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EXPERT FORUM

# Prostate Issues and Erectile Dysfunction

Making Education Easy 2023

## About the speakers

**Dr Jason Du**
**BHB, MBChB, PGDipSurgAnat, FRACS (Urol)**
Jason is a NZ trained urologist and urological surgeon with a special interest in urologic oncology and robotic surgery, especially prostate, bladder and kidney cancers. Jason also has extensive experience in managing kidney stone disease and benign prostatic hyperplasia. Jason works at North Shore Hospital as the lead robotic surgeon, and at the Urology Institute.

**Dr Maria Pearce**
**MBChB (Otago), FRANZCR**
Maria is a consultant radiation oncologist and manages the radiotherapy treatment at Auckland Radiation Oncology (ARO). In addition to her clinical role at ARO and previously Auckland City Hospital, Maria was also the Chief Pathology Examiner for the Royal Australian and New Zealand College of Radiologists (RANZCR), of which she is a Fellow.

**Dr Andrew Williams**
**BMedSc, MBChB, FRACS (Urol)**
Andrew is a urologist with subspecialist training in robotics and complex cancer surgery. Andrew works as a consultant urologist at Auckland District Health Board and Counties Manukau District Health Board, and consults at OnesixOne, Pukekohe Family Health Centre, Ormiston Specialists and EastCare Specialist Centre.

**Simon van Rij**
**FRACS, MBChB, BSc, PG Dip Sports Medicine**
Simon is a NZ trained urologist and robotic surgeon with a passion for mens health. He specialises in prostate conditions including diagnosing and managing prostate cancer. For benign prostate conditions he offers new emerging procedures alongside traditional laser techniques.

**Dr John Tuckey**
**MMedSc FRACS**
John is a urologist in Auckland with a special interest in erectile dysfunction, Peyronie's disease and penile prosthesis surgery. John consults at Ascot Central and has a public appointment at Auckland Hospital.

**Abbreviations used in this review**
**AS** = active surveillance
**BMI** = body mass index
**BP** = blood pressure
**BPH** = benign prostatic hyperplasia
**CNS** = central nervous system
**ED** = erectile dysfunction
**GP** = general practitioner
**IIEF** = International Index of Erectile Function
**LUTS** = lower urinary tract symptoms
**MP-MRI** = multiparametric magnetic resonance imaging
**PDE-5** = phosphodiesterase type 5
**PSA** = prostate-specific antigen
**QoL** = quality of life
**RR** = relative risk

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This publication summarises presentations by Dr Jason Du, Dr Maria Pearce, Dr Andrew Williams and Dr Simon van Rij who spoke on prostate issues, and by Dr John Tuckey who spoke on Erectile Dysfunction at the 2023 Goodfellow Symposium in Auckland in March. This review is sponsored by MercyAscot.

## PSA SCREENING
*Dr Jason Du*

Dr Du began his presentation by asking attendees to raise their hand if they would offer, discuss and arrange a PSA for a male patient aged ≥40 years. Approximately one-third of attendees indicated that they would. He reminded attendees that prostate cancer is fairly common in New Zealand, with 4000 men diagnosed and 700 dying annually from this disease.

### Is PSA a good screening test?

Dr Du explained that PSA fits the criteria for a good screening test, being simple, cheap and acceptable for patients, safe to perform, able to provide valid, reliable and reproducible results, and able to detect disease early in its natural history before the onset of symptoms. Furthermore, effective therapy is available to alter the course of prostate cancer, emphasising the importance of early diagnosis.

### Does PSA screening reduce prostate cancer mortality?

Findings from the European Randomized Study of Screening for Prostate Cancer involving over 180,000 men, published in the New England Journal of Medicine in 2012, found that after 11 years of follow-up, PSA-based screening significantly reduced mortality from prostate cancer, with a relative reduction in the risk of death in the screening group of 21% (RR 0.79: 95% CI 0.68-0.91; p = 0.001).[1] Furthermore, at this time point, the number needed to screen to prevent one death was 1055 and the number needed to diagnose was 37. Follow-up of this study cohort 5 years later (16 years of follow-up), revealed that in order to prevent one death from prostate cancer, the number needed to screen had decreased to 570 and the number needed to diagnose to 18.[2] Dr Du pointed out that these numbers are similar to those seen with other tests such as mammograms.

### Risk stratification

A study from Olmsted County has shown that even just a single PSA measurement for a patient in their 40s is very useful for predicting future risk of prostate cancer.[3] The study involved a random sample of 268 men aged 40-49 years followed for a median of 16.3 years. The risk of Gleason 6 prostate cancer diagnosis by 55 years was 0.6% (95% CI 0%-1.7%) for men with a baseline PSA <1.0 ng/mL and 15.7% (95% CI 6.5%-24.9%) for men with a baseline PSA ≥ 1.0 ng/mL.

### Frameshift in diagnosis of prostate cancer

Dr Du explained that previously, men with an elevated PSA were referred and underwent a transrectal ultrasound-guided (TRUS) prostate biopsy. He pointed out that this has been a point of contention and that the procedure carries a 3% risk of sepsis. The new gold-standard for such men for the diagnosis of prostate cancer is multiparametric magnetic resonance imaging (MP-MRI) of the prostate. Via this modality, the entire prostate gland can be visualised and local and pelvic nodal staging can be undertaken. A recent study published in the New England Journal of Medicine supported the use of MP-MRI prior to biopsy in men with an elevated PSA, showing that this screening procedure reduces the number of men needing to undergo a biopsy, thus reducing overdiagnosis.[4] In a study published in The Lancet, MP-MRI was shown to improve diagnostic accuracy, reduce diagnosis of clinically insignificant prostate cancer, and improve the detection of clinically significant prostate cancer.[5]

As an example of the utility of MP-MRI in the diagnosis of prostate cancer, Dr Du gave the example of a typical patient with a borderline elevated PSA of approximately 4.5 ng/mL. In this patient MP-MRI revealed a prostate weighing approximately 70 gm with no concerning lesions. In this case the elevated PSA was considered probably due to BPH and this patient was not subjected to a biopsy, but rather monitored to observe their PSA trend over time. He pointed out that it must be keep in mind that MP-MRI of the prostate carries about a 10% false-negative rate for prostate cancer detection.

