Contemporary cost-analysis comparison of direct-to-consumer vs. traditional prescriptions of phosphodiesterase-5 inhibitors

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After a focused telehealth visit, patients can now access phosphodiesterase-5 inhibitor (PDE5 inhibitor) prescriptions through online direct-to-consumer (DTC) healthcare companies. This study seeks to quantify the cost of DTC PDE5 inhibitor treatment compared to a traditional physician visit and local pharmacy prescription. Two DTC companies, two compounding pharmacies with national reach, three online Canadian pharmacies, and sixteen American pharmacy chains were queried for prices of 90-day regimens of common PDE5 inhibitors. Prices for chains were determined using their publicly available price on GoodRx® with coupon. Cost of physician visit was determined using 2020 Center for Medicare and Medicaid Services reimbursement for a level 3 new patient visit. For sildenafil 20 mg, a physician visit and local prescription cost a low of $125.45 compared to $144.35 for compounding, $169.34 for Canadian, and $195.00 for DTC. For sildenafil 100 mg, a physician visit and local prescription cost a low of $137.16 compared to $289.35 for compounding, $200.36 for Canadian, and $900.00 for DTC. For tadalafil 5 mg, a physician visit and local prescription cost a low of $125.80 compared to $169.35 for compounding, $195.34 for Canadian, and $720.00 for DTC. For tadalafil 20 mg, a physician visit and local prescription cost a low of $161.00 compared to $289.35 for compounding, $229.00 for Canadian, and $2880.00 for DTC. Thus, local pharmacies, in conjunction with online coupons, consistently provide a markedly less-expensive option for fulfillment of PDE5 inhibitor prescriptions than online DTC services.

INTRODUCTION

Erectile dysfunction (ED) is a highly prevalent condition and is increasingly being recognized in men younger than 40 years of age [1]. It is associated with underlying comorbidities such as cardiovascular disease [2] and metabolic syndrome [3], and it has been shown that men with ED have a significantly higher chance of a cardiovascular event in the years following diagnosis [4]. Multiple factors may contribute to ED, including hypertension [5], diabetes [6], psychological disorders [7], medications [8], hypogonadism [9], and sleep disorders [10].

Many men may either delay or bypass presenting to a physician to discuss ED. Some studies estimate that less than 25% of patients with sexual dysfunction sought care from a physician [11]. Patients are concerned that physicians may dismiss their complaints or fail to offer medical therapy, or have difficulty discussing sexual health due to privacy or embarrassment [12].

Treatment of men with ED changed dramatically with the advent of phosphodiesterase-5 (PDE5) inhibitors such as sildenafil (Viagra®) and tadalafil (Cialis®), which are both available in cheaper generic formulations [13]. In the United States, these medications require a prescription and have historically required a visit to a physician. However, in recent years, there has been a substantial increase in telehealth and online direct-to-consumer (DTC) healthcare companies. Patients now have alternative access to these medications without a traditional office visit. Internet-based DTC prescription platforms offer electronic consultation for evaluation and pharmacologic treatment of ED without a physical exam or in-person visit [14].

Seemingly in response to the rising prevalence of ED in younger men [15], DTC prescription websites are being marketed and utilized with increasing frequency, with one recent study finding that from 2017 to 2019 the total number of unique, quarterly visitors to these sites increased by 1688% from over 650,000 to over 11 million, and in 2019 there were on average 4.9 million visits each month to all DTC prescribing sites [14, 16]. The popularity of these websites offering remote diagnosis may be associated with the promise of discrete evaluation and treatment of ED [14]. However, there is significant concern that DTC platforms selling PDE5 inhibitors in this manner overlook critical pathology and operate in conflict with American Urological Association (AUA) guidelines on ED [17], yet patients may believe they are receiving adequate medical assessment [16].

