



Trends in reported male sexual dysfunction over the past decade: an evolving landscape

Edoardo Pozzi ^{1,2} · Paolo Capogrosso¹ · Luca Boeri ^{1,3} · Walter Cazzaniga^{1,2} · Rayan Matloob¹ · Eugenio Ventimiglia¹ · Davide Oreggia^{1,2} · Nicolò Schifano^{1,2} · Luigi Candela^{1,2} · Costantino Abbate¹ · Francesco Montorsi^{1,2} · Andrea Salonia ^{1,2}

Received: 2 March 2020 / Revised: 29 May 2020 / Accepted: 17 June 2020
© The Author(s), under exclusive licence to Springer Nature Limited 2020

Abstract

We investigated changes in patterns of reported male SDs at a single academic centre over a 10-year time frame. Comprehensive data of 2013 patients consecutively assessed for the first time by a single Sexual Medicine expert between 2006 and 2019 has been analysed. All patients were assessed with a thorough sexual and medical history. Primary reason for seeking medical help at first assessment was recorded for all patients and categorized as: erectile dysfunction (ED), premature ejaculation (PE), low/reduced sexual desire/interest (LSD/I), Peyronie's disease (PD), and other SDs. Linear and logistic regression models tested the association between different reasons for seeking medical help and the time at first evaluation. Local polynomial regression model explored the probability of reporting different SDs over the analysed time frame. Median (IQR) age at first clinical assessment was 50 (38–61) years. Overall, most patients were assessed for ED (824; 41%), followed by PD (369; 18%), PE (322; 16%), LSD/I (204; 10%) and other SDs (294; 15%). Significant changes in terms of reported SD over the analysed time frame were observed. The likelihood of assessing patients for ED significantly increased up to 2013, with a decrease in the past 5 years ($p < 0.001$). PE assessment at presentation linearly decreased over time (OR: 0.94; 95% CI: 0.91–0.96; $p < 0.001$). Patients assessed during the past few years were more likely to report PD (OR: 1.20; 95% CI: 1.15–1.25; $p < 0.001$) and LSD/I (OR: 1.21; 95% CI: 1.16–1.26; $p < 0.001$), with a linear increase over the evaluated time frame. Likewise, patients were also more likely to report other SDs (Coeff: 1.06; 95% CI: 1.02–1.10; $p = 0.004$), with a linear increase over time. These results may reflect real changes in SD incidence, increased public awareness towards different SDs and the possible impact of novel treatments available on the market throughout the same time frame.

Introduction

Sexual dysfunction (SD) is historically defined as a difficulty experienced by an individual or a couple during any stage of a normal sexual activity affecting physical pleasure, desire, preference, arousal or orgasm, with several updated

specifications over times [1–3]. Male patients presenting for SD mostly complain of erectile dysfunction (ED), premature ejaculation (PE), Peyronie's disease (PD) and lower sexual desire/interest (LSD/I) [4]. Over the past decades, public awareness campaigns and newly developed therapeutic and diagnostic strategies have played a major role in terms of patients' complaints about sexual function impairment, with not irrelevant impact towards the reasons for seeking medical help and the consequent incidence of reported sexual disorders in the real-life setting.

Eminent example of this is the advent of phosphodiesterase type 5 inhibitors (PDE5i), which led to a 2% increase in the number of patients seeking medical help for ED, along with an extraordinary amount of new studies on overall health of male patients seeking medical help for a problem—i.e. ED, which mostly went from being disease per se to epiphenomenon and symptom of different problems [5]. In this context, the association between ED and

These authors contributed equally: Edoardo Pozzi, Paolo Capogrosso

✉ Andrea Salonia
salonia.andrea@hsr.it

¹ Division of Experimental Oncology/Unit of Urology, URI, IRCCS Ospedale San Raffaele, Milan, Italy

² University Vita-Salute San Raffaele, Milan, Italy

³ Department of Urology, Foundation IRCCS Ca' Granda – Ospedale Maggiore Policlinico, University of Milan, Milan, Italy

the development of specific diseases and the linkage with common risk factors such as diabetes, hormonal dysregulation and metabolic syndrome have changed both patients' and physicians' perception over this condition [6–10].

Though numbers are certainly different, the same may hold true for other disorders, thus including both PE and PD [11–14]. Indeed, on the one hand, the advent of Dapoxetine and newly developed topical compounds for PE and, on the other, the growing use of extracorporeal shock wave therapy and collagenase *Clostridium histolyticum* (CCH) injections for PD might have ultimately influenced the raw rate of patients seeking expert consultation throughout times [15–18].

