# THE MANUAL

CUTTING-EDGE MEN'S HEALTHCARE

Australian Prostate Cancer Research

prostatecancerresearch.org.au

# Contents




Proudly supported by TOLMAR AUSTRALIA we CARE






# Editorial

Welcome to the second edition of The MANUAL. Following the Prostate Cancer World Congress in Cairns in late August, this edition of The MANUAL highlights several key issues in prostate cancer care.

By all of our metrics the Congress was an outstanding success. There were 700 delegates closeted in Cairns for a week and socially and scientifically the event was peerless. I do pay tribute to energy and drive of Sally Marasco who just “gets it done”. We started the meeting at Royal Melbourne in 2000 and it has grown from 25 delegates to 950 in Melbourne in 2013. The highlight for me was the dinner in the oil tanks just out of Cairns town proper. These tanks housed oil supplies for the Australian and US navies in the Second World War. They have now been turned into a reception centre in the rainforest.

Two of our international guests, Patrick Walsh and Bill Catalona, whom I believe are two of the most outstanding Doctors/Urologists in recent history, were interviewed. They pioneered the reduction in the morbidity of therapy and the 42% decline in US mortality from prostate cancer since the late 1980’s. It was truly spellbinding and a privilege to listen to these two men interviewed about their careers, their ethical views, and excitement for what has been achieved with early diagnosis and safe curative prostate cancer surgery.

This week the Journal of Urology [1] published an assessment of the impact on PSA testing of the USPC taskforce recommendations against prostate cancer screening [2]. There has been a dramatic drop in prostate cancer diagnosis across all grades of cancer, including a decline in diagnosis of intermediate and high-grade disease i.e. the cancers where early diagnosis can save lives.

In 2012, the NIH [3] published the USA prostate cancer mortality decline of 42% from 1990 due to early diagnosis (PSA) and curative intervention. We do acknowledge the overtreatment of some of those patients with low risk disease who now would be placed on Active Surveillance. We know from our Victorian Registry data (personal communication) that we place 40% of men with low risk prostate cancer on Active Surveillance (2014). We are now also better informed about lethality of aggressive prostate cancer.

Already in my own practice I am seeing more advanced disease at presentation, coinciding with a decline in testing in Victoria in recent years.

If there is no diagnosis we cannot stratify for risk and allow for early intervention where appropriate and active surveillance for those who don’t need immediate treatment.

It is clearly enunciated in the Melbourne Consensus Statement on Prostate Cancer Testing, statement 3 “we must uncouple diagnosis from treatment“ [4]. Not knowing whether a man has prostate cancer by doing away with PSA testing “burns bridges“.

We know mostly when and who to treat and what treatments work well [5]. To me the prostate cancer testing debate resonates with the contemporary discussion regarding childhood immunisation for infectious diseases. Some parents, who clearly cannot remember the devastating epidemics of polio and other childhood illnesses, refuse to immunise their children. Prostate cancer practitioners, who did not live in the quite recent era where the initial presentation of prostate cancer was bone metastasis +/- crush fracture to the vertebra and sometimes paraplegia, may be unknowingly steering us backwards.

At the recent 2013 AUA meeting Adams et al, report on the fate of men not screened for prostate cancer, i.e. those men who present with a PSA >100 [6]. There was a 9.7% three year survival, a 19.7% cord compression rate, and a 64% hospitalisation rate. Those who don’t learn the lessons of history are condemned to repeat them.

**Prof Anthony J Costello**
Executive Editor

**Dr Fairleigh Reeves**
Editor


**References**

**[1]** Barry MJ, Nelson JB. Patients Present with More Advanced Prostate Cancer since the USPSTF Screening Recommendations. The Journal of urology. 2015 **[2]** U.S. Preventative Services Task Force. Prostate Cancer: Screening.[cited October 2]; Available from: http://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/prostate-cancer-screening **[3]** Etzioni R, Gulati R, Tsodikov A, et al. Cancer. 2012: 118:5955-63 **[4]** Murphy DG, Ahlering T, Catalona WJ, et al. BJU international. 2014 Nov 8: 113:186-8 **[5]** Costello AJ, Murphy DG. The Medical Journal of Australia. 2010: 193:4-5 **[6]** Adams W, Elliott C, Reese J. The fate of men presenting with PSA over 100 ng/ml: What happens when we do not screen for prostate cancer? Journal of Urology; 2013, p. E608-E9

# Prostate cancer histology:
## moving beyond the Gleason score after 40 years

**Dr Andrew Ryan**
TissuPath, Mount Waverley, Victoria

Despite rarely having direct patient contact, pathologists play a crucial role in the diagnosis and management of most cancer patients. Our main responsibility is to deliver an accurate and concise report containing information about the specific type of tumour biopsied, as wel asl prognostic information ascertained through macroscopic and microscopic examination and ancillary testing.

Gleason grading of prostate carcinoma has been a cornerstone of prognostic information for four decades. Originally conceived by Donald Gleason in 1965, the Gleason grading system is an assessment of the architectural growth pattern of the tumour, with specific growth patterns attributed scores ranging from 1 to 5. The most common and second most common patterns are then presented as a sum score (3+4=7 means pattern 3 is the most common and pattern 4 the second most common pattern).

The Gleason grading system has been revised several times (1970's, 2005, 2014), the most modern iteration now technically a 'modified modified Gleason grading system'. However these modifications not only failed to address several flaws identified in the original system, but also created additional issues including:

- Use of patterns 1 and 2 have been discouraged in modern versions of the system (some of the lesions originally graded as 1 and 2 were likely lesions that we now recognise as benign). This has resulted in Gleason score 6 (3+3) being the lowest grade; seemingly not a big issue until clinicians worldwide tried to sell active surveillance to their patients who had tumours with a score of 6 out of 10!
- Artificial grouping of patients was occurring in clinical (nomogram) and research settings (eg D'Amico, 2-6, 7, 8-10) without proper validation and without standardisation.
- With the system name maintained throughout, tumour data acquired under different iterations of the grading system was sometimes being incorrectly pooled or compared; not entirely apples and oranges, but still bad science.

With these issues in mind, a new grading system has been designed by Epstein et al. [1] (a Johns Hopkins pathologist). While the foundations of the new grading system have not changed (still based on the architectural pattern of the tumour), there has been:

- Simplification of the way tumour architecture will be assessed; tumour components to be assessed as 'well formed glands' (equivalent to pattern 3), 'poorly formed or complex glands' (equivalent to pattern 4) or 'no gland formation' (equivalent to pattern 5),
- A change to the way the results of the assessment are presented to the treating clinicians and their patients. Now, rather than a sum score, tumours will be classified into one of 5 'grade group' (see table 1). This is a marked simplification from the 25 potential grade combinations under the old system.

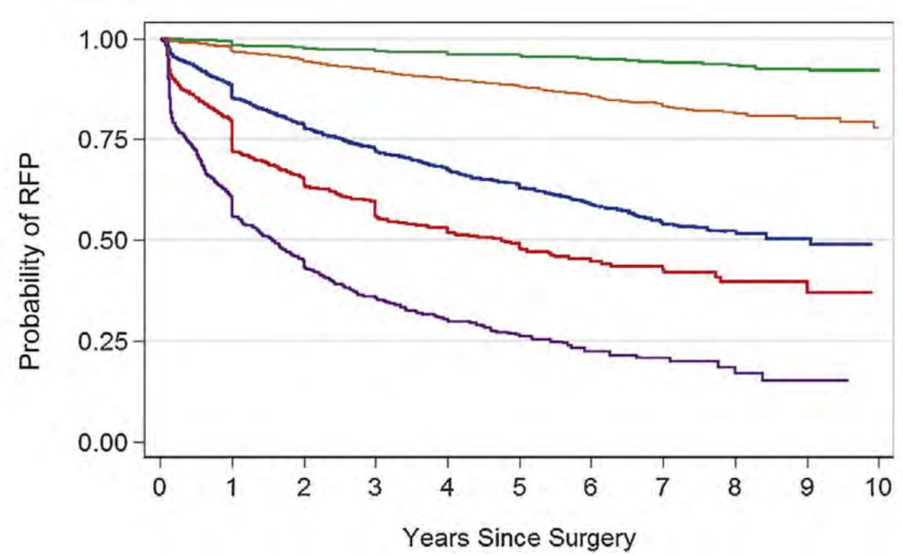
| Histologic definition of new grading system | | |
|---|---|---|
| **Grade Group 1** | (Gleason Score 3 + 3 = 6) | Only individual discrete well-formed glands |
| **Grade Group 2** | (Gleason Score 3 + 4 = 7) | Predominantly well-formed glands with lesser component of poorly formed/fused/cribriform glands |
| **Grade Group 3** | (Gleason Score 4 + 3 = 7) | Predominantly poorly formed glands with lesser component of poorly formed/fused/cribriform glands[1] |
| **Grade Group 4** | (Gleason Score = 8) | Only poorly formed/fused/cribriform glands, or<br>Predominantly well-formed glands and lesser component lacking glands[11]<br>Predominantly lacking glands and lesser component of well formed glands[11] |
| **Grade Group 5** | (Gleason Scores = 9-10) | Lack of gland formation (or with necrosis) with or without poorly formed/fused/cribriform glands[1] |

[1] For cases with >95% poorly formed/fused/cribriform glands or lack of glands on a core or at radical prostatectomy, the component of <5% well-formed glands is not factored into the grade
[11] Poorly formed/fused/cribriform glands can be a more minor component

**Table 1** – Histologic definition of new grading system (reproduced from [1] with permission)



In a validation study of >20,000 men treated by radical prostatectomy and >5000 men treated with radiotherapy, this new 5 tiered system was found by Epstein et al to stratify men into clearly discernible prognostic groups based on biochemical recurrence (Fig 1). The 5 tiered system outperformed other 3 and 4 tier combinations tested, and importantly, clearly separated the often aggregated 'Gleason 7' into two clearly distinct prognostic groups; grade group 2 (3+4=7) and grade group 3 (4+3=7). Stratification was demonstrated using both radical prostatectomy grading (Fig 1) and pre-prostatectomy biopsy grade, and was also demonstrated in patients receiving primary radiotherapy treatment.




| Number at risk | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **≤6** | 7397 | 6973 | 5104 | 4064 | 3226 | 2461 | 1768 | 1186 | 670 | 278 | 108 |
| **3+4** | 8353 | 7202 | 5298 | 3983 | 2955 | 2091 | 1299 | 778 | 393 | 135 | 45 |
| **4+3** | 3106 | 2452 | 1605 | 1152 | 839 | 569 | 350 | 199 | 90 | 38 | 15 |
| **8** | 917 | 678 | 412 | 280 | 191 | 129 | 86 | 59 | 35 | 14 | 7 |
| **≥9** | 1051 | 578 | 325 | 194 | 118 | 73 | 41 | 24 | 12 | 4 | 2 |

Gleason score ≤6, **Grade Group 1**
Gleason score 3+4 **Grade Group 2**
Gleason score 4+3 **Grade Group 3**
Gleason score 8 **Grade Group 4**
Gleason score ≥9, **Grade Group 5**

**Fig. 1 – Recurrence-free progression following radical prostatectomy stratified by prostatectomy grade.**
RFP = recurrence-free progression (reproduced from [1] with permission)

The new system also has the significant benefit of presenting the lowest grade tumours as the lowest grade group (ie grade group 1) rather than as 6 on a scale of 10. It is hoped that this will contribute to continued improvement in patient acceptance of active surveillance with a subsequent decrease in the overtreatment of low-grade prostate cancer detected by prostate-specific antigen (PSA).