While there is still much to be studied regarding the potential adverse consequences of obtaining medical prescriptions via online DTC platforms, to date there has been no published information regarding the costs of using these platforms relative to a traditional office visit, especially with the availability of online discounts. This study seeks to compare the costs associated with online DTC PDE5 inhibitor treatment compared to a traditional physician visit and local pharmacy prescription fulfillment.
MATERIALS AND METHODS
Pharmacy and medication selection
Sixteen local pharmacy chains with available public prices on GoodRx (https://www.goodrx.com) were included. National pharmacies that were subsidiaries of the same corporation were grouped together and considered one pharmacy, as prices were identical between each subsidiary. To approximate a national distribution of prices and pharmacy chains, prices were determined for five zip codes across the United States: 92612 (Irvine, CA), 44101 (Cleveland, OH), 10001 (New York, NY), 75201 (Dallas, TX), and 35230 (Birmingham, AL). In addition, Costco (https://www.costco.com) alone was queried, excluding membership, in a single zip code, 92697 (Irvine, CA). Hims (https://www.hims.com) and Ro® (Roman; https://www.getroman.com), the two largest DTC companies with readily available prescriptions for PDE5 inhibitor medications, were included. Three online Canadian International Pharmacy Association–licensed Canadian pharmacies that offer shipping to the United States were included. Finally, two compounding pharmacies with national reach that offer shipping across the United States were included. Prices were compared for a 90-day supply of 20 and 100 mg doses of sildenafil and 5 and 20 mg doses of tadalafil. These usually represent the two most commonly prescribed PDE5 inhibitors in practice, in the quantity determined based on the available regimen closest to 90 doses. The price per dose was calculated. Data were collected during 2021.

Cost of a physician visit was determined using the 2020 Center for Medicare and Medicaid Services reimbursement schedule for a level 3 new patient visit, the most commonly coded visit for an ED consult in our practice.

Outcomes
The primary outcome was the price difference between the lowest available prices from online DTC companies compared to local pharmacies. The secondary outcomes were the price differences between all the groups including Canadian and compounding pharmacies, as well as the mean price differences between the groups.

Statistical analysis
One-way ANOVA and Tukey’s test comparisons were used to determine statistical significance between continuous variables. All statistical analysis was performed using R [18].

RESULTS
For a 90-dose supply of sildenafil 20 mg, a physician visit and local prescription cost a mean of $191.51 with a low of $125.79 (σ = 136.50), compounding pharmacy prescription cost a mean of $218.28 with a low of $144.35 (σ = 104.55), and Canadian pharmacy prescription cost a mean of $240.25 with a low of $169.34 (σ = 68.66), compared to a mean of $227.50 and a low of $195.34 (σ = 12.05), compared to an average of $272.50 and low of $270.00 for DTC (σ = 10.60). Finally, for tadalafil 20 mg, a physician visit and local prescription cost a mean of $643.70 with a low of $161.00 (σ = 690.64), compounding pharmacy prescription cost a mean of $359.33 with a low of $289.35 (σ = 98.96), and Canadian pharmacy prescription cost a mean of $291.74 with a low of $229.00 (σ = 59.74), compared to a mean of $3427.50 and a low of $2880.00 for DTC (σ = 774.28) (Table 1 and Fig. 1). Physician visit with prescription fulfillment through Costco, excluding membership, cost $159.34 for sildenafil 20 mg, $193.40 for sildenafil 100 mg, $126.34 for tadalafil 5 mg, and $161.34 for tadalafil 20 mg.

There were no statistically significant differences in mean price between the four groups for sildenafil 20 or 100 mg. However, tadalafil 5 mg from DTC companies was significantly more expensive than local prescription (p < 0.01), Canadian (p < 0.01), and compounding pharmacies (p < 0.01). Similarly, tadalafil 20 mg was significantly more expensive from DTC companies than local prescription (p < 0.01), Canadian (p < 0.01), and compounding pharmacies (p < 0.01).

