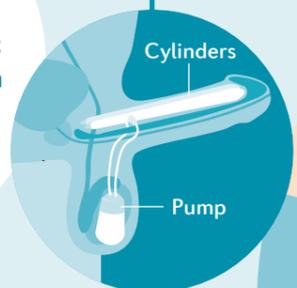


For the Primer, visit [doi:10.1038/nrdp.2016.3](https://doi.org/10.1038/nrdp.2016.3)

➔ Erectile dysfunction is the inability to achieve or maintain an erection for satisfactory sexual performance. Historically viewed as a psychogenic condition, erectile dysfunction is now known to have an organic cause in >80% of cases.

Rx MANAGEMENT

Surgical intervention is generally the final option after conservative options have been attempted, these include implantation of rigid or pump-based prostheses



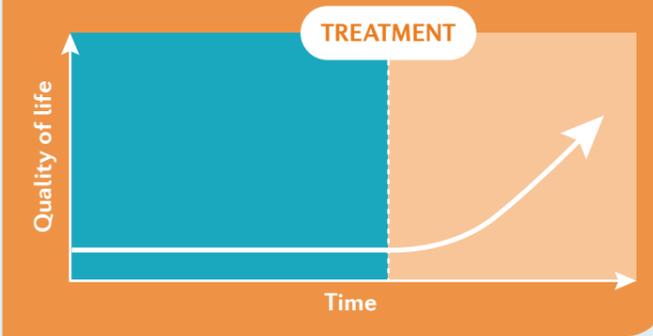
Lifestyle modifications include cessation of smoking, increased exercise and improvements to diet

PDE5 inhibitors such as sildenafil, vardenafil, avanafil and tadalafil are typical first-line therapies



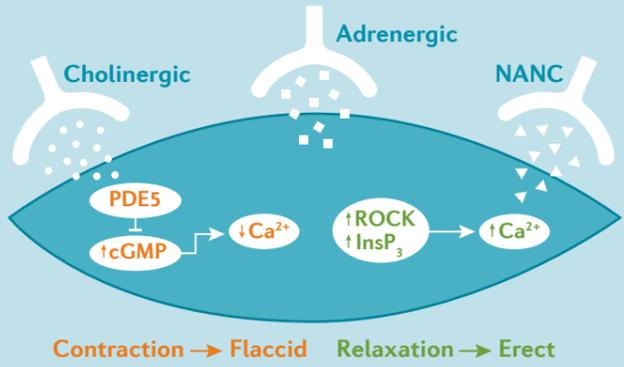
QUALITY OF LIFE

Erectile dysfunction is strongly associated with depressive symptoms. Men report anxiety related to sexual performance and avoid engaging in sexual relations. Many men also avoid seeking treatment for their erectile dysfunction. Even when using erectile dysfunction treatments, fear that these might fail leads to avoidance of sexual situations. Furthermore, erectile dysfunction has negative quality of life consequences for the patient's partner, and the couple overall. For example, female partners of men with erectile dysfunction have been shown to have lower overall and individual domain scores on the Female Sexual Function Index than women whose partners do not have erectile dysfunction. These deficits in quality of life in patients and their partners have been shown to be reversible upon treatment in the affected man.



MECHANISMS

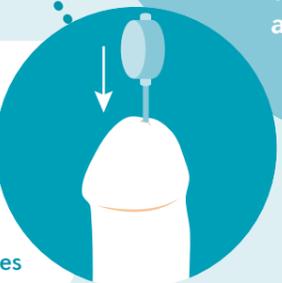
Erection is controlled by numerous processes. In the flaccid state, intracellular Ca^{2+} levels in cavernous smooth muscle cells are maintained in part by the activity of norepinephrine, RHO-associated protein kinase (ROCK) and inositol trisphosphate ($InsP_3$), as well as endothelins and prostaglandins derived from the endothelium. These factors act to maintain the contraction of the smooth muscle, which minimizes blood inflow and enables venous outflow. Upon sexual stimulation (central or local), acetylcholine and nitric oxide released from nerve (including non-adrenergic non-cholinergic (NANC)) fibres promote the accumulation of cyclic GMP in smooth muscle cells, which in turn contributes to a decrease in intracellular Ca^{2+} levels. The smooth muscle relaxes, increasing arterial inflow and decreasing venous outflow — an erection ensues. Phosphodiesterase type 5 (PDE5) hydrolyses cGMP and contributes to returning the organ to its flaccid state. Erectile dysfunction can occur when the nerves, blood vessels and/or intracellular signalling are disturbed.



Erectile dysfunction is strongly related to age, health status and emotional function; the prevalence has been reported to range from 6% to 64% in men aged 40–79 years

To treat men with erectile dysfunction, surgical and nonsurgical approaches can be considered. Nonsurgical options include lifestyle modification and oral phosphodiesterase inhibitors. If these fail, surgical approaches — such as insertion of penile implants — can work.

Second-line therapies include intraurethral suppository of prostaglandin E1 and intracavernosal injection with vasoactive substances



If PDE5 inhibitors do not work, vacuum erection devices can be tried



DIAGNOSIS

Understanding whether the erectile dysfunction is psychogenic, vasculogenic, neurogenic, iatrogenic or endocrine in nature is central to determining the best way to treat

the patient. Physical examination, full sexual and medical history and biochemical assessments might be warranted. Alcohol consumption, smoking, obesity, diets low in fruits and

vegetables, low exercise intake and benign prostatic hyperplasia (enlargement of the prostate) are all risk factors for developing erectile dysfunction.

! Erectile dysfunction can be a manifestation of an underlying vascular disorder. Accordingly, men with erectile dysfunction should be assessed for cardiovascular disease such as coronary artery disease.

OUTLOOK

Although often regarded colloquially as miracle drugs, sildenafil and other PDE5 inhibitors are not effective in all men with erectile dysfunction. Accordingly, other drugs are currently in development, including ROCK inhibitors. Another bustling field within sexual medicine is that of regenerative medicine. Here, growth factor therapy, gene transfer therapy and tissue engineering are being explored with the aim of restoring erectile function.