The new grading system has been ratified by ISUP (International Society of Urological Pathology) and will be included in the upcoming 2016 WHO Classification of tumours of the urinary system and male genital organs. It is recommended that Pathologists use the new ISUP/Epstein grade group system in conjunction with the Gleason grading system until the former is widely accepted and practiced.

**References**

**[1]** Epstein JI, Zelefsky MJ, Sjoberg DD, et al. A contemporary prostate cancer grading system: a validated alternative to the Gleason score. European urology. 2015

# The role of active surveillance
## in prostate cancer management

**Dr Roderick C.N. van den Bergh**
Urology Fellow
Royal Melbourne Hospital / Peter MacCallum Cancer Centre

In the early 1990s, serum prostate specific antigen (PSA) became available as a marker for prostate cancer. As it allowed for early detection of a lethal disease in still asymptomatic cases, this simple blood test truly has changed the field of prostate cancer diagnosis. It was hypothesized that by detecting the disease in an early stage, options for curative treatment were still an option, leading to more favorable outcomes. A large European randomized study indeed found that population-based screening using PSA significantly reduces the mortality rates due to prostate cancer [1]. The decreasing numbers of deaths due to prostate cancer in countries in which PSA has been introduced confirms this favorable effect from an epidemiological point of view [2]. The reduction in the number of patients developing metastases, which heavily impacts quality of life, was even more profound. While 20 years ago most prostate cancer patients presented with painful bone metastases, the majority now is detected in a localised stage. It was however also found that when using PSA, it is important to screen the right patients; older men may benefit less from early detection. Also, a risk-based approach has been recommended to optimise the effect of screening. PSA results should ideally be combined with further clinical information such as age, digital rectal examination, prostate volume, and imaging results [3].

Prostate cancer screening however comes at a price. Although the diagnosis in men who would develop symptomatic prostate cancer later during their life is advanced to a phase in which opportunities for curative treatment are still available, some others are diagnosed with a relatively low risk type of the disease. This low risk prostate cancer would sometimes not have given any symptoms during their life. Overdiagnosis is the main disadvantage of screening. Besides the heavy psychological impact of being diagnosed, many patients receive radical therapy despite the very low risk of progression and some of them can be considered overtreated. Dependent on the therapy chosen (surgery, external or internal radiation), this can potentially lead to erectile dysfunction, incontinence, and bowel problems in men who would not have had any problems of their prostate during their lifetime.

Active surveillance has developed as a potential solution for overtreatment. This strategy entails selecting patients with low risk disease who are unlikely to benefit from radical therapy because their disease has a very favourable natural course. These men are then followed using a fixed protocol to detect biological progression and to correct for initial under staging [4]. Deferred curative therapy is initiated only when indications for higher risk disease are found or based on patient preference. Active surveillance thus disconnects the direct link between diagnosis and treatment.

**Active surveillance is different from watchful waiting. Active surveillance is intended to offer curative treatment when there are signs of disease progression during the strict follow-up and is for relatively healthy men. Watchful waiting offers palliative therapy when the disease has progressed to a symptomatic stage and is usually applied in men not fit for surgery or radiation.**

The selection of prostate cancer patients who are likely to have an indolent disease course when remaining untreated is a heavily debated topic. Although adequate risk estimation is generally possible, it is currently impossible to 100% certainly select men with indolent disease. A small chance of including patients who actually harbour higher risk disease remains. However, the potential delay in treatment resulting from the initial expectant management has not been found to unfavourably impact outcomes.

**The most widely applied criteria for eligibility for active surveillance are organ-confined prostate cancer at digital rectal examination, with a PSA =<10, a PSA density (PSA divided by prostate volume) <0.2, a low Gleason score of 6 (histological aggressiveness) and a limited number of prostate biopsy cores invaded with cancer (indicating low volume disease)**.

The recent improvements in imaging of the prostate using MRI have also impacted the selection for active surveillance and applied more often in these cases, although not yet a standard part of the selection process. Also, transperineal template biopsies versus transrectal biopsies are known to reduce the misclassification of prostate cancer and are sometimes applied in active surveillance candidates.

After selection, patients are followed according to a fixed protocol. Besides frequently repeating PSA tests, digital rectal examination and repeat prostate biopsies are performed. As the course of the PSA is not always related to repeat biopsy findings, repeat biopsy is usually done after one year, independent of the PSA values. Again, during follow-up, the role of MRI and template biopsies is still evolving.

The uptake of active surveillance in the recent years has varied by country and region but is generally encouraging. The strategy was reported to be frequently used (35.9% of very low and low-risk men) in Victorian patients [5]. Recent reports show that the number of prostate cancer patients, despite very low risk disease, still receive immediate surgery or radiation therapy is very low and that an initial strategy of expectant management is now almost always elected in these cases. Five years after inclusion for active surveillance, around ⅔ of patients still have not received active therapy and treatment is thus successfully avoided. After 10 years, around ½ are still on active surveillance. There are no indications for an unfavourable impact on oncological outcomes. The psychological impact of active surveillance seems also to be limited. However, it should be noted that a selection bias is present in which only the patients who are keen on delaying treatment and avoiding side effects do actually choose active surveillance [6].

Active surveillance has so far been a successful strategy to delay or avoid the side effects of active treatment in patients who would not have any symptoms of their disease if they had never been diagnosed at all. The strategy largely covers the main side effect of screening, which will continue to happen, either as opportunistic screening in individuals or as population based screening. As the risk estimation of diagnosed prostate tumours improves, the indication for active surveillance will decrease as well. MRI and serum biomarkers are the topic of many research efforts currently and will be incorporated to improve active surveillance protocols. At the same time, the psychological and physical burden for patients diagnosed with a low risk prostate cancer needs to be kept as low as possible. The future will both improve the selection process with lower misclassification rates of active surveillance candidates, but also expand the eligibility for active surveillance, for example in older patients. Not treating prostate cancer has never been so important.

**References**

**[1]** Schröder FH, Hugosson J, Roobol MJ, et al. The Lancet. 2014: 384:2027-35 **[2]** Etzioni R, Gulati R, Tsodikov A, et al. Cancer. 2012: 118:5955-63 **[3]** Zhu X, Albertsen PC, Andriole GL, Roobol MJ, Schröder FH, Vickers AJ. European urology. 2012: 61:652-61 **[4]** Loeb S, Bruinsma SM, Nicholson J, et al. European urology. 2015: 67:619-26 **[5]** Weerakoon M, Papa N, Lawrentschuk N, et al. BJU international. 2015: 115:50-6 **[6]** Klotz L, Vesprini D, Sethukavalan P, et al. Journal of Clinical Oncology. 2014: 33:272-7

# Overview of **androgen deprivation therapy**

**Azik Hoffman and Laurence Klotz**
University of Toronto, Division of Urology, Sunnybrook Health Sciences Centre

In the 75 years since the landmark publication of Nobel Prize-winning Huggins and Hodges on castration as a treatment for metastatic carcinoma of the prostate (CAP) [1], great progress has been made in our understanding of the androgen receptor pathway and the ways it can be manipulated. However, the basics of androgen deprivation therapy (ADT) remains the same.

It relies on the knowledge that in CAP cells, dihydrotestosterone binds to the androgen receptor resulting in nuclear translocation, binding to androgen response elements in the genome, gene upregulation and mitosis. Blocking that mechanism results in CAP cell death by apoptosis. The work of Andrew Schally, another Nobel-prize winner, on LHRH and the discovery of Prostate Specific Antigen (PSA) modified the diagnosis and treatment of CAP, and dramatically altered the population of patients in whom ADT is initiated. Locally advanced, recurrent, and metastatic CAP is diagnosed based on PSA level and PSA kinetics, most times prior to other clinical or radiological findings. New emerging stages of the disease, such as rising PSA post-primary treatment and non-metastatic castrate resistant prostate cancer (CRPC) are now widely recognized. Patients are often started on ADT based on rising PSA level only. Early diagnosis of CAP and ADT efficacy results in a median life expectancy of over 15 years at diagnosis. Therefore ADT initiation, choice of drug and treatment strategy should be considered in the context of life expectancy, CAP complication prevention and long term ADT side effects.

**Methods of ADT** - For the first 40 years that it was utilized, androgen ablation was administered continuously, using surgery or drugs to produce castrate serum levels of testosterone. A number of ways to achieve castration were utilized. Bilateral orchidectomy, achieving a quick castration (aprox. 24 hours) is considered safe and efficient but was abandoned as other pharmacological treatments emerged. Still, it is an option when an effective and inexpensive treatment is needed [2]. It is the standard of care for advanced prostate cancer in most of the developing world. Diethylsilbestrol (oestrogen), a well-known treatment in the early years, is currently not used in the primary setting. Nonsteroidal antiandrogens (which block the androgen receptor) and lutenizing hormone-releasing hormone (LHRH) agonists (which bind to LHRH receptor and prevent circadian release of LH, resulting in testosterone production inhibition) gained popularity over the last two decades. As of today, LHRH agonist injections remain the mainstay of treatment given their simple administration method and relative long T1/2. In 2008, the LHRH antagonist Degeralix was approved by the FDA to treat advanced prostate cancer. The new formulation reduced previously reported anaphylactic reaction to older LHRH agonists. Degarelix has been shown to produce quicker serum testosterone reduction, with an acceptable safety profile and a mechanism of action that obviates the testosterone surges associated with LHRH agonist use [3, 4]. It also results in lower levels of FSH, and has been reported to have less risk of cardiovascular disease in patients with pre-existing CV conditions.

All methods of castration are associated with adverse effects including loss of libido, erectile dysfunction, hot flashes, loss of bone density and fracture susceptibility, loss of muscle mass, changes in blood lipids, insulin resistance, weight gain, fatigue, gynecomastia and mood swings [5]. Among these, two should be mentioned in particular. In 2010, the FDA released a warning regarding increased risk of diabetes and cardiovascular disease. Keating et al [6] reported increased risk of diabetes, coronary events, stroke and an increase of sudden cardiac death with hazard ratios of 1.2 to 2.2. Another large cohort [7] estimated total Cardio vascular risk to be HR- 1.21, with CVD risk highest during the first 6 months of ADT. The risk was particularly higher in men who had experienced two or more previous cardiovascular events. Pre-clinical research has suggested this may be due to the effects of FSH and/or LHRH agonists on endothelial plaque stability, resulting in an increased risk of plaque rupture and thrombosis [8]. Secondly, ADT results in loss of bone mineral density [9] and an increased risk of fractures, morbidity and mortality. In the presence of approved preventive treatment (Zoladronic acid and Denosumab), an effort should be made towards prevention of osteoporosis. A recent review [10] concluded a significantly increased risk of overall fracture of 23% (RR- 1.23), and a 17% (RR- 1.17) increase in cardiovascular related mortality compared with men with CAP not receiving ADT. Several randomized trials have demonstrated that co-administration of a bisphosphonate (ie, Aledronate 70 mg per week) [11, 12] or Denosomab every 6 months, [13] reverses the ADT related loss of BMD.