Recently published data have shown that novelties in terms of clinical management of SDs have driven patient interest in seeking web information in the past few years [19]. Whether this interest was eventually translated into actively seeking medical help, it is currently unknown. Thereof, the landscape of patients requiring clinical care for SDs could have changed in the past few years with a consequent need for a proper practical knowledge by healthcare professionals.

In this study, we aimed to investigate the changes in patterns of reported SDs over a relatively short period of time at a single academic Sexual Medicine outpatient clinic.

Material and methods

Comprehensive data of a cohort of 2013 consecutive patients assessed for the first time for SDs by a single expert between 2006 and 2019 were analysed. All patients were assessed with a comprehensive medical and sexual history. Comorbidities were scored with the Charlson Comorbidity Index [20]. Patients were also assessed in terms of socio-demographic characteristics, thus including recreational habits (i.e., smoking history, alcohol intake, illicit drugs) and regular physical exercise (defined as at least 2 hours/week) at the time of first clinical evaluation. Smoking habits were assessed and categorized into two groups as follows: no smokers (never smoked) and ex-smokers/active smokers. Similarly, alcohol consumption was categorized as abstainers (no alcohol consumption) and drinkers (any amount per week).

Primary reason at first outpatient assessment was recorded for all patients and categorized as: (i) ED, (ii) PE, (iii) PD, (iv) LSD/I, and (v) other SDs. ED was defined as the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance [21]. Either lifelong or acquired PE was defined according the classification criteria suggested by the International Society for Sexual Medicine (ISSM) Ad Hoc Committee [22, 23]. Low

sexual desire was defined using the 'umbrella' criteria taken from the Standard Operational Procedures of ISSM as the reduction in the usual level of SD/I and was defined throughout the study timeline as a clinical condition where a man complains of a modification in his usual level of sexual interest or desire [3, 24, 25]. Diagnosis of PD was achieved with a comprehensive medical and sexual history, physical examination and, in some cases, sonographic evaluation of the penile shaft confirmed the presence of fibrotic plaque/s, thus establishing the final diagnosis of PD [26]. Sexual dysfunctions other than ED, PE, LSD/I and PD were categorized as 'other SDs' (e.g. delayed ejaculation/anejaculation, reduced semen volume, penile morphometric alterations other than PD/penile dysmorphism, orgasmic dysfunction, etc.). Data collection followed the principles outlined in the Declaration of Helsinki. All patients signed an informed consent agreeing to share their own anonymous information for future studies. The study was approved by the Ethics Committee of our centre (IRCCS OSR Prot. 2014 – Pazienti Ambulatoriali). The Strengthening the Reporting of Observational Studies in Epidemiology checklist was followed to ensure high-quality presentation of the study [27].

Statistical analysis

Prevalence of ED, PE, LSD/I and PD was recorded for each year between 2006 and 2019 at a single, tertiary, referral academic centre. Local polynomial regression model was applied to explore and graphically display patients' likelihood of reporting different SDs over the analysed time frame. Regression models tested the association between different reasons for seeking medical help and the time at first evaluation.

Statistical analyses were conducted using Stata version 14.0 (Stata Corp., College Station, TX, USA), with a two-sided significance level set at $p < 0.05$.

Results

The overall number of patients assessed for SDs linearly increased over the past decade (Fig. 1).

Table 1 shows descriptive statistics of the whole cohort. Median (interquartile range) age at first clinical assessment was 50 (38–61) years. ED was the most frequently reported sexual complain (41%), followed by PD (18%), PE (16%), LSD/I (10%) and other SDs (15%) (Table 1).

Figure 2 graphically displays the probability of reporting different SDs over the analysed time frame. Patients assessed in the past few years were more likely to report PD (odds ratio (OR): 1.20; 95% confidence interval (CI): 1.15–1.25;

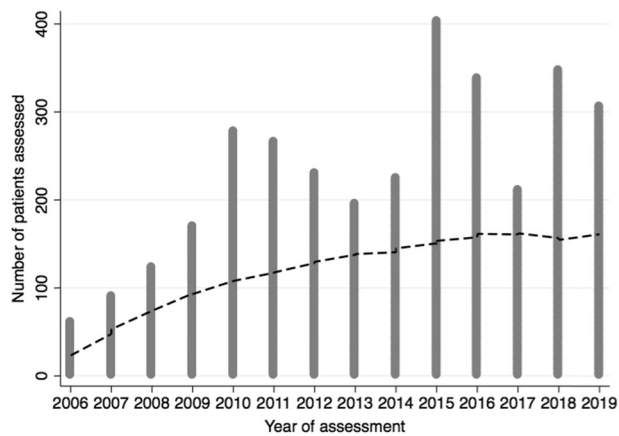


Fig. 1 Patients seeking help for sexual dysfunction (any type) over time. The dashed line represents the increasing trend of patients assessed over time estimated with local polynomial smoothing.