DISCUSSION
First introduced in the mid-1990s, PDE5 inhibitors are a well-researched and efficacious first-line pharmacological option for the treatment of ED [17, 19, 20]. As sildenafil, and later tadalafil, have become generic, out-of-pocket costs to patients have decreased substantially. However, the available literature on the economics of PDE5 inhibitors is dated and does not account for the role of internet-based methods of prescription fulfillment [21]. In the era of generic PDE5 inhibitors and the increasing public awareness of sexual health, online DTC companies such as Ro® (Roman) and Hims® have emerged as a potential new paradigm in sexual medicine and men’s health. These companies offer low-commitment, low-pressure alternatives for men seeking medical management of ED, and they often direct marketing efforts at young men who may be hesitant to seek medical attention from a physician for sexual function [14]. Our investigation, however, reveals that DTC prescriptions are markedly more expensive with significant drawbacks when compared to a traditional physician visit with local prescription fulfillment.

We found that for a 90-dose supply, a physician visit and local pharmacy prescription was consistently less expensive than online DTC, with the lowest available prices 30% less for sildenafil 20 mg, 85% less for sildenafil 100 mg, 83% less for tadalafil 5 mg, and 94% less for tadalafil 20 mg. Mean prices were consistently lower for

| Table 1. Comparison of direct-to-consumer vs. traditional prescriptions of PDE5 inhibitors. |
| --- |
| Sildenafil | Sildenafil | Tadalafil | Tadalafil |
| 20 mg | 100 mg | 5 mg | 20 mg |
| **Physician visit plus local pharmacy** | | | |
| Mean | $191.51 | $524.11 | $205.79 | $643.70 |
| Low | $125.45 | $137.16 | $125.80 | $161.00 |
| **Physician visit plus compounding pharmacy** | | | |
| Mean | $218.28 | $401.78 | $179.33 | $359.33 |
| Low | $144.35 | $289.35 | $169.34 | $289.35 |
| **Physician visit plus online licensed Canadian pharmacy** | | | |
| Mean | $240.25 | $252.63 | $207.59 | $291.74 |
| Low | $169.34 | $200.36 | $195.34 | $229.00 |
| **Price difference between lowest categories** | | | |
| Mean | $69.55 | $762.84 | $594.20 | $2719.00 |
A thorough medical, sexual and psychosocial history, a physical examination, and selective laboratory testing for all men presenting with symptoms of ED [17]. This includes vital signs for cardiovascular health screening, morning serum total testosterone levels, and a thorough physical examination to assess for penile lesions, deformities, and evidence of Peyronie’s disease (PD), all of which may impact management [17].

ED may be an early harbinger of structural, systemic, or psychiatric disease, especially in the younger population to whom DTC services are often marketed. Men with ED experience increased risk for cardiovascular disease and coronary artery disease, and associations are seen between ED and hyperlipidemia, diabetes mellitus, obesity, and hypertension [23–25]. In addition, a comparison of men under 40 at low risk for coronary artery disease with similar men without ED suggests that young men with ED may exhibit subclinical cardiovascular disease and be at markedly higher risk for developing such conditions later in life [26]. While PD is typically associated with aging, 8.2% men with PD are under 40, of whom 21% experience ED [27]. Psychogenic factors may play a significant role in the pathogenesis of ED in this younger population, with some studies suggesting up to 83% of cases involve a significant psychogenic component [28, 29]. A self-reported, online questionnaire administered by DTC companies may fail to identify such comorbidities, as it precludes the ability to physically examine the patient or properly identify and counsel on potential psychogenic factors. In a 2020 study, the specific content of DTC screening questionnaires was compared to the comorbidities present in a cohort of men under 40 presenting with ED [16]. In that cohort, 15% of patients were obese, 20% diabetic or prediabetic, 54% had dyslipidemia, 20% were hypogonadal, and 35% had varicoceles; all of these findings would have been missed by the DTC questionnaires [16].