**Indications for ADT** - Although ADT treatment is more established in advanced locoregional and metastatic disease, the risk-benefit ratio in earlier stages remains poorly defined [14]. In men with non-metastatic disease, the use of primary ADT as monotherapy has not shown a benefit and is not recommended. ADT combined with conventional-dose RT (<72Gy) for patients with high-risk disease delays progression and prolongs survival [15]. In men with biochemical recurrence, the optimal timing of initiation of ADT is unresolved [16, 17]. Common practice is to initiate ADT for a rising PSA, rather than wait for metastatic disease. However, no randomized trial has examined this specific approach. EORTC 30891 [18] randomizing untreated patients between early and delayed ADT, showed an 11% survival benefit favouring earlier treatment. Stratification analysis showed the benefit of earlier therapy in men under 70 whose PSA was > 20, and in men over 70 whose PSA was > 50, or in those with a PSA DT <= 12 months. These PSA levels should serve as a rough guide for the timing of intervention in men with biochemical failure, perhaps adjusted downwards by ~30% if the prostate is absent.



| Possible adverse effect | Treatment / prophlaxis |
|---|---|
| Loss of libido | Intermittent ADT |
| Erectile dysfunction | PDE5 inhibitors, intracavernosal injections |
| Hot flashes | DES, Cyproterone acetate, Venlafaxine, Clonidine |
| Gynecomastia and breast pain | Prophylactic radition, liposuction, mamectomy, Tamoxifen, aromatase inhibitors |
| Increase in body fat | Diet |
| Muscle wasting | Exercise |
| Diabetes | Diet and weight control |
| Cardiovascular disease | Smoking cessation, monitor BP and serum lipid |
| Cognitive decline | Memory excercise |
| Decrease in bone mineral density | Excercise, addd calcium + vit. D3, biphosphonates |

**Intermittent therapy** - Intermittent therapy for men with biochemical failure has been shown to be non-inferior to continuous lifelong therapy [19], and is warranted in most patients. This approach, first reported in 1986, has proven to be effective when managed wisely, by properly selecting patients, strictly following maintenance of T castration level and switching to continuous therapy when indicated [20-22]. Currently, it offers improved quality of life in selected patients due to testosterone recovery during off-treatment periods. However, some principals should be followed [23]: Only drugs leading to castration should be considered, the initial cycle must last between 6 and 9 mo, and the treatment is stopped only if patients have a clear PSA response, empirically defined as a PSA level <4 ng/ml in metastatic patients or <0.5 ng/ml in relapsing patients. The treatment is resumed when there is either clinical progression or the PSA value rises above an empirically fixed threshold. Treatment is continued as in the induction cycle or until PSA reaches nadir. A strict follow-up is mandatory. In the context of salvage radiation therapy, additional ADT was proven to have biochemical and clinical progression benefit, yet an overall survival benefit has not been demonstrated [19, 24, 25]. In men with more advanced disease, immediate ADT therapy is a common practice. The Eastern Cooperative Oncology Group (ECOG) 3886 trial influenced common clinical practice by showing improved OS and CSS in node positive disease patients after RP who were started on ADT immediately vs. at diagnosis of bone metastasis [26]. However, reasonable modifications of this approach, including the use of intermittent ADT in men with node positive disease, or delaying ADT until PSA failure (rather than metastatic disease), have never been studied in a prospective randomized trial. Both approaches are widely used. Patients with metastatic PCa experience reduced risk of complications and a survival benefit with immediate ADT initiation [27]. As a consequence of the adverse effects of ADT on metabolism and quality of life, an intermittent therapy approach has gained popularity.

Given the known adverse effects of ADT, routine follow up is important. Patients should first be evaluated at 3 and 6 months after the initiation of treatment, including serum PSA measurement, DRE, serum testosterone, and evaluation of response and side effects. Follow-up should be tailored for the individual patient according to disease stage symptoms, prognostic factors, and the treatment given, usually every 3-6 months. The testosterone serum level should be monitored closely to ensure adequate testosterone suppression. If IAD therapy was chosen, testosterone should be monitored during the off-treatment interval [23]. Routine monitoring of weight, blood glucose, diabetes re-evaluation and blood lipids should be performed on a regular basis. Suggested interventions to reduce adverse effects impact is summarized in table 1.

In conclusion, Androgen ablation therapy is an effective treatment for patients with advanced prostate cancer. Although not curative on its own, it improves survival. It enhances the effectiveness of radiation treatment. The adverse impact on quality-of-life should be taken into consideration, particularly when ADT is used over a long period of time. Intermittent therapy may reduce this QOL impact. Treatment should be tailored to the patient, who must be monitored routinely for response, adverse effects and disease progression.

**References**

**[1]** Huggins C, Hodges C. Cancer Res. 1941: 1:293-7 **[2]** Bourke L, Kirkbride P, Hooper R, et al. British journal of cancer. 2013: 108:9-13 **[3]** Klotz L, Boccon-Gibod L, Shore ND, et al. BJU international. 2008: 102:1531-8 **[4]** Van Poppel H, Tombal B, Jean J, et al. European Urology. 2008: 54:805-15 **[5]** National Comprehensive Cancer Network. NCCN Guidelines for Patients®: Prostate Cancer. Vol. Version 1. 2013 Ed. Fort Washington, Pa http://www.nccn.org/patients/guidelines/prostate **[6]** Keating NL, O'Malley AJ, Freedland SJ, Smith MR. Journal of the National Cancer Institute. 2009: 102:39-46 **[7]** O'Farrell S, Garmo H, Holmberg L, et al. Journal of Clinical Oncology. 2015: 33:1243-51 **[8]** Pinthus J. Canadian Urological Association Journal. 2015: 9:226-7 **[9]** Eastham JA. The Journal of urology. 2007: 177:17-24 **[10]** Taylor LG, Canfield SE, Du XL. Cancer. 2009: 115:2388-99 **[11]** Klotz LH, McNeill IY, Kebabdjian M, et al. European urology. 2013: 63:927-35 **[12]** Greenspan SL, Nelson JB, Trump DL, et al. Journal of Clinical Oncology. 2008: 26:4426-34 **[13]** Skolarus TA, Caram MV, Shahinian VB. Current opinion in urology. 2014: 24:601-7 **[14]** National Comprehensive Cancer Network. NCCN guidelines for patients: Prostate cancer. Available from: http://www.nccn.org/patients/guidelines/prostate **[15]** Pagliarulo V, Bracarda S, Eisenberger MA, et al. European urology. 2012: 61:11-25 **[16]** Freedland SJ, Humphreys EB, Mangold LA, et al. JAMA. 2005: 294:433-9 **[17]** Makarov DV, Humphreys EB, Mangold LA, et al. The Journal of urology. 2008: 179:156-62 **[18]** Studer UE, Whelan P, Wimpissinger F, et al. European Urology. 2014: 66:829-38 **[19]** Shipley W, Hunt D, Lukka H, et al. International Journal of Radiation Oncology Biology Physics. 2010: 78:S27 **[20]** Klotz LH, Herr HW, Morse MJ, Whitmore WF. Cancer. 1986: 58:2546-50 **[21]** Crook JM, O'Callaghan CJ, Duncan G, et al. New England Journal of Medicine. 2012: 367:895-903 **[22]** Klotz L, Toren P. Current Oncology. 2012: 19:S13 **[23]** Heidenreich A, Bastian PJ, Bellmunt J, et al. European urology. 2014: 65:467-79 **[24]** Bolla M, van Poppel H, Collette L, et al. The Lancet. 2005: 366:572-8 **[25]** Thompson IM, Tangen CM, Paradelo J, et al. The Journal of urology. 2009: 181:956-62 **[26]** Messing EM, Manola J, Sarosdy M, et al. NEJM. 1999: 341:1781-8 **[27]** Adib R, Anderson J, Ashken M, et al. British Journal of Urology. 1997: 79:235-46

# Androgen deprivation therapy: what is the role of the general practitioner?

**Dr Jane Crowe**
General Practitioner
Epworth Prostate Centre

**Ms Helen Crowe**
Urology Nurse Practitioner
Epworth Prostate Centre

In 1944 Charles Huggins received the Nobel Prize for discovering the role testosterone played in prostate cancer. As a result surgical castration by means of bilateral orchidectomy became the treatment for advanced prostate cancer. Androgen deprivation therapy (ADT) by way of chemical or surgical castration still plays an integral part in the management of prostate cancer [1]. ADT is generally used as a treatment option for patients with metastatic prostate cancer [2]. It is also often used as neoadjuvant/adjuvant therapy in combination with radiotherapy for treatment of localized disease [3].

ADT may be given as continuous therapy, usually 3, 4 or 6 monthly injections, or may be intermittent, with the ADT being commenced and continued for a prescribed time (often 9-12 months) then ceased. The patient's PSA is monitored regularly and used as a trigger for the recommencement of ADT. Intermittent therapy may allow patients relief from the troublesome side effects by recovery of testosterone. There is conflicting evidence about the optimal use of ADT, and the risks and benefits of continuous versus intermittent therapy [4-6]. Most patients will progress to develop a resistance to their ADT, known as castrate resistant disease, evidence by a rising prostate specific antigen (PSA) or radiographic evidence of disease progression in the context of castrate levels of testosterone [1]. The time to castrate resistance varies considerably. These patients will then require additional therapies to control their disease.

ADT can result in physical (cardiovascular), psychological, metabolic and bone effects (Table 1), which vary in severity from being mild to intolerable for some patients. The GP needs to be aware of these side effects so they can play a role in monitoring and support of men on ADT as part of a multidisciplinary team.

This therapy is usually commenced by the patient's treating specialist, with follow-up care given by the GP to actively supervise the patient's side effects. In practice unfortunately, many GPs are unaware of the monitoring practices required for patients on ADT.

**GP Management:**

The patient, and importantly their partner, require education about ADT and its role in prostate cancer treatment. It is helpful to talk to men and their partners about ADT and to discuss the possible side effects, management, and the optimal follow up program before commencement of therapy. The commonly experienced side effects of ADT, and possible management of these, are listed in Table 1.

