowest and highest mean PPUs. We also reported factors associated with this variability including pharmacy type, geographic location, dosage, and quantity prescribed. Our analysis made it clear that PDE5 inhibitors pricing does not appear to follow regional characteristics for all classes of drugs. PDE5 inhibitors are sometimes not covered by insurance leading to high cost of treatment and treatment noncompliance which makes such drugs an ideal candidate to study the price variability. <sup>11,18</sup>

In this study, chain pharmacies offered more affordable prices compared to independent pharmacies for the majority of PDE5 inhibitors. This price difference was more pronounced for certain generic drugs (Table 2). In a cost analysis of four PDE5 inhibitors (ie, sildenafil [Viagra] 100 mg, tadalafil [Cialis] 5 mg, vardenafil [Levitra] 20 mg, and avanafil [Stendra] 200 mg) in 2018, Mishra et al found that independent pharmacies provided the lowest cost for three of the four PDE5 inhibitors (ie, sildenafil, tadalafil, and avanafil) compared to other pharmacies within a 25mile radius of their institution in Cleveland, Ohio. 11 However, our study indicated chain pharmacies provided cheaper cash prices for sildenafil (Viagra) 100 mg and tadalafil (Cialis) 5 mg at the national scale. In line with our findings, they reported wide price variability especially among independent pharmacies. Of note, sildenafil was the only generic PDE5 inhibitors available at the time of Mishra's study and generic tadalafil was released during the writing of their article. This could have impacted their findings. In another study of 16 different generic and brand-name commonly used nonurologic drugs, Luo et al reported that independent pharmacies and small chain stores offered higher cash prices for generic drugs while big box pharmacies had the lowest prices. 19 Additionally, relative differences in cash prices for brand-name drugs were modest across types of retail pharmacies. We observed a similar finding where the largest price difference for brand-name and generic drugs by type of pharmacy was 10.8% and 83.7%, respectively.

Drug prices are meant to be adjusted by pharmacies according to the geographic location to meet a fair market value for the medication for that specific region. To examine this for ED drugs, we stratified cash prices by the top 10 MSAs in the US and compared several socioeconomic factors. We observed a wide variability in cash prices of PDE5 inhibitors among the largest metro areas in the US. For example, the commonly prescribed sildenafil (Viagra) 100 mg ranged from \$27.9 ± 16.4 in the Miami MSA to \$49.1 ± 14.6 in the Houston MSA, a 76% price difference. However, the pricing for most drugs did not have a clear association with the socioeconomic factors in each MSA. While socioeconomic factors may be associated with pricing in some regions, unadjusted drug pricing across MSAs can

lead to decreased affordability and poor patient adherence to medication regimen. 12,20,21

Many physicians are not aware of the cost of the drug they prescribe or do not discuss the cost with their patients. One underlying cause is the separate roles of physicians, pharmacists, and payers which has insulated physicians from knowing the drug prices or considering them in their decisions. 22,23 Increased awareness of both physicians and patients on drug costs and alternatives can play a major role in reducing drug expenditures and improving medication adherence. Clinicians can use information on price variability across manufacturer, dosage, and quantity to make more informed decisions on the most cost-effective medication regimen for a patient. For example, switching from brand to generic sildenafil 50 mg can offer average savings of \$45.4 per pill at chain pharmacies and \$44.9 per pill at independent pharmacies. Where clinically appropriate, savings could also be achieved by adjusting quantity and dosage, such as substituting one tadalafil 10 mg tablet (average PPU \$60.2 at chain pharmacies and \$71.3 at independent pharmacies) for two tadalafil 5 mg tablets (average PPU \$10.2 at chain pharmacies and \$12.9 at independent pharmacies).

Additionally, many patients are not aware of the large price variability for many drugs. It has been shown that patients' pharmacy choice is more influenced by convenience rather than cost.<sup>24</sup> However, Brodsky et al found that price education ultimately impacted intent to research prescription drug prices before selecting a pharmacy.<sup>24</sup> Educating patients about the observed variability by pharmacy type and geographic location can encourage them to do comparison shopping by using online platforms or visiting different pharmacies in order to find the lowest prices.