While our investigation provides evidence that DTC companies are a more expensive option for prescription fulfillment than traditional physician visits and local pharmacies, it is not surprising that prices are higher given the for-profit nature of these companies. Yet, these sites continue to grow exponentially [14]. In order to provide the appropriate care and possibly inform practice habits for a changing demographic, clinicians should practice habits for a changing demographic, clinicians should...
consider why patients are willing to pay this premium, possibly due to convenience, perceived privacy, difficulty with physician access, and/or simply lack of awareness of such drawbacks. In a 2020 study of a German online platform similar to Ro® and Hims®, 48% of patients reported convenience as the primary rationale for pursuing DTC prescriptions, 23% discretion, and 13% shame. Only 4.6% reported price as their primary reason [30]. Awareness may also play a role, as 88% of patients report referral to DTC service through advertising or online media, and media coverage of such services is largely positive [16, 30].

While online DTC companies are potentially providing men with more convenience and perceived privacy, it is the urology community's obligation to promote the best and safest clinical care for our patients. Expanding the use of telemedicine in sexual medicine, as has been done during the COVID-19 pandemic, may be an appropriate avenue to address some of the concerns that lead patients to seek online DTC treatment [31, 32]. While telemedicine is often appropriate for follow-up visits, its role in the evaluation of new patients is not well defined, and in-person examination may be necessary for the establishment of a physician-patient relationship [33, 34]. Telemedicine is a valuable tool, and while appropriate in many situations, we believe clinical judgment should be applied in cases where the urologist feels an in-person evaluation may be necessary. In fact, determination of the necessity of a referral, and ease of pursuing that referral, is an advantage "traditional" telemedicine has over DTC companies [32]. In addition, increasing public awareness of the drawbacks of online DTC platforms, as the AUA has done in a press release in 2021, may help shift the balance toward evidence-based care [35].

Of note, online medication coupon providers, such as GoodRx®, used in our study, have their own drawbacks for prescribers and patients. As with any free online service, it must be monetized through advertisements or user data. In the past, GoodRx® has received criticism for sharing user data with companies including Google and Facebook; however, for now, this policy has changed [36]. Such concerns will remain with any such service and their use should be approached with caution and due diligence on the part of both patient and physician.

This study is limited by the narrow scope of prices analyzed. Local, non-chain pharmacies were not included and thus the relative cost of fulfilling prescriptions at such locations cannot be assessed. Similarly, while five zip codes provide an approximately representative sample of prices in major urban and suburban areas across the United States, it is not truly comprehensive. Insurance coverage was not considered as it varies significantly by insurance plan; however, insurance coverage would likely reduce the cost of a physician visit and local pharmacy prescription as these are well-known services to insurance providers, unlike online DTC offerings. Finally, local physician visits and prescription fulfillments may incur additional costs to the patient not assessed in this study, such as those of public transportation, parking, or missed work. Special consideration should be made for the unique socioeconomic situation of individual patients, and changes made to a traditional schedule as necessary or appropriate.

Our findings suggest that a physician visit and medication filled by local pharmacies, in conjunction with online coupons, consistently provide a markedly less-expensive option for fulfillment of PDE5 inhibitor prescriptions than online DTC services, compounding, or Canadian pharmacies, in addition to the established benefits of physician visits. This is most pronounced if a patient has flexibility in where he fills his prescription and can use the available local price.

DATA AVAILABILITY

Additional data are available upon request.

REFERENCES

1. Capogrosso P, Collichia M, Ventimiglia E, Castagna G, Clementi MC, Suardi N, et al. One patient out of four with newly diagnosed erectile dysfunction is a young man—worrisome picture from the everyday clinical practice. J Sex Med. 2013;10:1833–41.

2. Thompson IM, Tangen CM, Goodman PJ, Probstfield JL, Moinpour CM, Coltman CA. Erectile dysfunction and subsequent cardiovascular disease. JAMA. 2005;294:2996–3002.