A typical clinical assessment and consultation for a patient on ADT would include the following:

1. **General assessment.**
   - Prostate cancer history
   - Medical history
   - Psychosocial history
   - Sexual functioning
   - Diet and exercise, alcohol intake, smoking
   - Identification of any symptoms attributable to ADT
2. **Examination.**
   - General physical examination including height and weight to determine BMI, waist circumference, blood pressure.
   - Screen for mood, anxiety or other mental health disorders.
3. **Investigations.**
   - Pathology: FBE, OGTT, Vitamin D, calcium, Urea & Electrolytes, creatinine, fasting lipids, liver function tests.
   - Dexa bone density scan (MBS reimbursement for men with hypogonadism).
   - Lateral X-Ray thoracolumbar spine to look for asymptomatic compression fracture(s).
4. **Educate the patient and his partner and devise a management plan for his symptoms and ADT effects.**

   Refer to specialists and allied health as required. Ensure there is good communication between all of the patient's treating health professionals.
5. **Referral options**
   - Dietician
   - Exercise physiologist (ESSA.org.au is the website for the association of accredited exercise physiologists)
   - Psychologist
   - Sexual therapist (http://societyaustraliansexologists.org.au is the website for the accredited sex therapists)
   - Continence physiotherapist (not specific for ADT), but may be required
   - Urologist
   - Endocrinologist
   - Cardiologist
   - Radiation Oncologist
   - Urology/prostate cancer nurse
6. **Plans that allow for Allied health Medicare rebates for patients**
   - GP Management Plan, Team Care Arrangement
   - Mental health care plan
7. **Review the patient 3-6 monthly depending on clinical condition and management**

In summary, men on ADT for prostate cancer may develop significant side effects. A GP, who is proactive regarding patient education, and in monitoring and managing side effects as part of a multidisciplinary team, can start to improve the health and quality of life of these patients and their partners.



| Side effects | Management options |
|---|---|
| **Flushes / sweats** | **Avoid possible triggers e.g. spicy foods, alcohol , caffeine, stress, nicotine, heavy clothing [7]**<br>Carry a face cloth and wear layers, natural fibre clothing.<br>**Acupuncture: auricular acupuncture, weekly for 10 weeks [8]**<br>Gabapentin 900mg daily [9, 10]<br>**Clonidine [11]**<br>SSRIs [12]<br>**Venlafaxine [13]**<br>Complementary medicines: There is little data available to support the use of complementary therapies. Further work is needed to determine safety and efficacy before any can be recommended.<br>**Hormonal treatment: with oestrogen and cyproterone can be effective but have a side effect of significant increased cardiovascular risk, and are not commonly used [14]** |
| **Cognition / mood and depression** | Psychological (or psychiatric referral) for patient and/or partner, antidepressants.<br>**Exercise prescription may help with depression and fatigue [12, 13]**<br>May require cessation of ADT if depression is severe enough.<br>**Memory aids e.g. lists, appointments diaries to help forgetfulness**<br>Patient support groups<br>**Mindfulness** |
| **Fatigue** | Exercise prescription [15, 16]<br>**Lifestyle changes/balance counseling** |
| **Sexual dysfunction** | Prescribed exercise has been shown to improve sexual dysfunction in some men on ADT [17]<br>**Psychological counseling for patient and his partner**<br>PDE5 inhibitors, Intracavernosal injections, Vacuum constriction devices, or penile prostheses [14]<br>**Referral to a sex therapist** |
| **Sarcopaenia and reduced bone** | Lifestyle measures: smoking cessation and reduction in alcohol intake [18]<br>**Baseline bone density soon after androgen deprivation therapy is initiated [17] repeated after one year, and then as indicated.**<br>Baseline lateral thoracolumbar spine X-Ray to screen for asymptomatic osteoporotic fractures [17]<br>**Exercise for bone and muscle strengthening exercise [17]**<br>Reduce falls risk<br>**Ensure adequate calcium in diet, or advise a calcium supplement daily [17]**<br>Ensure adequate Vitamin D levels >75nmol/L [17]<br>**Obtain dental review before commencing antiresorptive medication.**<br>Treat osteoporosis with antiresorptive agent if fracture present or T score below -2.0. (18) (NB PBS reimbursement requires T score <-2.5) |
| **Metabolic syndrome and increased risk of diabetes and cardiovascular disease** | **Lifestyle measures: healthy weight, smoking cessation, exercise**<br>Monitor BMI, blood pressure and fasting lipids,<br>**OGTT at initiation and annually.**<br>Intensive lifestyle intervention to prevent weight gain and worsening of insulin resistance.<br>**Tight control of CVS risk factors (BP aim for <130/80) [17]** |
| **Anaemia** | Normocytic normochromic (usually mild) [14] |
| **Gynaecomastia** | **Radiation may reduce breast tenderness [14]**<br>Mastectomy [19]<br>**Aromatase inhibitors and short term tamoxifen may reduce the pain [14]** |

**References**

**[1]** Rhee H, Gunter JH, Heathcote P, et al. BJU international. 2015: 115:3-13 **[2]** Sharifi N, Gulley JL, Dahut WL. JAMA. 2005: 294:238-44 **[3]** Studer UE, Whelan P, Wimpissinger F, et al. European urology. 2014: 66:829-38 **[4]** Alva A, Hussain M. Intermittent Androgen Deprivation Therapy in Advanced Prostate Cancer. Current treatment options in oncology. 2014: 15:127-36 **[5]** Brungs D, Chen J, Masson P, Epstein R. Prostate cancer and prostatic diseases. 2014: 17:105-11 **[6]** Wolff JM, Abrahamsson PA, Irani J, Calais da Silva F. BJU international. 2014: 114:476-83 **[7]** Boekhout AH, Beijnen JH, Schellens JH. The oncologist. 2006: 11:641-54 **[8]** Harding C, Harris A, Chadwick D. BJU international. 2009: 103:186-90 **[9]** Loprinzi C, Dueck A, Khoyratty B, et al. Annals of oncology. 2009: 30:379-83 **[10]** Jeffery SM, Pepe JJ, Popovich LM, Vitagliano G. Annals of Pharmacotherapy. 2002: 36:433-6 **[11]** Kouriefs C, Georgiou M, Ravi R. BJU international. 2002: 89:379-83 **[12]** Loprinzi CL, Sloan JA, Perez EA, et al. Journal of clinical oncology. 2002: 20:1578-83 **[13]** Quella SK, Loprinzi CL, Sloan J, et al. The Journal of urology. 1999: 162:98-102 **[14]** Kumar RJ. Reviews in urology. 2005: 7:S37 **[15]** Cormie P, Galvão DA, Spry N, et al. BJU international. 2015: 115:256-66 **[16]** Cavallini G, Caracciolo S, Vitali G, Modenini F, Biagiotti G. Urology. 2004: 63:641-6 **[17]** Cormie P, Newton R, Taaffe D, et al. Prostate cancer and prostatic diseases. 2013: 16:170-5 **[18]** Grossmann M, Hamilton EJ, Gilfillan C, Bolton D, Joon DL, Zajac JD. Med J Aust. 2011: 194:301-6 **[19]** Thompson CA, Shanafelt TD, Loprinzi CL. The oncologist. 2003: 8:474-87

# Nursing support for men
## with prostate cancer

**Evie Mertens**
Department of Urology,
The Royal Melbourne Hospital

Urology Nurses are integral members of the multidisciplinary team. They are highly specialized, often with postgraduate qualifications specific to prostate cancer and Urology and Continence nursing. Those specializing in prostate cancer play a pivotal role in providing ongoing education and supportive care to patients and partners with prostate cancer, from diagnosis through to treatment and follow up.

Nurses are often excellent communicators, and developing rapport with the patient and partner from the first consultation is particularly important, as personal topics are broached regarding sexual function and continence. Patients may share information with their nurse that they withhold from the medical team, finding it too embarrassing to discuss certain health care needs or concerns.

A recent survey of 1001 men across 7 countries highlighted this issue, finding '81% of men living with prostate cancer had unmet supportive care needs' [1]. Of those men surveyed, lack of advice from a nurse or advice and support from a nurse were associated with unmet psychological, sexual and health information needs [1]. This survey highlights the significance of the urology nurse addressing the educational and supportive requirements of prostate cancer patients.

Receiving a cancer diagnosis can be a traumatic experience for both the patient and their partner. Historically patients were given their diagnosis and received treatment without adequate education or involvement in the treatment decision. Patients often felt hurried, unable to ask questions about their own health care. Utilising a urology nurse specializing in prostate cancer care enables the patient and partner to receive education using laymen's terms regarding diagnosis, treatment options, side effects of treatment, and follow up. Deciding on treatment can be extremely stressful for patients and partners. Treatment regret can have a huge impact on quality of life, and reducing treatment regret may improve mental health [2]. The prostate cancer urology nurse can ensure patients are seen by both a radiation oncologist and urologist to discuss treatment options, and can provide education and unbiased information regarding surgery or radiotherapy and the side effects of treatment. Linking patients in with their closest prostate cancer support group, and other members of the multidisciplinary team including psychologists and continence physiotherapists ensures the patient receives the best care possible.

At the Prostate Cancer Centre in Melbourne, several specialist clinics are now available to assist men living with prostate cancer. Those patients undergoing Robotic Radical Prostatectomy are enrolled in our Prehabilitation clinic: a multidisciplinary clinic with a urology nurse, continence physiotherapist and exercise physiologist. During a one-hour consultation with the urology nurse the patient and partner are educated on Gleason score, anatomy and function of the urinary tract, surgical procedure, ward stay, incontinence aides, erectile dysfunction, incontinence and penile rehabilitation. The continence physiotherapist then educates the patient on pelvic floor exercises and the exercise physiotherapist prescribes an exercise regime. Sexual function can be an ongoing issue following curative treatment. A sexual function nurse led clinic runs fortnightly at the Centre with consultant support. The urology nurse is able to educate patients on penile rehabilitation, PDE5 Inhibitors, vacuum erection devices and provide lessons in intracavernosal injection therapy. For those patients with advanced disease on androgen deprivation therapy (ADT), there is an ADT clinic where the patient is seen by a GP, urology nurse and exercise physiologist. The urology nurse provides education on the role of testosterone in the body, hormone treatment, side effects of hormone treatment and management of side effects. The GP conducts a comprehensive health check and the exercise physiologist prescribes an exercise regime to combat the side effects of hormone treatment.

While service delivery and roles vary between institutions, urology nurses caring for men and partners with prostate cancer share a common goal: to improve patient outcomes through education, support and care facilitation. They are the patient advocate and work hard within the multidisciplinary team to ensure the patient and their partner receives the best outcome. In 2012, the Prostate Cancer Foundation of Australia, funded by Movember, launched a specialist prostate cancer program. Thirteen nurses with prostate cancer care training were rolled out to metropolitan and remote communities throughout Australia, to play a direct role in providing prostate cancer supportive care to patients and family members with prostate cancer. The successful program has now expanded to include twenty-six specialist nurses. Together with urology nurses working in a similar role, Australian men now have improved access to specialist nurses to help meet their ongoing supportive care needs.

**References**

**[1]** Cockle-Hearne J, Charnay-Sonnek F, Denis L, et al. British journal of cancer. 2013: 109:2121-30 **[2]** Ratcliff CG, Cohen L, Pettaway CA, Parker PA. 2013: 21:3337-43



APCR
Prostate Cancer Centre

Now open for GP referral. Bulk-billed specialists and allied health services from some of Victoria's leading practitioners.