Dr Du explained that when a suspicious lesion is identified by prostate MP-MRI, instead of performing a transrectal prostate biopsy, it is now more common to undertake a targeted transperineal biopsy under either local or general anaesthetic. With this procedure, an ultrasound probe is placed into the rectum for visualisation of the prostate and together with the MRI image the biopsy can be targeted to the suspicious lesion. Because the rectum is not breached, the sepsis rate with this procedure is considerably lower (<0.3%) than that with TRUS biopsy of the prostate. The targeted transperineal biopsy also allows for sampling of anterior tumours, something not possible with the traditional transrectal route.

## Frameshift in management of prostate cancer

When a patient is diagnosed with prostate cancer, their cancer is graded. The International Society of Urological Pathology (ISUP) grading system for prostate cancer, which ranges from 1 (low risk disease) to 5 (high-risk disease) is now used in favour of the Gleason scoring system (**Table 1**).

**Table 1.** ISUP and Gleason grading systems for prostate cancer[6]

| Risk Group* | ISUP Grade Group | Gleason Score |
|---|---|---|
| Low/Very Low | Grade Group 1 | Gleason Score ≤ 6 |
| Intermediate (Favourable/Unfavourable | Grade Group 2 | Gleason Score 7 (3 + 4) |
| | Grade Group 3 | Gleason Score 7 (4 + 3) |
| High/Very High | Grade Group 4 | Gleason Score 8 |
| | Grade Group 5 | Gleason Score 9-10 |

**Risk groups are defined by the Grade Group of the cancer and other measures including PSA, clinical tumour stage (T stage), PSA density, and number of positive biopsy cores*

Dr Du explains to his patients that prostate cancer is a spectrum, ranging from the kitten variety to the tiger variety, with the behaviour and natural history of the disease very different depending on whether it falls into a low- or high-risk category. He pointed out that 20 years ago, a lot of men with low-risk prostate cancer were treated via either surgery or radiotherapy, but it was subsequently realised that almost all of these men actually did not need treatment because low-risk prostate cancer is very indolent. He added that in 2023, the majority of men with low-risk prostate cancer receive active surveillance (AS).

### Active surveillance

AS is considered suitable for men with low-risk prostate cancer as the majority of these men do not progress. AS involves regular PSA monitoring with follow-up MP-MRIs and biopsy, if necessary. AS reduces harm from over treatment and provides for the ability to identify those who need treatment, without compromising outcomes. The New Zealand Ministry of Health guidance on using AS to manage men with low-risk prostate cancer is available from: https://www.health.govt.nz

### Individualised treatment of prostate cancer – precision oncology

For those men who do require treatment of their prostate cancer, the improvements in diagnostics and risk stratification mean that individualised treatment plans can be offered. Such treatment is based on the man's prostate cancer risk category and may involve AS (for low-risk disease), surgery (intermediate- or high-risk disease), radiotherapy (intermediate- or high-risk disease), or watchful waiting (for men who are comorbid or who have a <10-year life expectancy).

### TAKE-HOME MESSAGES:

- PSA is a good screening test for men ≥40 years of age, particularly those with a family history of prostate cancer and for those with >10-year life expectancy
- PSA screening reduces prostate cancer mortality
- PSA enables risk stratification, even with just a single test for men in their 40s
- There has been a frameshift in diagnostics and management of prostate cancer, thus reducing harm from over diagnosis/over treatment
- Early detection and risk stratification of prostate cancer allows for the delivery of an individualised treatment plan.

## RADIATION THERAPY FOR PROSTATE CANCER

*Dr Maria Pearce*

Dr Pearce explained that radiation therapy involves the use of ionising radiation to treat cancer. Radiation therapy is also occasionally used to treat benign conditions. The different types of radiation include linear-accelerator-based whereby photon x-rays are generated by accelerating electrons to a high speed using microwave energy, brachytherapy (seed radiation) whereby radioactive seeds, ribbons or wires are inserted into tumours, particle radiation (not available in Australasia), and the CyberKnife, which uses stereotactic body radiation therapy (SBRT) and is fully robotic and available in Auckland. Dr Pearce pointed out that radiation therapy cannot distinguish between cancer cells and normal cells; however, normal cells divide slower and are able to repair the DNA damage caused by the radiation. Dr Pearce explained that prior to radiation therapy, the patient undergoes a planning CT scan and if necessary, an MRI, to identify the tumour and tattoos are placed on the skin to indicate its location. While undergoing radiation treatment, the patient is immobilised by being put in a vacuum bag. When treating the head and neck region a plastic mask is used.

Dr Pearce's explained that previously when treating prostate cancer via external beam radiation therapy, one beam was used from the front and two from the side, but the radiation dose to the bladder and rectum was very high. Now, the machine rotates around the patient and the dosage and shape of radiation can be altered to deliver a higher dose to the tumour and a lower dose to the surrounding tissue. With the CyberKnife it is now possible to give high doses of radiation over a short period of time. With the linear accelerator, patients typically have 20 treatments, but with the CyberKnife sufficient treatment can be achieved with five treatments.