Table 1 Descriptive statistics of the whole cohort ($N = 2013$).

Age (years; median (IQR))	50 (38–61)
BMI (kg/m^2); median (IQR)	25 (23.1–27.4)
CCI [N (%)]	
0	1621 (81)
≥ 1	392 (19)
DM type 1	38 (1.9)
DM type 2	123 (6.1)
CVD	83 (4.1)
Hypertension	543 (27)
Alcohol intake [N (%)]	618 (31)
Cigarette smoking [N (%)]	
No	1168 (58)
Current smoker	443 (22)
Ex-smoker	383 (19)
Regular physical activity [N (%)]	1087 (54)
Sexual dysfunction [N (%)]	
Erectile dysfunction	824 (41)
Premature ejaculation	322 (16)
Peyronie's disease	369 (18)
Low sexual desire/interest	204 (10)
Other SDs	294 (15)

BMI body mass index, CCI Charlson Comorbidity Index.

$p < 0.001$; Table 2) and LSD/I (OR: 1.21; 95% CI: 1.16–1.26; $p < 0.001$; Table 2) with a linear increase over the evaluated time frame. Conversely, the probability of reporting ED showed a significant increase up to 2013, with a subsequent slight decrease in the past 5 years ($p < 0.0001$). The likelihood of reporting PE at first assessment linearly decreased over time (OR: 0.94; 95% CI: 0.91–0.96; $p < 0.001$). We also observed an increase in patients seeking first assessment for SDs other than ED, PD, PE and LSD/I (Table 2; $p = 0.004$).

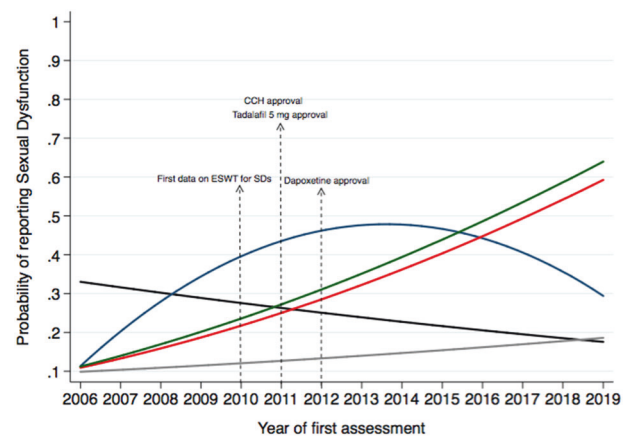


Fig. 2 Probability of reporting different sexual dysfunctions over time. Blue line represents erectile dysfunction over time; black line depicts premature ejaculation; green line represents Peyronie's disease; red line represents low sexual desire/interest; and grey line represents other sexual issues.

Table 2 Regression analysis testing the probability of being assessed for specific SDs (any) according to year of first assessment (2006–2019).

Predicted variable	OR	95% CI	p value
Low sexual desire/interest	1.21	1.16–1.26	<0.001
Peyronie's disease	1.20	1.15–1.25	<0.001
Premature ejaculation	0.94	0.91–0.96	<0.001
Erectile dysfunction ^a	—	—	<0.001
Other SDs	1.06	1.02–1.10	0.004

SD sexual dysfunctions, OR odds ratio.

^aModelled with non-linear terms.

Table 3 Univariate regression estimating the association between year of first assessment, patients' clinical characteristics and lifestyle habits accordingly.

Predicted variable	Coeff	95% CI	p value
Age	−0.15	−0.31 to 0.01	0.04
BMI	−0.58	−1.34 to 0.17	0.1
Predicted variable	OR	95% CI	p value
CCI (0 vs ≥ 1)	0.93	0.91 to 0.95	<0.001
Smokers	1.11	1.08 to 1.13	<0.001
Regular physical activity	1.03	1.02 to 1.06	<0.001
Alcohol use	−0.004	−0.01 to 0.001	0.1

BMI body mass index, CCI Charlson Comorbidity Index.