Australia's first public, bulk-billing healthcare centre dedicated to the multi-disciplinary and long-term supportof Australian men with prostate cancer and other urological conditions

www.prostatecentre.org.au

Urology • Radiation Oncology • Medical Oncology • Specialist Nursing • Psychology • Physiotherapy • Nutrition • Onsite Pathology

Open 9am - 5pm Monday to Friday

a:14-20 Blackwood Street, North Melbourne, VIC, 3051 t: (03) 8373 7600 e: info@prostatecentre.org.au w: prostatecentre.org.au

# Understanding **urinary incontinence after radical prostatectomy**

**Dr Fairleigh Reeves**
Departments of Urology and Surgery,
Royal Melbourne Hospital, University of Melbourne

## Normal anatomy of male urinary continence

In order to understand both the pathophysiology and treatment of incontinence after surgery, it is important to first appreciate the normal anatomy.

Male urinary continence requires the coordinated function of several sets of muscles. Foremost is the male urethral sphincter. This comprises an internal smooth muscle sphincter (also known as the lissosphincter) and the striated external urethral sphincter (also known as the rhabdosphincter) [1].

The lissosphincter is important for continence at rest and also prevents retrograde ejaculation. It receives autonomic innervation.

In contrast, the rhabdosphincter is important for maintenance of continence in conditions of stress. It is weakness of this muscle that is most often implicated post-prostatectomy urinary incontinence. The rhabdosphincter is a horseshoe or omega shaped muscle [2], which has the bulk of its muscle at the anterolateral aspect of the membranous urethra, and inserts posteriorly into the perineal body. Its muscle fibres however also extend proximally, where they thin out over the bladder base and intermingle with the smooth muscle fibres of the bladder [1, 3].

While the rhabdosphincter lies in close proximity to the muscles of the pelvic floor they are in fact independent, separated by connective tissue [4].

The muscular pelvic floor, formed by levator ani also plays an important role in the maintenance of continence [5]. Of particular importance, the most central portion of levator ani consists of specialized thickened muscular slings, which are anchored to the pubic bone anteriorly and pass around the viscera of the pelvis. These muscular slings include puborectalis [5] and puboperineales (also known as levator urethrae or levator prostate [6]).

Functional imaging with transperineal ultrasound has greatly improved our understanding of the coordinated actions of the muscles of continence. Figure 1, illustrates the complementary movement generated by activation of these muscles in men. By measuring the displacement of anatomic points with transperineal ultrasound, Stafford and colleagues were able to demonstrate the various actions of these muscles. That is, the striated urethral sphincter compresses the urethra in a dorsal direction, against the perineal body. Whereas the puborectalis muscle of levator ani displaces the urethra in the opposite direction, anterosuperiorly [7]. Similarly, based on 3D images constructed from MRI, Myers and colleagues suggest that puboperineales achieves quick stop urinary control by compressing the urethra anteriorly against the pubic bone [8].

## Why does incontinence occur after radical prostatectomy?

Although urodynamic studies have shown that weakness of the rhabdosphincter is implicated in the majority of cases [9], the precise mechanism underlying this sphincter weakness is not well understood and is likely multifactorial.

## Who is most at risk?

A number of factors have been associated with continence outcomes. Older patient age has been associated with poorer continence outcomes [10]. However, in a local series published by Basto and colleagues, there was no significant difference between continence rates at 12 months in men younger than 70 years old compared to those 70 or older. Therefore, age should not be a reason to deny older men with reasonable life expectancy curative surgical treatment of localized prostate cancer [11]. Urinary continence outcomes are also affected by the presence of prior radiotherapy. Salvage radical prostatectomy (following prior radiotherapy) is generally associated with a higher risk of incontinence that primary surgery.  Conversely, rates of postoperative and late urinary complications following radical prostatectomy are significantly reduced if the procedure is performed in a high-volume centre and by a surgeon who performs a high number of these procedures [12]. Other patient factors that were identified in a meta-analysis, include body mass index, comorbidity index, lower urinary tract symptoms and prostate volume [10]. However, these are not consistently reported.

Despite, various advancements in surgical technique, we have not yet been able to eliminate the risk of post-prostatectomy incontinence. More research is needed to elucidate the precise anatomy of urinary continence so that we can tailor treatment to avoid incontinence.



## What can clinicians do?

The most important thing that clinicians can do is to be proactive in the management of urinary incontinence. Unfortunately, we can be a poor judge of our patients' symptoms. Studies have shown that physician ratings of patient symptoms do not correlate well with patient self-assessments of health related quality of life and are likely to underestimate patient symptoms [13]. This reminds us that we must always actively ask our patients about their continence status so that we can facilitate early intervention and referral to appropriate clinicians for further evaluation and treatment.

A broad spectrum of effective interventions are available to these patients, further details of which are encompassed in the articles by Dr Borin, Ms Morrison and Ms Heerey in this edition of The MANual.

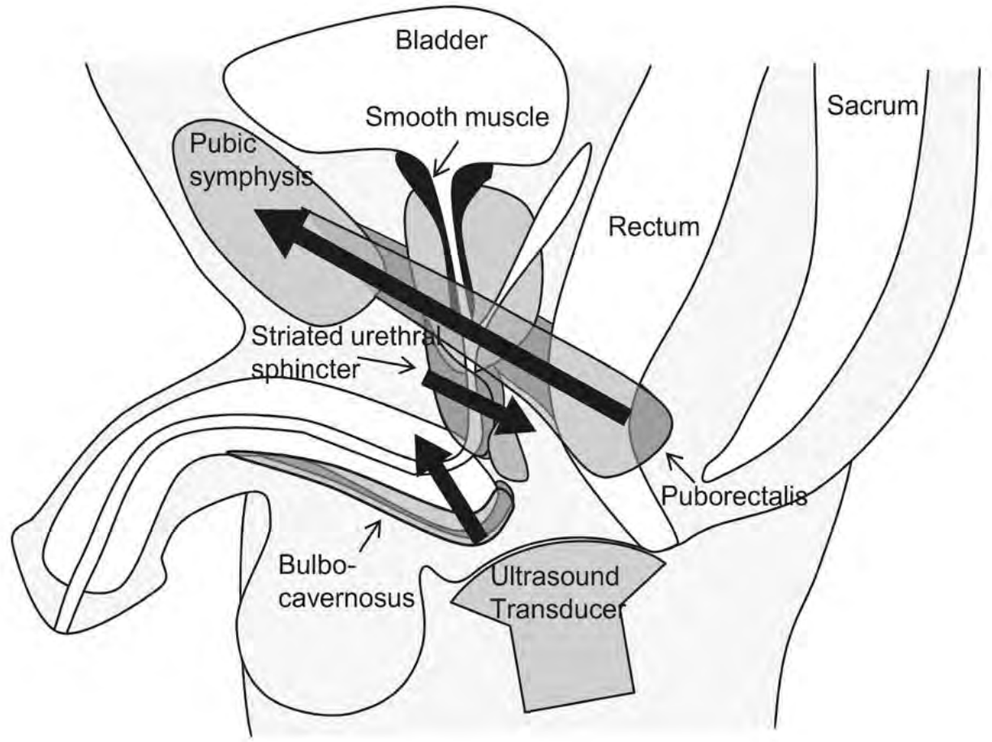



**Figure 1.** Anatomical depiction of the male pelvic floor and associated structures viewed in the midsagittal plane with an ultrasound transducer placed on the perineum. Bold arrows indicate hypothesized direction of movement during voluntary muscle contraction based on anatomy (Reproduced from [7] with permission)

**References**

**[1]** Koraitim MM. J Urol. 2008 Jun: 179,:1683-9 **[2]** Ludwikowski B, Oesch Hayward I, Brenner E, Fritsch H. BJU Int. 2001 May: 87:565-8 **[3]** Oelrich TM. Am J Anat. 1980 Jul: 158:229-46 **[4]** Dorschner W, Biesold M, Schmidt F, Stolzenburg JU. J Urol. 1999 Dec: 162:1942-5 **[5]** Stoker J. Best Practice & Research Clinical Gastroenterology. 2009: 23:463-75 **[6]** Walz J, Burnett AL, Costello AJ, et al. European Urology. 2010 Mar: 57:179-92 **[7]** Stafford RE, Ashton-Miller JA, Constantinou CE, Hodges PW. Urology. 2013 Apr: 81:685-9 **[8]** Myers RP, Cahill DR, Kay PA, et al. J Urol. 2000 Oct: 164:1412-5 **[9]** Ficazzola MA, Nitti VW. J Urol. 1998 Oct: 160:1317-20 **[10]** Ficarra V, Novara G, Rosen RC, et al. European Urology. 2012 Sep: 62:405-17 **[11]** Basto MY, Vidyasagar C, te Marvelde L, et al. BJU Int. 2014 Jun **[12]** Begg CB, Riedel ER, Bach PB, et al. N Engl J Med. 2002 May 11: 346:1138-44 **[13]** Litwin MS, Lubeck DP, Henning JM, Carroll PR. JURO. 1998 Jul: 159:1988-92

# The role of **physiotherapy in post-prostatectomy urinary incontinence**

**Ms Shan Morrison**
Specialist Continence and Women's Health Physiotherapist
Managing Director of Women's and Men's Health Physiotherapy

**Ms Rachel Heerey**
Physiotherapist at APCR Prostate Cancer Centre
& Women's and Men's Health Physiotherapy

Urinary incontinence is a common problem for men after surgery for prostate cancer [1], and it can have a huge impact on quality of life. Pelvic floor muscle training is an essential component of a conservative management program for post-prostatectomy incontinence. A Cochrane review published in 2015 reported moderate evidence that pelvic floor muscle training commenced prior to radical prostatectomy is effective in hastening recovery of continence [2].

Urinary incontinence after radical prostatectomy can be a mild problem, needing pads to manage it for only a few weeks, or more severe and requiring protective pads for up to a year. This leakage will often happen with sudden movements, physical activity, or coughing and sneezing. How much urine leaks and how long this incontinence lasts is difficult to predict. Fortunately, urine leakage can be reduced by learning to use the pelvic floor muscles effectively. The pelvic floor muscles control the bladder and flow of urine. Exercising them effectively will help men regain bladder control earlier after surgery. Ideally the exercises are started before surgery, but they can also help bladder control if they are started after surgery.

### What causes post-prostatectomy incontinence?

Aetiology of post-prostatectomy incontinence is complex. The most well recognised cause of post-prostatectomy incontinence is intrinsic sphincter deficiency or weakness. However, there is poor understanding and awareness about the contribution of bladder overactivity, as much of the literature is focused on sphincteric weakness. Bladder overactivity can be pre-existing, or it can be de novo after surgery. De novo bladder overactivity is believed to be caused by partial decentralisation of the bladder during or after surgery, or by urine escaping into the proximal urethra due to sphincteric weakness, which can then trigger a bladder contraction [3, 4]. Bladder overactivity is relatively common after radical prostatectomy, occurring in 21- 63% of men, however is rarely the sole cause of post-prostatectomy incontinence [4]. Current research suggests that the aetiology of post-prostatectomy incontinence is multifactorial, and so management must include a thorough history, and an individualised treatment approach.