3. Esposito K, Giugliano D, Obesity, the metabolic syndrome, and sexual dysfunction. Int J Impot Res. 2005;17:391–8.

4. Uddin SM, Mirbolouk M, Dardari Z, Feldman DJ, CAINozos-Achirica M, Defilipis AP, et al. Erectile dysfunction as an independent predictor of future cardiovascular events: the multi-ethnic study of atherosclerosis. Circulation. 2018;138:540–2.

5. Wang XY, Huang W, Zhang Y. Relation between hypertension and erectile dysfunction: a meta-analysis of cross-section studies. Int J Impot Res. 2018;30:141–6.

6. Koudrat Y, Pizzol D, Cosco T, Thompson T, Carmagni M, Bertoldo A, et al. High prevalence of erectile dysfunction in diabetes: a systematic review and meta-analysis of 145 studies. Diabet Med. 2017;34:1185–92.

7. Quek KF, Sallam AA, Ng CH, Chua CB. Prevalence of sexual problems and its association with social, psychological and physical factors among men in a Malaysian population: a cross-sectional study. J Sex Med. 2008;5:70–76.

8. Razdan S, Greer AB, Patel A, Alammeddin M, Jue JS, Ramsamy R. Effect of pre-
scription medications on erectile dysfunction. Postgrad Med J. 2018;94:171–8.

9. Corona G, Isidori AM, Aversa A, Burnett AL, Maggi M. Endocrinologic control of men's sexual desire and arousal/erectile dysfunction. J Sex Med. 2016;13:317–37.

10. Cho JW, Duffy JF, Sleep, sleep disorders, and sexual dysfunction. World J Mens Health. 2019;37:261–75.

11. Laumann EO, Glasser DB, Neves RC, Moreira ED Jr, Group GI. A population-based survey of sexual activity, sexual problems and associated help-seeking behavior patterns in mature adults in the United States of America. Int J Impot Res. 2009;21:171–8.

12. Althof SE, Rosen RC, Perelman MA, Rubio-Aurioles E. Standard operating proce-
dures for taking a sexual history. J Sex Med. 2013;10:26–35.

13. Huang SA, Lie JD. Phosphodiesterase-5 (PDE5) inhibitors in the management of erectile dysfunction. P T. 2013;38:407–19.

14. Wackerbarth JJ, Fantus RJ, Darves-Bornoz A, Hehemann MC, Helfand BT, Keeter MK, et al. Examining online traffic patterns to popular direct-to-consumer websites for evaluation and treatment of erectile dysfunction. Sex Med. 2021;9:100289.

15. Shamblou R, Ghaneh M. Erectile dysfunction. Lancet. 2013;381:153–65.

16. Shahinyan RH, Amighi A, Carey AN, Yoffe DA, Hodge DC, Pollard ME, et al. Direct-
to-consumer internet prescription platforms overlook crucial pathology found during traditional office evaluation of young men with erectile dysfunction. Urology. 2020;143:165–72.

17. Burnett AL, Nehra A, Breau RH, Culkin DJ, Faraday MM, Hakim LS, et al. Erectile dysfunction: AUA guideline. J Urol. 2018;200:633–41.

18. R Core Team. R: a language and environment for statistical computing. In: R Foundation for Statistical Computing. Vienna, Austria: 2020.

19. Boeillit M, Allen MM, Ballard SA, Gep-Attee S, Muirhead GJ, Naylor AM, et al. Sildenafil: an orally active type 5 cyclic GMP-specific phosphodiesterase inhibitor for the treatment of penile erectile dysfunction. Int J Impot Res. 1996;8:47–52.

20. Berner MM, Kriston L, Harms A. Efficacy of PDE5-inhibitors for erectile dysfunc-
tion. A comparative meta-analysis of fixed-dose regimen randomized controlled trials administering the International Index of Erectile Function in broad-spectrum populations. Int J Impot Res. 2006;18:229–35.

21. Rezaee ME, Ward CE, Brandes ER, Munarriz RM, Gross MS. A review of economic evaluations of erectile dysfunction therapies. Sex Med Rev. 2020;8:497–503.