Despite relatively high costs associated with PDE5 inhibitors and large variability in their pricing, they have remained the first-line treatment for ED. Previous studies have indicated that PDE5 inhibitors are in fact less costly compared to more invasive treatment options. In a study published in 2000, Tan investigated various ED treatments in a hypothetical managed-care model of 100,000 members. 25 He found out that treatment with sildenafil was associated with the lowest cost among the 6 treatment options (ie, intracavernosal injection, penile prosthesis device, oral sildenafil, testosterone transdermal patch, transurethral alprostadil suppository, and vacuum erection device). In addition, the average cost per patient work-up in the sildenafil group was the least which could be due largely to the limited diagnostic work-up required before initiation of PDE5 inhibitors. More recently in 2020, Hansen et al assessed the cost-effectiveness of three separate PDE5 inhibitors including sildenafil, tadalafil, and vardenafil in ED therapy in a Norwegian setting.<sup>26</sup> They found that treatment with sildenafil was the most cost-effective option compared to tadalafil, vardenafil, and no treatment. They also

UROLOGY 183, 2024 131

included a pricing scenario based on patent expiration of tadalafil and vardenafil which indicated similar findings.

In this study, we reported the cash prices which would be an appropriate indicator for studying the economics of PDE5 inhibitors, because these drugs are still considered "lifestyle" drugs and thus are not covered by many public and private payers. <sup>27</sup> Given the effectiveness of PDE5 inhibitors, and increased awareness that supports their use as a medical treatment rather than a lifestyle drug, a reassessment for coverage of ED medications and sexual medicine specialist consultation is needed to subsidize the cost of ED care. <sup>28</sup>

We studied the price variability among several types of pharmacies. There are other emerging ways that patients can get prescriptions for treatment of ED. With the emergence of the COVID-19 pandemic, the use of telemedicine and online platforms for electronic consultation has increased dramatically representing a paradigm shift in the way that patients seek care for ED. Telemedicine has been shown to be a cost-effective route for the delivery of medical care in patients with ED.<sup>29</sup> Given the nature of ED that generally does not require in-person visits, many online men's health direct-toconsumer (DTC) platforms have launched in the past few years offering electronic consultation and prescription without the need for a physical exam or in-person visit.<sup>30</sup> The number of unique visitors to these websites has increased by 1688%, from 655,733 visits in Q4 2017 to over 11 million visits in Q4 2019.<sup>30</sup> In addition, it has been shown that these DTC platforms sell generic sildenafil at excessively high prices.<sup>28</sup> A recent study investigated the costs associated with DTC platforms in the management of ED and compared them to a traditional physician visit and local pharmacy prescription fulfillment.<sup>31</sup> The authors found that DTC prescriptions were markedly more expensive and local pharmacies, in conjunction with online coupons, consistently provide a markedly less expensive prices for PDE5 inhibitors.

Our study has several limitations that should be acknowledged. First, we present mean price differences for a large sample of prescription claims, which may not be distributionally robust. While we aggregate claims-level data to pharmacy-level prices, our tests of statistical significance may also be overpowered due to our large sample of pharmacies and detect statistically significant price differences that are not necessarily clinically or economically significant. Future research should evaluate the magnitude of price differences that may have clinical impact on patient behavior. As our data reflects retail pharmacy claims, we were also not able to include certain types of pharmacies and prescription platforms including hospital-associated pharmacies, mail pharmacies, or DTC platforms. Furthermore, we did not account for point-of-sale discounts offered by the chain or independent pharmacies. We anticipate the real prices that patients pay for PDE5 inhibitor prescriptions using discount codes and online coupons would be lower than the prices reported in this paper. It is also possible that the use of online coupons will reduce the variability in the prices of these drugs. In addition to the discounts, some pharmacies may offer to price match their competitors, which is not accounted for in this study. Reported prices would be lower if the patient had insurance coverage for the medications. Lastly, our study focused solely on cash prices, which could restrict the generalizability of our findings to insured patients, who may pay as little as \$1 to \$4 per unit. <sup>28</sup> It is worth noting that individuals without insurance are probably most affected by the significant variations in PDE5 inhibitor cash prices.

#### CONCLUSION

Although PDE5 inhibitors have been proved to be an effective class of drugs for ED, their use is sometimes limited due to cost. Using a large nationwide sample of pharmacies, we found a substantial variability in PDE5 inhibitor cash prices by retail pharmacy type, manufacturer, dosage, and quantity. We also found the pricing does not necessarily correlate with the regional socioeconomic factors. This highlights the importance of provider awareness and patient counseling on drug price including potentially assisting patients in identifying the most affordable medication regimen. This study could pave the road toward increased affordability, adherence, and inclusion in the use of this highly effective class of medications.

#### **Author contributions**

BN and BNB conceived on the study. AN, DL, and JV provided the data and performed data analysis. BN, AN, and DL wrote the manuscript. All authors critically reviewed the final manuscript.

#### **Declaration of Competing Interest**

Dr Nguyen, Ms Li, and Dr van Meijgaard are employees of GoodRx. These analyses are based on a representative sample of US pharmacy claims and not based on GoodRx transactions.

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**132** UROLOGY 183, 2024

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UROLOGY 183, 2024 133