### How can a pelvic floor physiotherapist help?

Pelvic floor physiotherapists specialise in the assessment and treatment of post-prostatectomy incontinence. A thorough subjective assessment, preferably performed pre-operatively ensures identification of pelvic floor muscle risk factors and pre-existing lower urinary tract or bowel symptoms that may impact on post-operative recovery. Understanding each man's lifestyle and general exercise habits also assists in setting realistic post-operative goals. Establishing baseline outcome measures ensures appropriate post-operative expectations with respect to function and time frames. These measures include bladder frequency volume and fluid intake charts.

It is essential that men have an individualised objective assessment of their pelvic floor muscles with a pelvic floor physiotherapist, to ensure they have the correct technique of activation. The pelvic floor can be effectively assessed via a digital rectal examination, or via transperineal ultrasound. Transperineal ultrasound is a new and exciting assessment technique that has many advantages. It is relatively novel in assessment of the male pelvic floor, although it has been used in female pelvic floor muscle dysfunction for the past 10 years. It has proven reliability and validity in men [5, 6], provides visual biofeedback, and allows simultaneous investigation of all the striated muscles involved in continence.

An individualised pelvic floor rehabilitation program is designed based on findings of a clinical reasoned assessment. This will vary in the components of pelvic floor muscle exercise prescription such as technique, dosage, positions and application to function and activities of daily living. Post operative progression of the program is also based on the degree of incontinence and rate of recovery, most accurately assess by a pad weigh diary. A pelvic floor physiotherapist will also treat any bladder overactivity or bowel dysfunction, ensure appropriate return to general exercise and provide education, guidance and support throughout the journey on the return to continence.

### Evolution of physiotherapy management

Physiotherapy management of post-prostatectomy incontinence has evolved over the past 2 decades. In the past, men attended physiotherapy after radical prostatectomy for pelvic floor exercises, the pelvic floor muscles were assessed via a digital rectal examination, and the training protocols used were predominately strength based. However, as our understanding of the male continence mechanism has evolved, physiotherapy management programs have continued to improve. There is now greater emphasis on pre-operative pelvic floor muscle training, as the evidence shows this is most beneficial [2]. This is thought to be due to enhanced motor skill learning before surgery, as after surgery muscle inhibition is present due to pain or inflammation. Physiotherapists have also evolved training programs to include functional pelvic floor exercises. Techniques to assess the pelvic floor have also progressed, with the use of transperineal ultrasound emerging in research and practice.

In the past, there was controversy about the efficacy of pelvic floor exercises in the treatment of post-prostatectomy incontinence, with some studies finding it beneficial, and some finding it not beneficial [7]. One key factor that needs to be critically analysed is the way that pelvic floor muscle exercises are taught. A common feature in studies finding no benefit of pelvic floor muscle training is a focus on anal sphincter activation, for example using verbal cues such as 'tighten around the anus', or the intensive use of anal biofeedback [8-10]. Conversely, studies that found pelvic floor muscle training effective, had minimal or no emphasis on the anal sphincter [11-13]. In an Australian study in 2015, Stafford and co-authors found that verbal cues with an anal focus create higher external anal sphincter activity, and verbal cues focusing on shortening the penis or flow stopping create the highest urethral pressure, hence being the most preferred [14]. It is likely that pelvic floor muscle training programs focusing on activation of the levator ani and urethral sphincter, rather than the anal sphincter, will continue to see a further improvement in the recovery rate of continence and degree of incontinence after surgery.

You can find a pelvic floor physiotherapist in your area via www.cfaphysios.com.au or www.physiotherapy.asn.au under 'Find A Physio'

**References**

**[1]** Ficarra V, Novara G, Rosen RC, et al. European Urology. 2012 Sep: 62:405-17 **[2]** Anderson C, Omar M, Campbell S, Hunter K, Cody J, Glazener C. Conservative management for postprostatectomy urinary incontinence (Review). Cochrane Database Syst Rev. 2015 **[3]** Haga N, Ogawa S, Yabe M, et al. Urology. 2014: 84:642-9 **[4]** Thiruchelvam N, Cruz F, Kirby M, Tubaro A, Chapple C, Sievert K. A review of detrusor overactivity and the overactive bladder after radical prostate cancer treatment. BJU international. 2015 **[5]** Neumann P, Panuccio C, Fuller A, Sutherland P. Australian and New Zealand Continence Journal. 2015: 21:84-8 **[6]** Stafford RE, Ashton-Miller JA, Constantinou CE, Hodges PW. Urology. 2013: 81:685-9 **[7]** Campbell SE, Glazener C, Hunter KF, Cody JD, Moore KN. Conservative management for postprostatectomy urinary incontinence. The Cochrane Library. 2012 **[8]** Dijkstra-Eshuis J, Van den Bos TW, Splinter R, et al. Neurourology and urodynamics. 2015: 34:144-50 **[9]** Geraerts I, Van Poppel H, Devoogdt N, et al. European urology. 2013: 64:766-72 **[10]** Glazener C, Boachie C, Buckley B, et al. The Lancet. 2011: 378:328-37 **[11]** Burgio KL, Goode PS, Urban DA, et al. The Journal of urology. 2006: 175:196-201 **[12]** Centemero A, Rigatti L, Giraudo D, et al. European urology. 2010: 57:1039-44 **[13]** Tienforti D, Sacco E, Marangi F, et al. BJU international. 2012: 110:1004-10 **[14]** Stafford RE, Ashton-Miller JA, Constantinou C, Coughlin G, Lutton NJ, Hodges PW. Pattern of activation of pelvic floor muscles in men differs with verbal instructions. Neurourology and urodynamics. 2015

# Evaluation and management of incontinence

## after treatment for prostate cancer

**Dr James F. Borin**
Department of Urology, New York University
MD New York University

The treatment options for localized prostate cancer have been expanding over the past decade. Newer treatments have not been shown to improve cancer control; however, there is some evidence of fewer side effects for the common complications of urinary incontinence and/or erectile dysfunction. These treatments include robotic prostatectomy, whole-gland and focal cryotherapy, high-intensity focused ultrasound and focal laser therapy as well as several types of experimental focal therapy. However, despite improvements in outcomes and a slow migration toward centralization of care, post-treatment incontinence remains a problem for a significant number of men.

Any examination into post-treatment incontinence must begin with the realization that not all men are continent prior to treatment. Men with large prostates and bladder outlet obstruction can suffer from post-void dribbling; in addition, overactive bladder can cause urge incontinence. In a U.S. national sample of men above age 50, 6.4% reported incontinence, but this number increased with age >70, BMI >30 and was significantly higher (21%) in men with moderate or severe depression [1].

Radical prostatectomy can improve some of the lower urinary tract symptoms associated with an enlarged prostate while radiation may temporarily worsen these symptoms. In the long term, radical prostatectomy is associated with a higher risk of urinary incontinence than radiation, but both of these treatments can cause incontinence. This has been attributed to urethral sphincter injury and to bladder dysfunction, for example detrusor overactivity or poor compliance.

One recent trial in Sweden evaluated 2431 men who underwent either robotic prostatectomy or open radical retropubic prostatectomy [2]. This was a prospective, controlled but non-randomized comparison trial. At 12 months, approximately 20% of men in each group had urinary incontinence as measured by needing to change pads at least once in 24 hours. About 6% of men had moderate incontinence—2-3 pads/day. Severe incontinence, >3 pads/day, was rarely reported by only 2-3% of patients. Of interest, however, was that while the primary end-point of incontinence was measured as the pad-free rate, 35% of men in each group reported daytime leakage, and about 56% of men experienced incontinence as defined as neither leak-free nor pad-free.

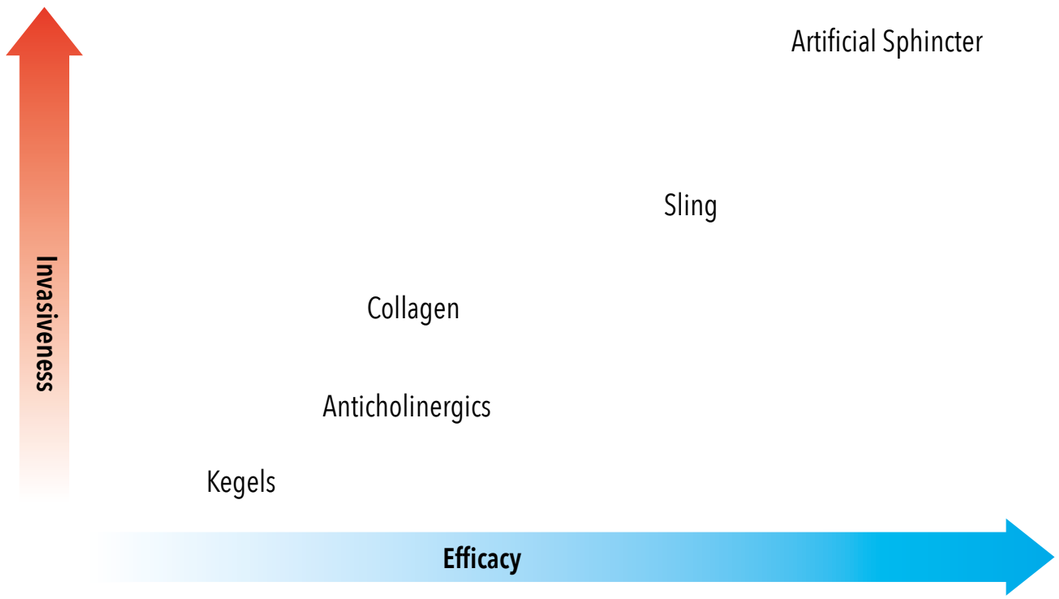



**Figure 1:** Therapeutic options for post-treatment urinary incontinence in men with prostate cancer.



### Patient Evaluation

Evaluation of patients with post-treatment incontinence focuses on elucidating the severity of incontinence as well as potentially reversible causes. Primary evaluation is made up of: patient history, physical examination, urinalysis, postvoid residual, voiding diary, and pad test [3]. More specialized examination, such as cystourethroscopy and urodynamics may be required if conservative measures fail [4].

There are several treatment options for addressing post-treatment incontinence which are based on the severity of the incontinence. For mild incontinence, noninvasive therapeutic strategies include conservative treatment, Kegel exercises with or without biofeedback, penile clamp and medication. Surgical intervention includes collagen injection, sling, or artificial urinary sphincter. [Figure 1]

### Non-invasive Therapy

A recent randomized controlled trial of patient-centered interventions randomized 279 patients to 3 groups: 1) Biofeedback pelvic floor muscle exercise (PFME) plus a support group; 2) Biofeedback PFME plus telephone contact; 3) Usual care [5]. Both biofeedback groups had a lower frequency of daily urinary leakage than the usual care group at 3 months but not at 6 months. Overall both biofeedback groups reported less symptom severity ($p \leq 0.001$) and fewer incontinence issues ($p \leq 0.01$) than the usual care group at 6 months. For patients with overactive bladder, either demonstrated by urodynamics or suggested by symptoms, antimuscarinic pharmacologic therapy may be beneficial [6].