22. Steidle CP, McCullough AR, Kaminetzky JC, Crowley AR, Siegel RL, Deriesthal H, et al. Early sildenafil dose optimization and personalized instruction improves the frequency, flexibility, and success of sexual intercourse in men with erectile dysfunction. Int J Impot Res. 2007;19:154–60.

23. Mostafavi H, Mori K, Hajebrarhani S, Abufaraj M, Karakiewicz PI, Shariat SF. Association of erectile dysfunction and cardiovascular disease: an umbrella review of systematic reviews and meta-analyses. BJU Int. 2021;128:3–11.

24. Fang MM, Bettencourt R, Barrett-Connor E. Heart disease risk factors predict erectile dysfunction 25 years later: the Rancho Bernardo Study. J Am Coll Cardiol. 2004;43:1405–11.

25. Feldman HA, Johannes CB, Derby CA, Kleinman KP, Mohr BA, Araujo AB, et al. Erectile dysfunction and coronary risk factors: prospective results from the Massachusetts male aging study. Prev Med. 2000;30:328–38.

26. Yao F, Huang Y, Zhang Y, Dong Y, Ma H, Deng C, et al. Subclinical endothelial dysfunction and low-grade inflammation play roles in the development of erectile dysfunction in young men with low risk of coronary heart disease. Int J Androl. 2012;35:653–9.
27. Tefekli A, Kandirali E, Erol H, Alp T, Köksal T, Kadioglu A. Peyronie's disease in men under age 40: characteristics and outcome. Int J Impot Res. 2001;13:18–23.

28. Nguyen HMT, Gabrielson AT, Hellstrom WJG. Erectile dysfunction in young men—a review of the prevalence and risk factors. Sex Med Rev. 2017;5:508–20.

29. Caskurlu T, Tasci AI, Resim S, Sahinkanat T, Ergenekon E. The etiology of erectile dysfunction and contributing factors in different age groups in Turkey. Int J Urol. 2004;11:525–9.

30. Rodler S, von Buren J, Buchner A, Stief C, Elkhanova K, Wulffing C, et al. Epidemiology and treatment barriers of patients with erectile dysfunction using an online prescription platform: a cross-sectional study. Sex Med. 2020;8:370–7.

31. Boehm K, Ziewers S, Brandt MP, Spanwasser P, Haack M, Willems F, et al. Telemedicine online visits in urology during the COVID-19 pandemic: potential, risk factors, and patients’ perspective. Eur Urol. 2020;78:16–20.

32. Rabinowitz MJ, Kohn TP, Ellimoottil C, Alam R, Liu JL, Herati AS. The impact of telemedicine on sexual medicine at a major academic center during the COVID-19 pandemic. Sex Med. 2021;9:100366.

33. Dooley AB, Houssaye N, Baum N. Use of telemedicine for sexual medicine patients. Sex Med Rev. 2020;8:507–17.

34. Association AM. 50-state survey: establishment of a patient-physician relationship via telemedicine. https://www.ama-assn.org/system/files/2018-10/ama-chart-telemedicine-patient-physician-relationship.pdf. Accessed 17 Dec 2021.

35. Association AU. Buyer beware: direct-to-consumer marketing not backed by science. In: Frey C, editor. American Urological Association. auanet.mediaroom.com. 2021.

36. Germain T. GoodRx Stops Sending Prescription Data to Facebook. 2020. https://www.consumerreports.org/health-privacy/goodrx-stops-sending-prescription-data-to-facebook-a6520868989/. Accessed 23 Sep 2021.

AUTHOR CONTRIBUTIONS
DS, FAY, LCJ: conceptualization, methodology; DS, LCJ: data collection, investigation; DS: formal analysis, visualization; DS, CAL, AB, FK, FAY, LCJ: manuscript preparation and editing; FAY, LCJ: supervision.

COMPETING INTERESTS
The authors declare no competing interests.

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