Moreover, patients' clinical characteristics at first presentation showed relevant changes over time (Table 3). Indeed, patients assessed throughout the past few years were younger ($p = 0.04$), reported less comorbidities ($p < 0.001$), were more likely current smokers ($p < 0.001$) and did practice physical activity on a regular basis ($p < 0.001$).

Discussion

Is it possible that a disease comes to the doctor's attention since it is susceptible to specific therapies? Likewise, is it plausible that, as the availability of treatments may change over times, the load of patients requesting a medical assessment may also change accordingly to such an extent that might also change the demography of Medicine? Our analyses have attempted to answer these questions in the sensitive and narrow field of Sexual Medicine; indeed, this study was aimed to detect significant changes of reported SDs over a relatively little time frame in patients presenting for an SD (any) as their primary complaint at a single Sexual Medicine outpatient clinic. Current findings suggested that the likelihood of assessing patients for ED increased up to 2013, with a subsequent gradual decrease over the years. On the contrary, the rate of patients complaining of PE linearly decreased over time. Of clinical interest, the patients evaluated in the past few years were more likely to be diagnosed with LSD/I and PD at first assessment. Both those latter conditions had showed a linear increment throughout the course of many years. Of further clinical relevance, we observed that patients presenting for ED were younger and younger over the years and with a lower load of comorbidities as compared with the ones evaluated in the past. Overall, these results suggest a significant change in the landscape of patients seeking medical help for SDs, with potential important implications both in epidemiological terms and in clinical practice. Indeed, the observed changes may be related to differences in terms of lifestyle, daily habits and public awareness that occurred over time—all changes that actually occurred—with a direct impact on the risk of developing or at least seeking help for SDs. As a consequence, this sort of evolution obliges physicians to face up to different patients' profile in the everyday clinical practice, along with potential novel treatments, or even simply different needs.

As for ED, a number of now historical studies had evaluated perception changes over this condition both in patients and among medical practitioners [28, 29]. So much has been said about the revolutionary power of PDE5i after their launch in the market, along with the concomitant explosion of Internet, both of which could have positively influenced the compliance of men seeking medical help for ED [30–33]. This is certainly a realistic deduction, although perhaps a little too simplistic and only partially true. Indeed, Salonia et al. [34], for instance, pointed out how a delay in seeking medical help in new-onset ED patients remained high, even after the introduction of PDE5i. In contrast, patients with higher degree of awareness on this condition were more likely to ask for expert medical attention [34], although the educational status had demonstrated not to significantly affect a patient's behaviour towards ED [35].

Moreover, a recent analysis has showed how age at first presentation for ED had decreased significantly over a relatively short period of time [36, 37], with these findings possibly being the consequence of an increased public awareness on ED, which would highlight the importance of sexual education programmes among younger generations. In addition, other studies demonstrated how general practitioners (GPs) underestimate and scantily investigate the presence of ED during their routine clinical work-up; in this context, GPs' reluctance in investigating ED, together with wrong feelings of inadequacy and erroneous beliefs among patients, play a major role in assessing precise incidence and prevalence of ED in the general population [6, 38].

As for PE, wide heterogeneity exist in terms of published disease prevalence, mainly as a consequence of differences in methodology, assessment tools, ethnic groups and age distribution among studies [14, 39]. Our cohort of patients presenting for SDs has been assessed with a consistent and homogenous approach over the years by a single expert; thereof, this would help and guarantee the accuracy of the diagnosis throughout the analysed time frame, thus limiting an internal bias that might impact towards data collection. Conversely, the problematic nature of the disorder and patients' poor compliance with therapies, including new ones developed and proposed over time [40], may have been responsible for the descending prevalence trend of patients seeking medical help for PE as their primary complaint, which was observed during the short time frame under investigation.

In contrast, we found that trends of reported LSD/I and PD were largely increasing over the years. The growing incidence of these two conditions might be ascribed to different factors. Of those, LSD/I may be correlated to the increasing incidence of reported depressive symptoms, even at younger ages, especially in men with concomitant ED [41–44]. In this context, the co-presence of depressive symptoms and LSD/I can drastically reduce patients' self-confidence and sense of masculinity, thus inducing a dangerous vicious cycle. Similarly, LSD/I could be found in men after pelvic surgery [45], and it is more and more clear how important it is to ask also about sexual desire in individuals previously considered only because of their complaints for postoperative urinary incontinence and ED [45–47]. Furthermore, the increased prevalence of LSD/I may also derive from a condition of hypogonadism, which must necessarily be investigated and excluded, as well as other forms of endocrine disorders [48, 49].