PACE-A, an international phase 3 randomised controlled trial comparing SBRT to surgery for localised prostate cancer found that at 2 years of follow-up, significantly fewer SBRT recipients than surgery recipients reported use of urinary pads (4.5% vs 46.9%; $p < 0.001$) and SBRT recipients had better erectile function, but a higher rate of bowel side effects.[7]

Dr Pearce explained that while patients with metastatic prostate cancer have traditionally received hormone therapy, this carries the risk of side effects. Such patients can now undergo prostate-specific membrane antigen positron emission tomography, which is able to detect early metastases. Dr Pearce emphasised that radiation treatment for these patients is successful at treating metastases in 85-90% of cases. There is a small risk of bone fracture for patients treated for bone metastases.

## PROSTATE CANCER SUPPORT

*Dr Andrew Williams*

### Treatment outcomes

Dr Williams pointed out that there are now a number of good treatment options for prostate cancer and that treatment outcomes and quality of life (QoL) have significantly improved for this patient group. It is now unusual for a treated patient to develop major incontinence or bowel dysfunction, and any issues that do arise generally have little impact on long-term QoL.

In New Zealand and Australia, urologists have a good understanding of their prostate cancer surgical outcomes, being sent feedback every 3 months in the form of a scatter plot graph indicating where they sit in relation to their peers with regard to patient urinary incontinence, bowel dysfunction, and sexual dysfunction post surgery. Dr William's data also reveals that his intervention rate for low-risk prostate cancer is only 2%, significantly lower than the rate of 60-70% in the US.

While these outcomes are very useful, it is recognised that the patient's experience and morbidity associated with prostate cancer are affected by the holistic experience and include factors such as stress, depression, and anxiety, and these domains are becoming an increasing area of interest for clinicians.

### Stress, depression, anxiety

While stress, depression and anxiety have been recognised as important factors for patients at the time of prostate cancer diagnosis, it is increasingly recognised that these domains are also associated with treatment delay and decision-making. Referral to treatment for prostate cancer across New Zealand from the time of a raised PSA measurement is frequently ≥3 months in private and ≥9 months in the public system. There is now also a focus on the management of post-treatment morbidity.

A study into the relationship between the severity of prostate cancer and stress and depression has been recently published.[8] In that study, over 15% of men diagnosed with prostate cancer were clinically diagnosed with depression following their diagnosis. Results showed that those diagnosed with PSA-detected cancer were just as stressed as those with clinically-detected prostate cancer, which is understandable. During and after treatment, anxiety was found to improve, but the incidence of depression increased.

### Improving outcomes for patients

#### Counselling support

Dr Williams explained that the recognition of depression and anxiety in patients undergoing diagnostic evaluation and treatment for prostate cancer is essential and pointed out that such patients will frequently be seen by GPs who need to be mindful that such patients are generally not good at opening up about their psychological symptoms. It is imperative that GPs keep an eye out for these men and help them access support. The New Zealand Prostate Cancer Foundation provides five free counselling sessions and also run support groups, including Rainbow support groups, for patients and their families.

#### Nurse-led care

Dr Williams and colleagues are currently advocating for specialist nursing support particularly for prostate cancer patients with incontinence and erectile dysfunction (ED). According to Dr Williams, it is well recognised that specialist nurses do a better job at discussing prostate cancer management with patients than doctors. Studies have shown that nurse-led education is cost-effective and leads to lower intervention rates in low-risk disease.[9,10] Nurse-led care frees up clinician time and is now becoming the standard of care in prostate cancer in Europe and North America.

#### Physiotherapy

It is also well recognised that patients undergoing radical prostatectomy will experience a degree of stress incontinence and that physiotherapy is of benefit for such men. Nowadays, physiotherapist care for these patients is readily available in public and private healthcare. Dr Williams pointed out that it doesn't take a lot to improve the outcomes of a man with urinary or bowel incontinence following prostate cancer surgery, with usually just one or two appointments necessary in order for them to feel more in control with their situation. Men may be given Kegel exercises, which have proven to be very effective for men with incontinence post prostate cancer surgery.[11]

While physiotherapy in New Zealand for prostate cancer patients accounts for only around 0.5% of the total cost of treatment, a number of health insurance companies will not cover this type of physiotherapist care. A study looking at outcomes with or without physiotherapy in men treated for prostate cancer has shown significant improvements in International Prostate Symptom Score 6 weeks post surgery and in Incontinence Score by 2 weeks post surgery in those receiving such therapy.[11]

#### Re-referral to urology

Dr Williams explained that patients using more than a pad a day following prostate cancer surgery need to be seen as there are a number small procedures that can help with artificial sphincters, with expensive procedures not generally necessary for significant improvement. He pointed out that a patient who for example plays tennis and suffers from minor incontinence can benefit as much from a procedure as someone who is actually fully wetting themselves, because their tennis may be very important for them.

#### Improving sexual function

Studies have shown that the average man with prostate cancer has mild ED at baseline and severe ED after surgery before slowly improving out to 2 years.[12,13] Dr Williams explained that patients who are more involved in their treatment and have greater hope for recovery of their sexual function seem to do better.

Dr Williams encourages regular use of the PDE-5 inhibitor sildenafil in patients suffering from ED post prostate cancer treatment, even if they don't achieve an erection, as there is data suggesting that it improves response over 2 years.[14] He pointed out that the price for sildenafil can vary from $2.50 to $11 per tablet, so it is best if patients shop around different pharmacies. The cost of taladafil can vary from $5-7 per tablet to $30 per tablet.

There is evidence that blood flow to the penis is crucial for long-term recovery, with a use it or lose it phenomenon.[15,16] Penile injectables are another option as are penile implants, and a number of insurers now fund penile implants for these men.