### Surgical Therapy

Because incontinence generally improves over the first 6-12 months after treatment, surgical intervention is generally not indicated for at least a year after prostate cancer treatment [6]. The mainstay of surgical therapy is the male sling and the artificial urinary sphincter. Collagen injections do not seem to deliver long-term efficacy and have largely been abandoned.

The degree of preoperative incontinence affects cure rates in sling surgery. Higher success rates for slings are seen for men with 24h pad weight < 400g which translates into 2 or fewer pads used in 24 hours [7]. The gold standard for post-prostatectomy incontinence surgery is the artificial urinary sphincter. Most studies demonstrate overall success rates > 80% which is variably defined as pad use of 0-1 pads/day or a 50% improvement in pad usage [8]. Mean infection and erosion rates are about 8.5% while device failure ranges from 2-14%. Overall, this translates into a 26% reoperation rate [9].

### New Directions

As more patients survive and thrive after cancer treatment, a greater emphasis on survivorship is emerging. The ProRehab study sought to evaluate the effects of a multimodal exercise program on physical fitness, quality of life and treatment-related adverse effects in patients following radical prostatectomy [10]. The trial involved a 15 month supervised exercise program post-prostatectomy of 60 min/week of aerobic, resistance and pelvic floor exercises as well as games and exercises that promote flexibility, coordination, relaxation skills, cognitive abilities, cooperation, and communication. There were no differences between the intervention and control groups in recovery of erectile function or physical activity levels. However, while both groups showed improvement over time in urinary function, there was a significant difference in the urinary symptom score ($p = .027$) favouring the intervention group. Finally, and perhaps of most importance, there were significant intervention-related improvements in physical fitness, urinary incontinence, physical, emotional, and social functioning, as well as further disease and treatment related side effects (dyspnea, urinary, and bowel symptoms) compared to the control group.

#### References

**[1]** Wu JM, Matthews CA, Vaughan CP, Markland AD. Journal of the American Geriatrics Society. 2015: 63:947-53 **[2]** Haglind E, Carlsson S, Stranne J, et al. European Urology. 2015: 68:216-25 **[3]** Radomski SB. Practical evaluation of post-prostatectomy incontinence. Canadian Urological Association Journal. 2013: 7:S186 **[4]** Bauer RM, Gozzi C, Hübner W, et al. European urology. 2011: 59:985-96 **[5]** Zhang AY, Bodner DR, Fu AZ, et al. Effects of Patient Centered Interventions on Persistent Urinary Incontinence after Prostate Cancer Treatment: A Randomized, Controlled Trial. The Journal of urology. 2015 **[6]** Lucas MG, Bosch RJ, Burkhard FC, et al. European Urology. 2012: 62:1130-42 **[7]** Serra AC, Folkersma LR, Domínguez-Escrig JL, Gómez-Ferrer Á, Rubio-Briones J, Narbón ES. Urology. 2013: 81:1034-9 **[8]** Van Bruwaene S, De Ridder D, van der Aa F. BJU international. 2015: 116:330-42 **[9]** Van der Aa F, Drake MJ, Kasyan GR, Petrolekas A, Cornu J-N, Group YAUFU. European urology. 2013: 63:681-9 **[10]** Zopf EM, Bloch W, Machtens S, et al. Integrative cancer therapies. 2015: 14:409-18

# Suicide risk after a prostate cancer diagnosis

**A/Prof David Smith**
Cancer Council NSW

**Prof Suzanne Chambers**
Menzies Health Institute Queensland
Griffith University

## Introduction

Australian men diagnosed with prostate cancer face a higher risk of suicide than their prostate cancer free peers. A recent Cancer Council NSW study found a 70% higher risk in prostate cancer patients. Those at greatest risk were men with locally advanced disease, single men and those living in major cities. Acknowledging this risk exists, instigating a system for early identification of vulnerable men and then implementing referral to appropriate services or programs can reduce the heavy burden that suicide has on this group of men.

## Background

Suicide is estimated to account for over 800,000 deaths annually worldwide [1]. While the trend in rates in Australia has fluctuated since records were first kept in 1920, suicide currently accounts for about 2,500 deaths annually, making it the 14th leading cause of all deaths [2]. Three quarters of suicides occur in males and while the most at risk group are those aged 25-54 years, older men, are also at risk. It is estimated that over 70% of suicides in those aged 60 years and over are related to a physical illness [3]. Unconfirmed suicides attributed to accidents or other causes and suicide attempts only add to the mortality and morbidity associated with self-harm.

## International Evidence Of Higher Risks

Suicide rates are higher in patients previously diagnosed with cancer than in the general population. Lung, oropharyngeal, breast and pancreatic cancers have previously been associated with high rates of suicide internationally [3]. Western Australian cancer patients were shown to have a 60% higher risk of suicide after diagnosis compared to matched population rates [4]. The long term risks of suicide after a diagnosis of prostate cancer varied from between about 4 times higher in men from Florida [5] to 2.6 times higher in Swedish men [6].

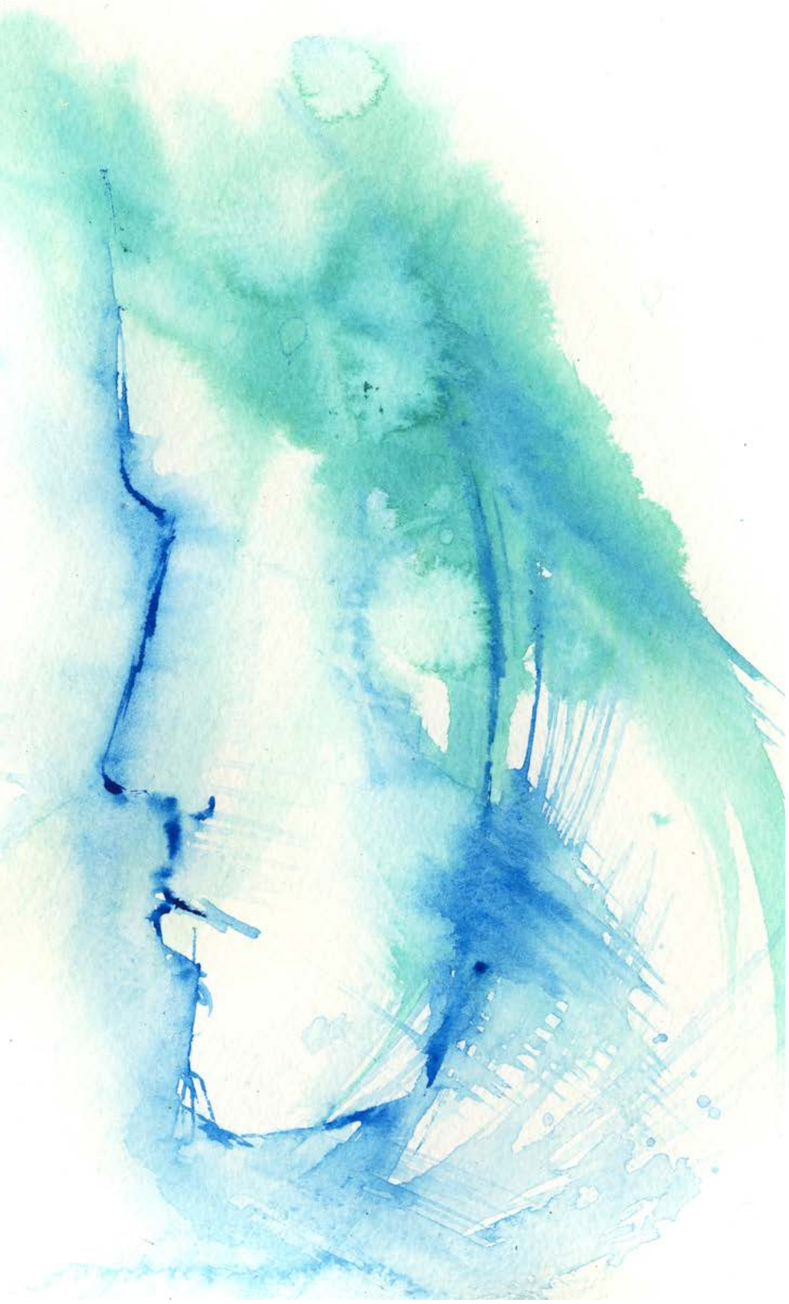
Having visited a physician one month prior to death and a recent diagnosis of depression have both been found to raise risk of suicide in men with prostate cancer [5].

A critical period shortly after diagnosis has been identified, with men at over 8 times at risk of suicide compared to cancer free men within one-week of diagnosis [6]. A further study demonstrated that risk was not only high in men with high-risk disease, but also in men with low-risk disease within the first six months of diagnosis [7]. Analyses of the USA SEER data has shown patients who were recommended treatment but did not receive it or refused it had a 32% higher risk of suicide than men with other cancers [8].

Clinical depression associated with a cancer diagnosis, distress associated with difficult treatment decisions, or longer-term treatment-related adverse effects such as urinary incontinence and erectile dysfunction that impair quality of life may contribute to heightened risks during the disease course. Prostate cancer patients can experience negative intrusive thoughts and significant declines in physical, mental, and social aspects of their lives, particularly within the first six months of diagnosis. In a large Australian population based study 54% of men with prostate cancer expressed some level of unmet psychological need, and one in five men had moderate to high unmet need for support about uncertainty about the future [9].

## Recent Cancer Council NSW Research

With this background it is therefore little surprise that a recent population-wide linkage study in New South Wales identified that men diagnosed with prostate cancer were at a 70% higher risk of death from suicide than age-matched men from the general population [10]. The study was based on 52,000 NSW men diagnosed with prostate cancer between 1997 and 2007. A total of 49 suicides were observed in the patient population. The highest risk occurred in men with locally advanced disease, men living in major cities and those who were single, divorced, separated or widowed. The majority of suicides occurred within six months of diagnosis. Data on the existence of pre-existing psychological or psychiatric illness were not available. Evidence that men are more likely to experience neuro-cognitive and mood function changes, depression, lack of energy and reduced vigour when treated with androgen deprivation therapy may account for some of the higher risk in men with locally advanced disease.



## What Should Be Done?

Although the absolute risks of suicide in Australian men with prostate cancer are modest, in relative terms the increased relative risk is alarming. Every suicide leaves a trail of destruction in its wake. Not only for families and friends but also emergency services workers and the health professionals who provide care and support for those affected. Our findings reflect only the tip of the iceberg in the spectrum of psychological stress that men with prostate cancer experience after diagnosis.