As for the increasing trend of patients presenting with PD, we strongly believe that it could be ascribed to the introduction of relatively novel medications, such as CCH intraplaque injections [50, 51]. The advent and the proven efficacy of CCH might have changed patients' reluctance in seeking medical attention for PD, due to the poor amount of

effective medical therapeutic measures previously offered other than surgery. In this context, a recent study suggested that people are surfing the web for sexual diseases and treatment options thus raising public awareness and encouraging men to seek expert medical help [15]. Even if this holds true, another recent study found that the reported prevalence of men with PD did not change after CCH entered the market [52]. Whatever is the truth, it is certainly true that future will tell us if this increased prevalence in men with PD that has been observed by all the urologists was only a straw fire, given the withdrawal of CCH itself from most of the markets [53]. Lastly, we observe an increasing trend of patients reporting SDs other than ED, PD, PE and LSD/I, which could be ascribed to an overall increased public awareness of sexual diseases; still, larger studies considering further experiences in different centres are certainly necessary to more comprehensively speculate on this single-centre findings.

Our study is certainly not devoid of limitations. First, it is a cross-sectional retrospective analysis at a single, tertiary, referral academic centre thus raising the possibility of selection biases. Second, the definitions of specific sexual dysfunctions (e.g. PE and LSD/I) have changed over time leading to possible cases left undiagnosed. Third, our data may not reflect an actual change of disease incidence, defined as the number of cases observed over 1 year, but rather a change in the prevalence of each condition among patients seeking help for SDs. Indeed, we observed a linear increase in the overall number of patients assessed for SDs at a single centre, with a concomitant modification of the relative prevalence of the various conditions. As such, the absolute number of patients assessed for either ED or PE, for instance, did not show an actual decrease in recent years but rather a decreasing trend when compared to the number of patients complaining of PD, LSD/I or other SDs. Thereof, larger cohort studies across different centres and populations are needed to validate our findings. Yet, all patients have been consistently analysed over time by a single expert physician, thus limiting at least potential heterogeneity associated with differences in diagnostic work-up methodology.

Conclusions

The landscape of patients seeking medical help for SDs has changed over the past decade. Recently, more patients have been assessed for LSD/I and PD as compared with a relative decline in men complaining of ED and PE. These data could reflect either changes in public awareness toward different conditions or true modifications in disease incidence. Thereof, physicians should be aware of the evolving profile of patients seeking medical advice for SDs in order to provide adequate and up-to-date clinical care.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. Laumann EO, Nicolosi A, Glasser DB, Paik A, Gingell C, Moreira E, et al. Sexual problems among women and men aged 40-80 y: prevalence and correlates identified in the Global Study of Sexual Attitudes and Behaviors. *Int J Impot Res.* 2005;17:39–57. <https://doi.org/10.1038/sj.ijir.3901250>.
2. Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and predictors. *JAMA.* 1999;281:537–44. <https://doi.org/10.1001/jama.281.6.537>.
3. McCabe MP, Sharlip ID, Atalla E, Balon R, Fisher AD, Laumann E, et al. Definitions of sexual dysfunctions in women and men: a Consensus Statement From the Fourth International Consultation on Sexual Medicine 2015. *J Sex Med.* 2016;13:135–43. <https://doi.org/10.1016/j.jsxm.2015.12.019>.
4. McCabe MP, Sharlip ID, Lewis R, Atalla E, Balon R, Fisher AD, et al. Incidence and prevalence of sexual dysfunction in women and men: a Consensus Statement from the Fourth International Consultation on Sexual Medicine 2015. *J Sex Med.* 2016;13:144–52. <https://doi.org/10.1016/j.jsxm.2015.12.034>.
5. Montorsi F, Briganti A, Salonia A, Rigatti P, Margonato A, Macchi A, et al. Erectile dysfunction prevalence, time of onset and association with risk factors in 300 consecutive patients with acute chest pain and angiographically documented coronary artery disease. *Eur Urol.* 2003;44:360–4. Discussion 364–5.
6. Ribeiro S, Alarcão V, Simões R, Miranda FL, Carreira M, Galvão-Teles A. General practitioners' procedures for sexual history taking and treating sexual dysfunction in primary care. *J Sex Med.* 2014;11:386–93. <https://doi.org/10.1111/jsm.12395>.
7. Boeri L, Capogrosso P, Ventimiglia E, Schifano N, Montanari E, Montorsi F, et al. Sexual dysfunction in men with prediabetes. *Sex Med Rev.* 2019. <https://doi.org/10.1016/j.sxmr.2018.11.008>.
8. Montorsi F, Adaikan G, Becher E, Giuliano F, Khoury S, Lue TF, et al. Summary of the recommendations on sexual dysfunctions in men. *J Sex Med.* 2010;7:3572–88. <https://doi.org/10.1111/j.1743-6109.2010.02062.x>.
9. Hatzimouratidis K, Salonia A, Adaikan G, Buvat J, Carrier S, El-Meliegy A, et al. Pharmacotherapy for erectile dysfunction: recommendations from the Fourth International Consultation for Sexual Medicine (ICSM 2015). *J Sex Med.* 2016;13:465–88. <https://doi.org/10.1016/j.jsxm.2016.01.016>.
10. Hui J, He S, Liu R, Zeng Q, Zhang H, Wei A. Trends in erectile dysfunction research from 2008 to 2018: a bibliometric analysis. *Int J Impot Res.* 2019. <https://doi.org/10.1038/s41443-019-0161-8>.
11. Martin S, Atlantis E, Wilson D, Lange K, Haren MT, Taylor A, et al. Clinical and biopsychosocial determinants of sexual dysfunction in middle-aged and older Australian men. *J Sex Med.* 2012;9:2093–103. <https://doi.org/10.1111/j.1743-6109.2012.02805.x>.
12. Pastuszak AW, Rodriguez KM, Solomon ZJ, Kohn TP, Lipshultz LI, Eisenberg ML. Increased risk of incident disease in men with Peyronie's disease: analysis of U.S. Claims data. *J Sex Med.* 2018;15:894–901. <https://doi.org/10.1016/j.jsxm.2018.04.640>.
13. Graham CA, Mercer CH, Tanton C, Jones KG, Johnson AM, Wellings K, et al. What factors are associated with reporting