### TAKE-HOME MESSAGES:

- Screen men with prostate cancer for depression/anxiety
- Refer to counselling/support groups if not already involved
- Initiate medical treatment if indicated
- Recognise patients with incontinence issues and refer to physiotherapy and urology
- Continue to trial PDE-5 inhibitors for a couple of years in patients with ED
- Offer treatments or referral to appropriate providers for advanced treatments.

## SO, THE PSA IS NORMAL

*Dr Simon van Rij*

### PSA follow-up

Dr van Rij stressed the importance of getting to the heart of why a patient may be presenting to the GP. Often patients are concerned about cancer and it is easy to end up in a cycle of more frequent PSA testing, something that can actually cause further anxiety. Dr van Rij suggests waiting a year before repeat PSA testing when the PSA is normal and for low-risk men waiting as long as 5 years. He says that the Prostate Cancer Working Group and Ministry of Health 2015 Prostate Cancer Management and Referral Guidance (available from: https://www.health.govt.nz) should be followed. The guideline definitions for an abnormal PSA level by age are shown in **Table 2**.

**Table 2.** Definitions for an abnormal PSA level, by age[17]

| Age Group | Abnormal PSA level (µ/L) |
|---|---|
| Men aged ≤ 70 years | ≥ 4.0 |
| Men aged 71-75 years | ≥ 10.0 |
| Men aged ≥ 76 years | ≥ 20.0 |

Dr van Rij explained that the PSA cut-off levels are higher in older patients because we are not trying to identify men with early disease, but rather those who are progressing and may develop metastatic disease. He adds that for men who have undergone an MRI and biopsy, their treatment plan can be tailored to them and a set new PSA level above which to refer can be established.

## Lower urinary tract symptoms in men

Dr van Rij pointed out that a lot of men present at the urology clinic because of lower urinary tract symptoms (LUTS). For these men, he follows the guidance of the Community HealthPathways Auckland Region (available from: https://aucklandregion.communityhealthpathways.org), first taking a history and determining the predominant symptom, investigating red flags such as recurrent urinary tracts infections (UTIs), previous urological surgery, overflow incontinence, and haematuria. He then risk-stratifies these men based on severity of symptoms, asking the International Prostate Symptom Score (IPSS) bothersome of urinary symptoms question `How would you feel if you had to live with your urinary condition the way it is now, no better, no worse, for the rest of your life?'. He also asks `Do you think your symptoms are bad enough that you would want to take medication to treat them?'. Differential diagnoses are considered. He undertakes a physical exam of the penis, bladder and prostate when indicated.

Dr van Rij, explained that when a patient presents with LUTS but no red flags, there is usually no need to do further testing, but instead start treatment. Further testing when indicated may include blood tests, ultrasound (if creatine is elevated, infection or incontinence are present), and mid-stream urine (if symptoms indicate infection). He would not necessarily undertake a PSA at this stage before discussing the pros and cons with the patient, and points out that there is no rush for the patient to make that decision.

### Treatment options for LUTS

Alpha blockers are considered first-line treatment for LUTS and Dr van Rij explains that 70% of men with LUTS starting such therapy will experience improvement in their symptoms. The most commonly used first-line agent in New Zealand for LUTS is doxazosin, a non-selective alpha blocker; tamsulosin (a selective alpha blocker) is available under Special Authority and Dr van Rij puts patients aged over 80 years straight onto tamsulosin as this medication's risk of postural hypotension is lower. He pointed out that alpha blockers may cause retrograde or loss of ejaculation and this can have a major impact on men's QoL, and that it is worth querying the patient about such symptoms.

Finasteride, a 5-alpha reductase inhibitor, is used as a second-line agent for LUTS and is available on Special Authority for men who have been intolerant to or progressed on an alpha blocker. It works very well in the right selected patient. This agent works by shrinking the prostate and Dr van Rij generally avoids using finasteride in young men. This is due to potential for sexual side effects and the fact that men in this age group usually already have small prostates with limited ability to shrink. Men treated with finasteride should be informed that symptoms may take up to 6 months to resolve.

Dr van Rij will sometimes prescribe solifenacin, a muscarinic receptor antagonist, for men with irritative bladder symptoms, such as urgency and frequency, but he no longer uses oxybutynin. He explains that one needs to be mindful of cognitive function in elderly patients treated with solifenacin.

Dr van Rij explained that nocturia may have a multifactorial cause and can be difficult to manage. He explains to men that their nocturia is likely due to their prostate, bladder, fluid balance, sleep and habits, with the latter more difficult to control. He added that GPs are experts in managing patients with nocturia, especially with regard to fluid management, blood pressure and sleep.

### When to refer and what happens next

Dr van Rij recommends that GPs refer patients who have urinary retention, who progress on medication, who are intolerant to medication, or who have red flags. Once a patient is referred to urology, options for treatment in the public system usually include transurethral resection of the prostate (TURP). There are other surgical/procedural options available in New Zealand, especially if men are worried about the effect of TURP on their sexual function.

## Case examples

Dr van Rij presented several cases examples of men presenting with prostate cancer.

**Case 1:** A 72-year-old man with a PSA of 6.5. In this man, the PSA measurement should be repeated. His physiological age rather than just his chronological age should be considered and if he is very fit and well for his age, then this should be included on the referral letter, as according to the Prostate Cancer Working Group and Ministry of Health 2015 Prostate Cancer Management and Referral Guidance, his PSA would not be considered abnormal, but given his potential lifespan, further assessment or treatment may be appropriate.

