Sexual dysfunction

PDE5 inhibitors have revolutionised treatment for ED – but for how long?

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There is no doubt that almost over night, phosphodiesterase 5 (PDE5) inhibitors changed the management of erectile dysfunction (ED) for people with diabetes. As the first successful licensed oral therapy for ED, together with their launch publicity, more people with diabetes than ever reported to their healthcare physicians and were eligible for treatment, but how long do people continue with their PDE5 therapy for? It has been difficult to answer this question since efficacy studies have tended to address the short-term outcome. Thus, the observational study to the right is of interest since it examines the continuation of sildenafil scripts for up to 3 years after initial uptake (Sato et al, 2007). In short, only a third of individuals continued with sildenafil after the first prescription. Given the fact that this drug is associated with a positive and fairly rapid effect, why is this drop-out rate so high? Sato et al's study identified that approximately a third of people did not return to their healthcare professional after the first prescription (for unidentified reasons) and of those who did, only a relatively small percentage reported treatment failure. However, the study does not address any further reasons for this high drop-out rate and deserves further evaluation. For example, does initial and subsequent lack of response to sildenafil suggest a lessening of effect or perhaps a failure to adequately counsel people on the use of this drug? In our own clinic, we identify that approximately a third of individuals who were deemed PDE5 inhibitor 'failures' later resume this therapy with a successful outcome once adequately instructed about its use. Side effects are reported but seem very low in published studies and our own clinical experience. Is libido simply less of an issue with advancing age or relationship for the individual and/or partner? Finally, we now recognise the close association between ED, heart disease and other cardiovascular risk factors. Thus, it is possible that coronary risk factors and disease per se or the drugs used to treat it may mitigate or prohibit the successful use of PDE5 inhibitors. It is important that we understand the time-related decline in individual use of PDE5 inhibitors since this may have important clinical implications.

ASIAN JOURNAL OF ANDROLOGY

Tadalafil three times a week versus on demand

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 The aim of this study was to compare three-times-weekly dosing of tadalafil with on-demand administration.

2 The Scheduled Use versus on-demand Regimen Evaluation (SURE) study involved 1058 men over 18 years of age (mean age: 54.8 years) who were affected with ED for at least 3 months. The study involved 94 urology centres in Italy.

3 Each individual was randomly assigned to either on-demand or three-times daily dosing of 20 mg tadalafil and crossed over to the alternative regimen following a 1-week washout.

4 A treatment preference questionnaire, completed 5–6 weeks after treatment commenced, showed that 59.1% preferred on-demand dosing and 41.9% preferred the three-times-weekly regimen.

5 Both regimens were efficacious and well tolerated.

6 The International Index of Erectile Function (IIEF) erectile function domain score and Sexual Encounter Profile (SEP) demonstrated a significantly greater improvement from the three-times-weekly regimen, although this difference was numerically minimal and lacking in clinical significance.

7 The authors concluded that tadalafil is effective in either dosing regimen and therefore, individuals should be given the choice according to personal needs.

Mirone V, Imbimbo C, Rossi A et al (2007) Evaluation of an alternative dosing regimen with tadalafil, three times per week, for men with erectile dysfunction: SURE study in Italy. *Asian Journal of Andrology* **9**: 395–402

INTERNATIONAL JOURNAL OF UROLOGY

High drop-out rate for sildenafil citrate treatment

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓

1 This study investigated the drop-out rate for sildenafil use after initial prescription and at 3-year follow up.

2 A total of 1036 men with ED who were taking sildenafil were analysed.

3 The Kaplan-Meier method was used to assess the drop-out rate during successful treatment and risk factors were measured using the Cox proportional hazards model.

4 The medical history of each individual was analysed based on an interview, a self-administered questionnaire and a physical examination.

5 Following initial prescription, 322 people (31%) had ceased taking sildenafil. The cumulative drop-out rate after 3 years of successful treatment was 48%.

6 Drop-out during successful treatment was associated with a lower International Index of Erectile Function (IIEF-5) score before treatment ($P < 0.029$ by the Cox proportional hazards model).

7 This study demonstrates a high drop-out rate from treatment with sildenafil during successful treatment. The authors suggest that adequate initial instruction, re-education, adequate dose titration and changes of treatment methods during long-term follow up are required for all individuals.

Sato Y, Tanda H, Kato S et al (2007) How long do patients with erectile dysfunction continue to use sildenafil citrate? Dropout rate from treatment course as outcome in real life. *International Journal of Urology* **14**: 339–42

'In men with diabetes and related impotence, endothelial microparticles are independently involved in the pathogenesis of erectile dysfunction.'