- lacking interest in sex and how do these vary by gender? Findings from the third British national survey of sexual attitudes and lifestyles. *BMJ Open* 2017. <https://doi.org/10.1136/bmjopen-2017-016942>.
14. Saitz TR, Serefoglu EC. The epidemiology of premature ejaculation. *Transl Androl Urol*. 2016;5:409–15. <https://doi.org/10.21037/tau.2016.05.11>.
 15. Russo GI, Cacciamani G, Cocci A, Kessler TM, Morgia G, Serefoglu EC, et al. Comparative effectiveness of intralesional therapy for Peyronie's disease in controlled clinical studies: a systematic review and network meta-analysis. *J Sex Med*. 2019;16:289–99. <https://doi.org/10.1016/j.jsxm.2018.12.011>.
 16. Russo A, Capogrosso P, Ventimiglia E, La Croce G, Boeri L, Montorsi F, et al. Efficacy and safety of dapoxetine in treatment of premature ejaculation: an evidence-based review. *Int J Clin Pract*. 2016;70:723–33. <https://doi.org/10.1111/ijcp.12843>.
 17. Di Mauro M, Russo GI, Della Camera PA, Di Maida F, Cito G, Mondaini N, et al. Extracorporeal shock wave therapy in Peyronie's disease: clinical efficacy and safety from a single-arm observational study. *World J Mens Health*. 2019;37:339–46. <https://doi.org/10.5534/wjmh.180100>.
 18. Porst H, Burri A. Novel treatment for premature ejaculation in the light of currently used therapies: a review. *Sex Med Rev*. 2019;7:129–40. <https://doi.org/10.1016/j.sxmr.2018.05.001>.
 19. Russo GI, di Mauro M, Cocci A, Cacciamani G, Cimino S, Serefoglu EC, et al. Consulting “Dr Google” for sexual dysfunction: a contemporary worldwide trend analysis. *Int J Impot Res*. 2019. <https://doi.org/10.1038/s41443-019-0203-2>.
 20. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373–83.
 21. NIH Consensus Conference. Impotence. NIH Consensus Development Panel on Impotence. *JAMA*. 1993;270:83–90.
 22. Althof SE, Abdo CHN, Dean J, Hackett G, McCabe M, McMahon CG, et al. International Society for Sexual Medicine's guidelines for the diagnosis and treatment of premature ejaculation. *J Sex Med*. 2010;7:2947–69. <https://doi.org/10.1111/j.1743-6109.2010.01975.x>.
 23. Serefoglu EC, McMahon CG, Waldinger MD, Althof SE, Shindel A, Adaiakan G, et al. An evidence-based unified definition of lifelong and acquired premature ejaculation: report of the second International Society for Sexual Medicine Ad Hoc Committee for the Definition of Premature Ejaculation. *J Sex Med*. 2014;11:1423–41. <https://doi.org/10.1111/jsm.12524>
 24. Rubio-Aurioles E, Bivalacqua TJ. Standard operational procedures for low sexual desire in men. *J Sex Med*. 2013;10:94–107. <https://doi.org/10.1111/j.1743-6109.2012.02778.x>.
 25. Salonia A, Clementi MC, Ventimiglia E, Colicchia M, Capogrosso P, Castiglione F, et al. Prevalence and predictors of concomitant low sexual desire/interest and new-onset erectile dysfunction - a picture from the everyday clinical practice. *Andrology*. 2014;2:702–8. <https://doi.org/10.1111/j.2047-2927.2014.00236.x>.
 26. Chung E, Ralph D, Kagioglu A, Garaffa G, Shamsodini A, Bivalacqua T, et al. Evidence-based management guidelines on Peyronie's disease. *J Sex Med*. 2016;13:905–23. <https://doi.org/10.1016/j.jsxm.2016.04.062>.
 27. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Epidemiology*. 2007;18:800–4. <https://doi.org/10.1097/EDE.0b013e3181577654>.
 28. Stevenson FA, Kerr C, Murray E, Nazareth I. Information from the Internet and the doctor-patient relationship: the patient perspective—a qualitative study. *BMC Fam Pract*. 2007;8:47. <https://doi.org/10.1186/1471-2296-8-47>.