**Case 2:** A 64-year-old male with a first PSA of 60 and a repeat PSA of 90. In this man, a digital rectal examination should be undertaken and if indicated biopsy and systemic staging urgently undertaken. This man was diagnosed with metastatic prostate cancer and treated promptly by the radiation oncology team with the aim of preventing neurological complications.

**Case 3:** A 47-year-old man with a family history of prostate cancer presents requesting a PSA measurement. This man's PSA can be tested, as it is a very good measurement for stratification of future risk of prostate cancer in this age group. It is good to establish a baseline PSA. Men from families with the *BRACA* mutation and history of early breast cancer and prostate cancer have a much higher risk of developing prostate cancer, and these individuals should be monitored carefully.

# MANAGING PATIENTS WITH ERECTILE DYSFUNCTION

***Dr John Tuckey***

## Introduction

Dr Tuckey, described ED as the inability to attain or maintain an erection adequate for sexual intimacy. According to a 2017 cross-sectional survey of 2000 New Zealand men, 38% in their 50s and 60% in their 60s reported ED.[18] These ED prevalence rates are similar to those seen in the 1980s Massachusetts Male Aging Study, in which 50% of men in their 50s and 60% of men in their 60s reported ED.[19] In the New Zealand study, one-quarter had moderate to severe ED, one-sixth were medically diagnosed and one-fifth were on treatment (77% PDE-5 inhibitors, 9% natural remedies, 4% injectables, 4% vacuum pump, 4% testosterone).[18]

## Why should we be proactive?

Dr Tuckey explained that ED can have a significant impact on a man's health and quality of life, contributing to low self-esteem, anxiety, depression, and suicidal ideation. ED may be responsible for difficulties in the man's relationship with his sexual partner, with performance anxiety and the avoidance of physical contact leading to the partner feeling unattractive and unloved.

## When is the best time to treat ED?

According to Dr Tuckey, treating ED as soon as possible is key to improving QoL and relationships. He also referred to a `use it or lose it' phenomenon where a lack of high oxygen content blood delivered to the corpora may result in corporal fibrosis and scarring leading to further difficulty achieving or sustaining an erection, and to atrophy and penile shortening. Penile shortening is common in the first year after radical prostatectomy, with an average length loss of 1cm.[20] The shortening appears to improve with time and the best predictor of length recovery appears to be preserved erectile function post surgery.

## How do men get an erection?

Dr Tuckey explained that erections are a cholinergic response mediated by nitric oxide via the parasympathetic nervous system. Tactile stimuli from the penis or scrotum send signals along the pudendal nerve to the spinal cord, while afferent signals from the brain in response to visual, auditory and olfactory stimuli travel via the hypogastric nerves to the pelvic plexus, then to the cavernosal nerves which surround the prostate and on to the penis where they induce dilatation of the helicine arteries and corporal smooth muscle relaxation, all mediated by the nitrous oxide system. A number of factors and disease processes including stress, anxiety, multiple sclerosis, Parkinson's disease, heart disease, hypotension, diabetes, radiotherapy or surgery of the prostate, and spinal surgery can all affect this pathway. Testosterone is important for nourishing the tissues and allowing for responsivity of the cavernosal tissue; low testosterone levels can cause a venous leak issue in the penis.

## Taking a history

Dr Tuckey pointed out that some men use the term ED to describe other symptoms such as low libido, early or late ejaculation, climacturia, or Peyronie's disease, so it is important to ask them to describe their problem when taking a history and to keep in mind that more than one of these issues may be present. He suggests querying about any other stressors in their relationships, at home or at work, and to ask how are the symptoms affecting their relationship with their partner and themselves, especially with regard to self-esteem, life outlook, and depression. He adds that in some cases there may be a simple explanation for their ED, like having a busy household and no space and time for physical intimacy, and that sometimes the partner may take the ED personally, feeling that they are no longer attractive to their partner.

Dr Tuckey always asked patients presenting with ED about their smoking history and use of alcohol, as both of these agents can affect ED. He explained that while small doses of alcohol may help ED by reducing anxiety, larger amounts can cause CNS depression, can reduce libido and can cause transient ED. Furthermore, chronic alcohol abuse can lower testosterone levels and increase oestrogen levels. He also asks about exercise (this can have beneficial effects), the use of medications, supplements, and other relevant history such as pelvic surgery, diabetes, cardiovascular disease, metabolic syndrome, and neurological disease. He explained that the severity of ED correlates strongly with the severity of cardiovascular disease and that in some men ED develops first due to penile arteries being smaller than the coronary arteries and therefore more susceptible to the impact of plaque formation. He adds that men presenting with ED and relevant risk factors should be evaluated for silent cardiovascular disease.

For assessing ED, Dr Tuckey recommends using the International Index of Erectile Function (IIEF)-5 questionnaire as a screening tool to learn how severe a man's ED is.[21] He says that the IIEF-5 can also be used at follow-up to assess response to treatment. For the physical examination, he suggests assessing the man's hands to see if there is potential for Peyronie's disease, assessing secondary sexual characteristics and determining if there is any curvature or nodularity of the penis. He added that stretched (flaccid) penile length is a useful proxy measurement for erect penile length. Blood tests should include testosterone, lipids, and HbA1c, examination of cardiovascular risk factors and BP measurement should be undertaken.

Dr Tuckey said that once all of the above have been assessed, there should be a fairly clear idea of the underlying issues behind the man's ED: stressors at work/home; hypogonadism; medications; vascular factors (in older men usually arterial, in younger men usually venous); neural factors.

## Behavioural modification

Dr Tuckey pointed out that behavioural modification is an area that GPs are familiar with, but the problem with ED is that patients want a quick solution and results are generally slower with behavioural modification. He added that there is evidence that exercise and diet can improve erections, particularly the Mediterranean diet and caloric restriction, and that obesity is an independent risk factor for ED.