'Men initiated on sildenafil are less likely to switch than those on tadalafil or vardenafil.'

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH

Endothelial microparticles are involved in the pathogenesis of ED

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 It is thought that cell-derived microparticles are involved in endothelial dysfunction and atherogenesis. As a result, the authors investigated the role of circulating microparticles in the pathogenesis of ED in people with diabetes.

2 Circulating microparticles and endothelial function were assessed in 30 men with diabetes and ED, and 20 age-matched controls without ED.

3 Circulating endothelial and platelet microparticles (EMPs and PMPs, respectively) in peripheral blood were quantified using flow cytometry.

4 Endothelium-dependent flow-mediated dilation (FMD) was assessed in the right brachial artery after reactive hyperaemia.

5 Men with diabetes had significantly higher numbers of EMP ($P=0.001$) and reduced FMP ($P=0.01$) compared with controls, with a significant inverse correlation between the number of circulating EMPs and the International Index of Erectile Function (IIEF) score ($r=0.457$; $P=0.01$).

6 In a multivariate analysis correcting for age, anthropometric indices, glucose and lipid parameters, FMD and PMP, EMP was identified as the only independent predictor or IIEF score ($P=0.03$).

7 In men with diabetes and related impotence, EMPs are independently involved in the pathogenesis of ED.

Esposito K, Ciotola M, Giugliano F et al (2007) Endothelial microparticles correlate with erectile dysfunction in diabetic men. *International Journal of Impotence Research* **19**: 161–6

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH

Physical activity associated with lower ED risk

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 A meta-analysis was conducted on seven cross sectional studies on ED with odds ratios (ORs) of physical activity.

2 Random effects models were used to pool the ORs and a summary estimate (0.53 [0.31, 0.91]) was derived for adjusted OR of physical activity in those with ED compared with those without.

3 A lower risk of ED was associated with moderate (0.63 [0.43, 0.93]) and high (0.42 [0.22, 0.82]) physical activity.

4 Tests did not detect significant publication bias and sensitivity analysis demonstrated that the summary estimate from the random effects model was robust to changes in study sample size and level of statistical adjustment.

5 Although causality cannot be assumed, further studies on the protective effect of physical activity in ED should be carried out using large-scale cohorts.

Cheng JY, Ng EM, Ko JS, Chen RY (2007) Physical activity and erectile dysfunction: meta-analysis of population-based studies. *International Journal of Impotence Research* **19**: 245–52

BJU INTERNATIONAL

Low rate of treatment switching in people taking sildenafil for ED

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 This study compared the rate of treatment switching in people with ED initiated on three PDE5 inhibitors: sildenafil, tadalafil or vardenafil.

2 Men initiating therapy between May 2003 and August 2004 with at least 6 months of prescription history before and after their initial PDE5 inhibitor prescription were included.

3 Switching was defined as the proportion of second PDE5 prescriptions that differed from the first.

4 Other factors such as dose, age and the presence of hypertension, dyslipidaemia, diabetes or depression were adjusted for using logistic regression.

5 Of 2703 men, 91 (3.4%) switched therapies. The choice of initial therapy was a highly significant predictor of switching. Men initiated on sildenafil were less likely to switch than those on tadalafil ($P=0.001$) or vardenafil ($P=0.003$).

6 These results suggest higher treatment satisfaction and preference with sildenafil.

Kell PD, Hvidsten K, Morant SV et al (2007) Factors that predict changing the type of phosphodiesterase type 5 inhibitor medication among men in the UK. *BJU International* **99**: 860–3

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH

High prevalence of Peyronie's disease in people with ED

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 This study investigated the prevalence of Peyronie's disease (PD) in people with diabetes and ED.

2 Of 206 people with diabetes, 42 (20.3%) had PD.

3 PD was significantly associated with risk factors of age, obesity and smoking and all people with PD also had ED. There was also a significant association between PD and ED duration.

4 Almost all individuals with PD (82.1%) had penile curvature and 25.4% had pain with or without erection.

5 The authors concluded that PD is very common among people with diabetes and ED. They suggest further work probing the mechanisms through which diabetes affects the pathogenesis of ED and PD.

Arafa M, Eid H, El-Badry A et al (2007) The prevalence of Peyronie's disease in diabetic patients with erectile dysfunction. *International Journal of Impotence Research* **19**: 213–7