 29. Gualtieri LN. The doctor as the second opinion and the internet as the first. In: *CHI 09 Extended Abstracts on Human Factors in Computing Systems*. Boston, MA, USA: Association for Computing Machinery; 2009. p. 2489–98. <https://doi.org/10.1145/1520340.1520352>.
 30. Davis NF, Smyth LG, Flood HD. Detecting internet activity for erectile dysfunction using search engine query data in the Republic of Ireland. *BJU Int*. 2012;110:E939–42. <https://doi.org/10.1111/j.1464-410X.2012.11237.x>.
 31. Tozdan S, Briken P. Age of onset and its correlates in men with sexual interest in children. *Sex Med*. 2018;7:61–71. <https://doi.org/10.1016/j.esxm.2018.10.004>.
 32. Smith WB, McCaslin IR, Gokce A, Mandava SH, Trost L, Hellstrom WJ. PDE5 inhibitors: considerations for preference and long-term adherence. *Int J Clin Pract*. 2013;67:768–80. <https://doi.org/10.1111/ijcp.12074>.
 33. Yafi FA, Jenkins L, Albersen M, Corona G, Isidori AM, Goldfarb S, et al. Erectile dysfunction. *Nat Rev Dis Prim*. 2016;2:16003. <https://doi.org/10.1038/nrdp.2016.3>.
 34. Salonia A, Ferrari M, Saccà A, Pellucchi F, Castagna G, Clementi MC, et al. Delay in seeking medical help in patients with new-onset erectile dysfunction remained high over and despite the PDE5 era—an ecological study. *J Sex Med*. 2012;9:3239–46. <https://doi.org/10.1111/j.1743-6109.2012.02953.x>.
 35. Salonia A, Abdollah F, Gallina A, Pellucchi F, Castillejos Molina RA, Maccagnano C, et al. Does educational status affect a patient's behavior toward erectile dysfunction? *J Sex Med*. 2008;5:1941–8. <https://doi.org/10.1111/j.1743-6109.2008.00810.x>.
 36. Capogrosso P, Ventimiglia E, Boeri L, Cazzaniga W, Chierigo F, Pederzoli F, et al. Age at first presentation for erectile dysfunction: analysis of changes over a 12-yr period. *Eur Urol Focus*. 2018. <https://doi.org/10.1016/j.euf.2018.02.006>.
 37. Capogrosso P, Colicchia 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. <https://doi.org/10.1111/jsm.12179>.
 38. Mas M, García-Giralda L, Rey JR, Martínez-Salamanca JI, Guirao L, Turbí C. Evaluating a continuous medical education program to improve general practitioners awareness and practice on erectile dysfunction as a cardiovascular risk factor. *J Sex Med*. 2011;8:1585–93. <https://doi.org/10.1111/j.1743-6109.2011.02244.x>.
 39. Verze P, Arcaniolo D, Palmieri A, Cai T, La Rocca R, Franco M, et al. Premature ejaculation among Italian men: prevalence and clinical correlates from an observational, non-interventional, cross-sectional, epidemiological study (IPER). *Sex Med*. 2018;6:193–202. <https://doi.org/10.1016/j.esxm.2018.04.005>.
 40. Castiglione F, Albersen M, Hedlund P, Gratzke C, Salonia A, Giuliano F. Current pharmacological management of premature ejaculation: a systematic review and meta-analysis. *Eur Urol*. 2016;69:904–16. <https://doi.org/10.1016/j.eururo.2015.12.028>.
 41. James SL, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;392:1789–858. [https://doi.org/10.1016/S0140-6736\(18\)32279-7](https://doi.org/10.1016/S0140-6736(18)32279-7).
 42. Sugimori H, Yoshida K, Tanaka T, Baba K, Nishida T, Nakazawa R, et al. Relationships between erectile dysfunction, depression, and anxiety in Japanese subjects. *J Sex Med*. 2005;2:390–6. <https://doi.org/10.1111/j.1743-6109.2005.20354.x>.