## Psychosexual counselling

Dr Tuckey explained that psychosexual counselling can be helpful for men with ED, especially those suffering from stress or relationship issue, and generally ≥5 sessions are necessary to see improvement, with a higher success rate (50-70%) if the partner attends.

## Herbal remedies and supplements

Some patients with ED have tried Herbal Ignite, which contains Horny Goat Weed, Tribulus terrestris and Avena sativa, and Dr Tuckey explained that there is some evidence that this agent has some PDE-5 inhibitor-like effects. He added that other supplements used for ED include ginseng and arginine, which act via the nitrous oxide pathway, and Ginkgo biloba which is purported to increase circulation.

## Low-intensity shock wave lithotripsy

Dr Tuckey described low-intensity shock wave lithotripsy and said that while this intervention is verified in musculoskeletal disorders, it is only experimental in ED. He added that the improvement in IIEF score is small and that some good randomised studies are required to determine its true benefit.

## PDE-5 inhibitors

PDE-5 inhibitors include sildenafil [Viagra®; Silvasta®; Vedafil®], tadalafil [Cialis®; Cilatil®], and vardenafil [Levitra®]. Dr Tuckey explained that PDE-5 inhibitors work by increasing the levels of cGMP and that nitrous oxide released by the nerves in response to sexual stimulation is a key part of the mechanism. Hence, PDE-5 inhibitors require intact nerves and this can be a challenge in some of the neurological conditions and post radical prostatectomy or radiotherapy for example.

Sildenafil has the shortest half-life at 3-5 hours, followed by vardenafil at 4-5 hours and tadalafil at 17.5 hours.[22-24] Dr Tuckey explained that PDE-5 inhibitors are effective in approx. 80% of men with ED. It is recommended that sildenafil is taken 30-60 minutes before sexual activity, vardenafil is taken 25-60 minutes before and tadalafil is taken at least 30 minutes before sexual activity and patients may be responsive for up to 36 hours.[22-24] Fatty food should be avoided when taking sildenafil as this reduces the rate of absorption of the agent.[22] Nitrates are contraindicated for all three agents.[22-24]

The most common side effects with the use of PDE-5 inhibitors are headache, indigestion, and flushing.[22-24] Priapism has been reported with these agents but is a rare side effect. Dr Tuckey added that despite their good safety profile, some patients and their partners are still concerned about the safety of PDE-5 inhibitors and may need reassuring. Sildenafil is funded by Pharmac via Special Authority for some patients with ED due to traumatic or non-traumatic spinal cord injury.

## What if sildenafil doesn't work?

Dr Tuckey suggested discussing with the patient how they are using their sildenafil: Are they waiting 30-60 minutes? Are they using stimulation? Are they taking sildenafil with fatty food? What doses have they tried, and have they tried any of the other PDE-5 inhibitors? Do they have any relevant comorbidities – neural injury, diabetic, post surgery? Dr Tuckey explained that there is a small incremental response rate when using sildenafil, so patients should not give up after trying just one or two times with the agent, but rather give up to six doses a go. He suggested that for those patients experiencing side effects of sildenafil, they may like to try a daily dose of tadalafil. He pointed out that this discussion can salvage around 30% of non-responders. If PDE-5 inhibitors simply don't work, there are other options including vacuum erection devices, intracavernosal injections, and penile prostheses

## Vacuum erection devices

Vacuum erection devices may be power or manually operated. They fit over the penis and the vacuum draws venous blood into the penis. Once the penis is erect, constriction rings are used to keep the blood in the corpora, but the device can also just be used to stretch the penis. Dr Tuckey explained that it is important to shave around the base of the penis to get a good seal and a lubricant can be used ensure a good seal. He added that vacuum devices are useful for reducing the penile length loss that is common after radical prostatectomy.

Dr Tuckey reported that vacuum erection devices can be difficult to use if dexterity is an issue, they are mostly used by those in a stable relationship, it is only the distal corpora that are engorged producing a hinge effect that is slightly different to a natural erection, and that they can be expensive at around $600 for a medical grade device, although sex shops have cheaper versions at around $50-$100.

## Intracavernosal injections

Dr Tuckey explained that intracavernosal injections with alprostadil (also known as prostaglandin E1) [CAVERJECT® IMPULSE], papaverine [DBL™ papaverine hydrochloride], or phentolamine are the next step for men whose ED has not been successfully treated with PDE-5 inhibitors or vacuum erection devices.[25,26]

Dr Tuckey explained that alprostadil causes vasodilation via the cyclic AMP pathway and smooth muscle relaxation, papaverine is a non-specific PDE-5 inhibitor, and phentolamine is an alpha-antagonist. There is also the option of using a combination of papaverine and phentolamine [Bi-Mix] or alprostadil, papaverine, and phentolamine [Tri-Mix].

Intracavernosal injections stimulate increased high oxygen content blood flow into the corpora, which nourishes the tissues, and according to Dr Tuckey, there is some evidence that the regular use of intracavernosal injections can result in the return of natural erections. He adds that they are stronger than PDE-5 inhibitors or vacuum devices, and they can produce a natural looking erection.

Dr Tuckey explained that although patients tend to be apprehensive about the self-administered injections, it is an easy technique to learn for most men and they usually report how much easier it is than they thought it would be. For those who are anxious, auto injectors can be helpful. Injections are into the shaft of the penis via a fine needle inserted at 10 or 2 o'clock. Patients are advised to press on the injection site to minimising scarring. Dr Tuckey recommends starting with a low dose of 5 µg alprostadil for example to avoid the risk priapism, titrating the dose each time until the desired effect is achieved. Erections usually occur within 5 minutes of the injection. If priapism (erection >4 hours duration) does occur, Dr Tuckey advises patients to take a cold shower and Coldrex containing phenylephrine and if it doesn't resolve, to head to the hospital for a drainage procedure.