43. Capogrosso P, Ventimiglia E, Boeri L, Pozzi E, Chierigo F, Schifano N, et al. Should we tailor the clinical management of erectile dysfunction according to different ages? *J Sex Med.* 2019;16:999–1004. <https://doi.org/10.1016/j.jsxm.2019.03.405>.
44. Pozzi E, Capogrosso P, Chierigo F, Pederzoli F, Ventimiglia E, Boeri L, et al. Clinical profile of young patients with erectile dysfunction: preliminary findings of a real-life cross-sectional study. *Eur Urol Focus.* 2020;6:184–9. <https://doi.org/10.1016/j.euf.2018.10.003>.
45. Boeri L, Capogrosso P, Ventimiglia E, Cazzaniga W, Pederzoli F, Gandaglia G, et al. Depressive symptoms and low sexual desire after radical prostatectomy: early and long-term outcomes in a real-life setting. *J Urol.* 2018;199:474–80. <https://doi.org/10.1016/j.juro.2017.08.104>.
46. Bravi CA, Tin A, Montorsi F, Mulhall JP, Eastham JA, Vickers AJ. Erectile function and sexual satisfaction: the importance of asking about sexual desire. *J Sex Med.* 2020;17:349–52. <https://doi.org/10.1016/j.jsxm.2019.09.024>.
47. Salonia A, Adaikan G, Buvat J, Carrier S, El-Meliegy A, Hatzimouratidis K, et al. Sexual rehabilitation after treatment for prostate cancer-Part 2: recommendations from the Fourth International Consultation for Sexual Medicine (ICSM 2015). *J Sex Med.* 2017;14:297–315. <https://doi.org/10.1016/j.jsxm.2016.11.324>.
48. Corona G, Isidori AM, Aversa A, Burnett AL, Maggi M. Endocrinologic control of men's sexual desire and arousal/erection. *J Sex Med.* 2016;13:317–37. <https://doi.org/10.1016/j.jsxm.2016.01.007>.
49. Salonia A, Rastrelli G, Hackett G, Seminara SB, Huhtaniemi IT, Rey RA, et al. Paediatric and adult-onset male hypogonadism. *Nat Rev Dis Prim.* 2019;5:38 <https://doi.org/10.1038/s41572-019-0087-y>.
50. Hellstrom WJG, Tue Nguyen HM, Alzweri L, Chung A, Virasoro R, Tapscott A, et al. Intralesional collagenase *Clostridium histolyticum* causes meaningful improvement in men with Peyronie's disease: results of a multi-institutional analysis. *J Urol.* 2019. <https://doi.org/10.1097/JU.000000000000032>.
51. Cocci A, Cito G, Urzì D, Minervini A, Di Maida F, Sessa F, et al. Sildenafil 25 mg ODT + collagenase *Clostridium histolyticum* vs collagenase *Clostridium histolyticum* alone for the management of Peyronie's disease: a matched-pair comparison analysis. *J Sex Med.* 2018;15:1472–7. <https://doi.org/10.1016/j.jsxm.2018.08.012>.
52. Sun AJ, Li S, Eisenberg ML. The impact of *Clostridium histolyticum* collagenase on the prevalence and management of Peyronie's disease in the United States. *World J Mens Health.* 2019;37:234–9. <https://doi.org/10.5534/wjmh.180073>.
53. Cocci A, Russo GI, Salamanca JIM, Ralph D, Palmieri A, Mondaini N. The end of an era: withdrawal of Xiapex (*Clostridium histolyticum* collagenase) from the European Market. *Eur Urol.* 2019. <https://doi.org/10.1016/j.eururo.2019.11.019>.