Dr Tuckey explained that CAVERJECT® IMPULSE is available in 10 µg and 20 µg doses. He added that CAVERJECT® IMPULSE is around twice as expensive as the injections that can be made up in the office. An advantage with CAVERJECT® IMPULSE is that it does not need to be stored in the fridge. He added that if patients experience penile aching with alprostadil they should be changed to Bi-Mix and if rigidity is an issue, then changed to Tri-Mix. Dr Tuckey added that intracavernosal injections can be very helpful with penile rehabilitation post surgery.

Dr Tuckey listed drawbacks of intracavernosal injections as follows: They can have a negative effect on spontaneity; They may not work if the patient injects them too deeply; Some patients do not respond at all; Some of the agents used require refrigeration.

## Penile prostheses

Penile prostheses are popular amongst Dr Tuckey's ED patients, as they are very reliable and durable, produce the same erection every time, restore spontaneity, and they are always with the patient. He added that penile prostheses produce a very rigid and natural looking erection, are discreet, and they can restore the patient's self-esteem, confidence and relationships. There have been over 100,000 penile prostheses implanted worldwide.

The two main types of penile prostheses are the malleable rod, one of each is inserted into each corpora, and the three-piece prosthesis, whereby a pump is inserted into the scrotum, a reservoir into the abdomen and a cylinder into each corpora. The three-piece devise is the most popular of the penile prostheses, with patient satisfaction rates of over 92%.[27] According to Dr Tukey, this level of satisfaction is higher than that with any of the other interventions for ED.

According to Dr Tuckey, penile prostheses are suitable for men who fail or dislike other treatments, for diabetics, for men who don't like using needles, and for men who want more spontaneity or a natural erection. They are also suitable for men with Peyronie's disease with unresponsive ED, and for those with ED after priapism. Penile prostheses are covered by insurers, but they are not available in the public system. Dr Tuckey stressed the importance of pre-operative counselling and that it is very important to set expectations. He explained that the glans doesn't engorge and it thus remains colder than with a normal erection. Complications are uncommon, but include infection and erosion. Mechanical reliability is good at about 70% at 15 years. Postoperatively men spend one night in hospital, have a 2-week recovery period, and the prosthesis is tested after 4-6 weeks.

## TAKE-HOME MESSAGES:

- ED is common in New Zealand and over 80% is unrecognised
- ED can have a major impact on a man's self-esteem and relationships
- ED is a marker for cardiovascular disease – consider referring if young or risk factors present
- Behavioural modification can be effective but takes time and effort
- Discuss the options – usually start with PDE-5 inhibitors
- Patients find intracavernosal injections much more comfortable than they expect
- Patients using injections appreciate the quality of the erection
- Penile prostheses have the highest satisfaction rates
- Penile prostheses solve the efficacy, reliability, and spontaneity of the other options.

## Case examples:

Dr Tuckey presented three cases of ED.

**Case 1.** Ken is a 65 CEO who comes to see you with a year history of ED – his erections are not rigid enough for intercourse. He has a very good relationship with his wife. His bloods are normal, his BMI is 32 and he is under considerable stress at work. What do you advise? 1. Exercise; 2. Caloric restriction; 3. Reduce stress – have a holiday; 4. Trial a PDE-5 inhibitor. Dr Tuckey, says that any of these options would be appropriate. Ken chose conservative measures; he had a holiday in Fiji and returns to say his erections are back to normal. However, he returns in 2 years and finds that even a holiday does not improve the quality of his erections. His BMI is now normal, he used to have intercourse three times per week and now has mild BPH symptoms. Dr Tuckey believes the best treatment at this stage would be tadalafil 5 mg daily, given that it is also helpful in BPH and its long half-life facilitates spontaneity.

**Case 2.** Bob is a 67-year-old man 3-months post radical prostatectomy who comes in for a routine BP check and prescription. Bob and his surgeon have been concentrating on his incontinence, which has just resolved. You mention that surgery can affect a patient's sex life and ask how he is? He replies he's not so good. Dr Tuckey recommends asking him about the following: ED, climacturia, painful orgasm. You prescribe sildenafil for his ED, but he does not respond to treatment. Dr Tuckey recommends asking him the following: Did he wait 30 minutes? Did he have a recent fatty meal? What dose did he use? How many tablets did he trial? It turns out he was using sildenafil appropriately. At this stage Dr Tuckey recommends prescribing alprostadil 5 µg. He tries alprostadil 5 µg but has stinging pain in his penis and only a partial erection. At this stage, Dr Tuckey recommends prescribing Bi-Mix. After 2 years of success with Bi-Mix it is no longer effective even at a higher dose. Dr Tuckey suggests that at this stage you could trial Tri-Mix (but it will likely cause him pain), or a recommend a vacuum device, or refer to discuss a prosthesis.

**Case 3.** Jim is a 68-year-old male who has recently come to your practice and is on intermittent hormonal therapy for advanced prostate cancer. His PSA is undetectable so his Zoladex® was stopped around 9 months ago. He comes in for a script and wonders if anything can be done about the lack of erections and his reduced libido. Dr Tuckey explained that the most relevant blood test at this stage is for testosterone. His testosterone result was normal. You find out he has been very stressed at home with business and family matters, which could explain his reduced libido. At this stage, Dr Tuckey suggests trialling him on intracavernosal injections because patients who have previously received hormonal therapy don't generally respond to PDE-5 inhibitors and can be difficult to treat. Intracavernosal injections were not effective so Dr Tuckey recommends trialling Tri-Mix or referring for a penile prosthesis.

**REFERENCES:**


1. Schröder FH et al. Prostate-cancer mortality at 11 years of follow-up. N Engl J Med. 2012;366(11):981-90
2. Hugosson J et al. A 16-yr follow-up of the eEuropean randomized study of screening for prostate cancer. Eur Urol. 2019;76(1):43-51
3. Weight CJ et al. Men (aged 40-49 years) with a single baseline prostate-specific antigen below 1.0 ng/mL have a very low long-term risk of prostate cancer: Results from a prospectively screened population cohort. Urology. 2013;82(6):1211-7
4. Hugosson J et al. Prostate cancer screening with PSA and MRI followed by targeted biopsy only. N Engl J Med. 2022;387(23):2126-2137
5. Ahmed HU et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): A paired validating confirmatory study. Lancet. 2017;389(10071):815-822
6. Prostate Cancer Foundation. ISUP and Gleason grading systems for prostate cancer. Available from https://www.pcf.org/about-prostate-cancer/diagnosis-staging-prostate-cancer/gleason-score-isup-grade/ (Accessed July 2023)
7. Van As NJ et al. PACE-A: An international phase 3 randomised controlled trial (RCT) comparing stereotactic body radiotherapy (SBRT) to surgery for localised prostate cancer (LPCa) – Primary endpoint analysis. J Clin Oncol. 2023;41(6 Suppl):298
8. Watts S et al. Depression and anxiety in prostate cancer: a systematic review and meta-analysis of prevalence rates. BMJ Open 2014;4(3):e003901
9. Martin E et al. Nurse-led active surveillance for prostate cancer is safe, effective and associated with high rates of patient satisfaction—results of an audit in the East of England. Ecancermedicalscience 2018;12:854
10. Kinsella N et al. Factors influencing men's choice of and adherence to active surveillance for low-risk prostate cancer: A mixed-method systematic review. Eur Urol. 2018;74(3):261-280
11. Milios JE et al. Pelvic floor muscle training in radical prostatectomy: a randomized controlled trial of the impacts on pelvic floor muscle function and urinary incontinence. BMC Urol. 2019;19(1):116
12. Sridhar AN et al. Recovery of baseline erectile function in men following radical prostatectomy for high-risk prostate cancer: A prospective analysis using validated measures. J Sex Med. 2016;13(3):435-43
13. Capogrosso P et al. Are we improving erectile function recovery after radical prostatectomy? Analysis of patients treated over the last decade. Eur Urol. 2019;75(2):221-228
14. Nathan A et al. Immediate post-operative PDE5i therapy improves early erectile function outcomes after robot assisted radical prostatectomy (RARP). J Robot Surg. 2022;16(1):37-43
15. Schwartz EJ et al. Sildenafil preserves intracorporeal smooth muscle after radical retropubic prostatectomy. J Urol. 2004;171(2 Pt 1):771-4
16. Gandaglia G et al. Penile rehabilitation after radical prostatectomy: does it work? Transl Androl Urol. 2015;4(2):110-23
17. Prostate Cancer Working Group and Ministry of Health 2015 Prostate Cancer Management and Referral Guidance. Available from: https://www.health.govt.nz (Accessed July 2023)
18. Quilter M et al. Male Sexual Function in New Zealand: A population-based cross-sectional survey of the prevalence of erectile dysfunction in men aged 40-70 Years. J Sex Med. 2017;14(7):928-936
19. Feldman HA et al. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. J Urol. 1994;151(1):54-61
20. Vasconcelos JS et al. The natural history of penile length after radical prostatectomy: a long-term prospective study. Urology. 2012;80(6):1293-6
21. Rhoden EL et al. The use of the simplified International Index of Erectile Function (IIEF-5) as a diagnostic tool to study the prevalence of erectile dysfunction. Int J Impot Res. 2002;14(4):245-50
22. Medsafe. New Zealand Medicines and Medical Devices Safety Authority. Viagra® Data Sheet. Date of revision 20 Jan 2023. Available from: https://www.medsafe.govt.nz/profs/Datasheet/v/viagratab.pdf (Accessed July 2023)
23. Medsafe. New Zealand Medicines and Medical Devices Safety Authority. Cialis® Data Sheet. Date of revision 18 March 2020. Available from: https://www.medsafe.govt.nz/profs/Datasheet/c/Cialistab.pdf (Accessed July 2023)
24. Medsafe. New Zealand Medicines and Medical Devices Safety Authority. Levitra® Data Sheet. Date of revision 10 Dec 2019. Available from: https://www.medsafe.govt.nz/profs/Datasheet/l/Levitratab.pdf (Accessed July 2023)
25. Medsafe. New Zealand Medicines and Medical Devices Safety Authority. CAVERJECT® IMPULSE Data Sheet. Date of revision 15 Jan 2019. Available from: https://www.medsafe.govt.nz/profs/Datasheet/c/caverjectImpulseinj.pdf (Accessed July 2023)
26. Medsafe. New Zealand Medicines and Medical Devices Safety Authority. DBL™ papaverine hydrochloride Data Sheet. Date of revision 30 Apr 2021. Available from: https://www.medsafe.govt.nz/profs/Datasheet/d/dblPapaverineHydrochlorideinj.pdf (Accessed July 2023)
27. Montorsi F et al. AMS three-piece inflatable implants for erectile dysfunction: a long-term multi-institutional study in 200 consecutive patients. Eur Urol. 2000;37(1):50-5


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