How we identify these vulnerable men and provide them with a practical toolkit of measures to reduce this risk is of high priority.

Identification of those at risk as early as possible in the diagnostic pathway to ensure assessment and appropriate referral to psychosocial care should be an integral part of the patients care plan [11] and indeed has been accepted as a standard of care internationally [12]. The use of a brief, simple, no cost, Distress Thermometer has been recommended with a prostate cancer specific version well validated in men with prostate cancer [13] and available from the Prostate Cancer Foundation of Australia. (http://www.prostate.org.au/media/458256/Prostate_Cancer_Distress_Form.pdf)

If anxiety, distress or depression are suspected or identified, a number of interventions can be activated depending on the needs of the man. These can include referral to appropriate care, peer support, exercise programs or group-based interventions [14].

## Conclusion

No man with prostate cancer should suffer alone. The most severe outcome associated with the distress of diagnosis or treatment is arguably suicide. Reducing the risk of suicide after prostate cancer is challenging but a systematic approach to identification and tailoring interventions to an individual can and will make a difference.

**References**

**[1]** World Health Organisation. WHO Mental Health Suicide Data. 2015 [cited 2015 Sept 24]; Available from: http://www.who.int/mental_health/prevention/suicide/suicideprevent/en/ **[2]** Australian Bureau of Statistics. Causes of Death, Australia, 2013. [cited 2015 Sept 24]; Available from: http://www.abs.gov.au/ausstats/abs@.nsf/mf/3303.0 **[3]** Misono S, Weiss NS, Fann JR, Redman M, Yueh B. Journal of Clinical Oncology. 2008: 26:4731-8 **[4]** Dormer NR, McCaul KA, Kristjanson LJ. Medical Journal of Australia. 2008: 188:140-3 **[5]** Llorente MD, Burke M, Gregory GR, et al. The American Journal of Geriatric Psychiatry. 2005: 13:195-201 **[6]** Fall K, Fang F, Mucci LA, et al. PLoS medicine. 2009: 6:1365 **[7]** Carlsson S, Sandin F, Fall K, et al. European journal of cancer. 2013: 49:1588-99 **[8]** Dalela D, Krishna N, Okwara J, et al. Suicide and accidental deaths among patients with non-metastatic prostate cancer. BJU international. 2015 **[9]** Smith DP, Supramaniam R, King MT, Ward J, Berry M, Armstrong BK. Journal of Clinical Oncology. 2007: 25:2560-6 **[10]** Smith DP, Bang A, Egger S, O'Connell D. Risk of suicide after a prostate cancer diagnosis: a population-wide study in New South Wales (NSW) Australia. BJU international. 2015: 116, Special Issue: Abstracts of the 2nd Prostate Cancer World Congress, Supplement S1:1-62 **[11]** Chambers S, Dunn J, Lazenby M, et al. ProsCare: A psychological care model for men with prostate cancer. Sydney: Prostate Cancer Foundation of Australia and Griffith University, Australia. 2013: **[12]** Holland J, Watson M, Dunn J. Psycho-Oncology. 2011: 20:677-80 **[13]** Chambers SK, Zajdlewicz L, Youlden DR, Holland JC, Dunn J. Psycho-Oncology. 2014: 23:195-203 **[14]** Chambers SK, Pinnock C, Lepore SJ, Hughes S, O'Connell DL. Patient education and counseling. 2011: 85:e75-e88

# How technology can help
## patients and clinicians

**Dr Addie Wootten**
Clinical Psychologist
Smiling Mind

We're currently living in world that is more connected than ever before. We're engaged with technology almost 24 hours a day. Information is at our fingertips whenever we need it and we can get answers to all our questions at the click of a button. So how do we harness the power of technology to improve education, awareness, clinical care, patient wellbeing and clinician knowledge? Here's a whirlwind tour of the latest and greatest technological advancements in prostate cancer.

**Online patient information and education**

www.PROSTMATE.org.au was developed by Australian Prostate Cancer Research (APCR) in collaboration with leading prostate cancer experts across Australia as a tool to deliver tailored information, tools to track treatments and test results and access to self-help programs as well as tele-health consultations with prostate cancer nurses. This is a free portal designed to support the whole family and anyone affected by prostate cancer can get involved. The nice thing about PROSTMATE is that it used technology to tailor information to minimize patient confusion.

If patients or their family are looking for the latest guidelines summarizing the evidence around management of cancer they can look at the Cancer Council Australia Wiki Platform. This platform can also be very useful for clinicians. This platform has a guideline on the management of locally advanced and metatstatic prostate cancer (http://wiki.cancer.org.au/australia/Guidelines:Prostate_cancer/Management/Locally_advanced_and_metastatic) and a draft guideline is currently open for public review about PSA testing and management of early prostate cancer (http://wiki.cancer.org.au/australia/Guidelines:PSA_testing).

Other information can be found on the Prostate Cancer Foundation of Australia website - http://www.prostate.org.au/awareness/general-information/what-you-need-to-know-about-prostate-cancer/

**Online patient wellbeing programs and their families**

Comprehensive wellbeing programs online are growing but very few exist that have been specifically designed for prostate cancer. www.MyRoadAhead.org is an online psychological intervention that we have been evaluating as part of our research program and we have found some very promising results. This 6-module psychological intervention is designed to support men in processing the emotional, physical and relationship impact of localized prostate cancer. Our research results indicate that this program significantly improved men's mood, their sexual satisfaction and their masculine self-esteem.

We've also developed an online psychological intervention for partners of men with prostate cancer who would like to reduce their stress, understand prostate cancer and the impact it can have on themselves and their partner and enhance their relationship and communication: www.partners.prostmate.org.au

Dr Leslie Schover from MD Anderson in the US has developed online counseling program for men with sexual difficulties following cancer. This program provides expert information, self-help tools and ways for partners to get involved too. www.hardtimessexandcancer.com

www.rekindleonline.org.au is another program that is currently undergoing research evaluation. Rekindle is a private, personalised online resource that addresses sexual concerns for all adults affected by cancer and while it was not specifically developed for prostate cancer it could offer some very important support to men experiencing significant sexual difficulties after prostate cancer treatment.

Mindfulness meditation has also been shown to be an effective intervention for men with prostate cancer, and it's also a very useful for practice for clinicians to use as well. However, finding someone to teach you mindfulness meditation can sometimes be difficult and as a result many people are turning to technology to learn how to practice Mindfulness. www.SmilingMind.com.au offers a free mindfulness App that offers mindfulness meditation programs for people of any age and is a great tool to help you get started with Mindfulness.

**Online resources for clinicians**

While there are many association guidelines available online (EAU, AUA, NCCN etc) there are also some new and very interesting online resources that are designed to improve the care we as clinicians provide to our patients.

A group of urologists and other clinicians have also started using twitter for an international journal club. It's an asynchronous chat over 48hrs on the first Sunday/Monday of the month. Use the hashtag #urojc for discussions and follow @iurojc to get involved. With almost 4,000 followers it's a good opportunity to discuss the latest papers with the experts across the world.

# Management of lower urinary tract symptoms
## caused by benign prostatic hyperplasia

**Paul Anderson**
Department of Urology,
The Royal Melbourne Hospital

Lower urinary tract symptoms (LUTS) caused by benign prostatic hyperplasia (BPH) are a common reason for men to seek medical attention. Some men have severe symptoms affecting their quality of life, while others have mild symptoms but seek medial advice fearing that they may be indicative of prostate cancer.

A spectrum of effective medical and surgical management options are available. Men with milder symptoms can frequently be managed with medical therapy, often appropriately initiated in general practice. Alpha-blockers (such as prazosin, alfuzosin, terazosin and tamsulosin) are still first-line therapy and work by relaxing smooth muscle at the bladder neck to reduce bladder outlet resistance. They all work rapidly and have similar efficacy, increasing flow rated by 20-25% and decreasing symptom scores (IPSS) by 30-40% [1]. For those that do not respond, there has been increasing interest in combined medical therapy.

Patients with large prostate glands (>40cm$^3$) and greater than average PSA levels (>1.4ng/ml) may benefit from the addition of a 5 alpha-reductase inhibior (5-ARI). These agents (such as finasteride or dutateride) block the conversion of testosterone to dihydrotestosterone and induce apoptosis in prostate epithelial cells leading to a reduction in prostate volume of 18-28% after 6-12 months [2]. In suitable patients this leads to greater efficacy than monotherapy [3], however, at a cost of increased rates of erectile dysfunction and some ongoing concern about an increased incidence of high grade prostate cancer [4]. As such, current prescribing recommendations call for specialist urological assessment prior to commencing 5-ARI therapy.

Recently, Tardalifil, a phosphodiesterise type-5 inhibitor (PDE-5), more commonly prescribed for the treatment of erectile dysfunction, has been shown to improve LUTS, but not flow rates [5]. This effect may be of benefit to those patients suffering from both conditions, but is probably not a cost effective therapy.

For men with more severe symptoms as well as those who cannot tolerate, or would prefer not to have oral therapy, surgery provides a very effective, definitive treatment for LUTS due to BPH. Transurethral resection of the prostate (TURP) remains the gold standard for surgical therapy. A meta-analysis of this widely available and reproducible technique showed a 162% improvement in flow rates and 70% reduction in symptom scores at 5 years [6]. Despite these results, there have been many competing technologies trying to achieve better outcomes.

Laser technologies, such as Greenlight photovaporisation of the prostate (GL-PVP) and Holmium laser enucleation of the prostate (HoLEP) have become increasingly more widely available. Both techniques result in outcomes similar to TURP but with reduced catheterization times and blood loss [7, 8]. Laser technologies are particularly useful in patients on anticoagulation, co-morbidity or with large prostate glands. Their uptake had been limited by the capital cost and skill dissemination, but now these technologies are quite widely available.

Another promising surgical therapy is Prostate Aquablation, an image-guided, robot controlled endoscopic therapy that uses a high-pressure jet of room temperature saline to quickly and accurately resect prostate tissue. Early studies (Phase II) carried out at our institution have been promising showing a 148% improvement in flow rate and 77% reduction in symptom scores at 12 months follow up [9]. All participants were discharged the next day, with patients noting minimal post-operative discomfort. We are currently recruiting patients for a Phase III study randomizing Aquablation to TURP.

Our dedicated LUTS clinic at the APCR Prostate Cancer Centre offers rapid patient assessment with on-site access to flowmetry, ultrasound, urodynamics and flexible cystoscopy, as well as the opportunity for patients to participate in the clinical trials evaluating the latest novel therapies. Referral information can be found at our website www.prostatecentre.org.au.

**References**

**[1]** Djavan B, Chapple C, Milani S, Marberger M. Urology. 2004: 64:1081-8 **[2]** Rittmaster RS, Norman RW, Thomas LN, Rowden G. The Journal of Clinical Endocrinology & Metabolism. 1996: 81:814-9 **[3]** McConnell JD, Roehrborn CG, Bautista OM, et al. New England Journal of Medicine. 2003: 349:2387-98 **[4]** Thompson Jr IM, Goodman PJ, Tangen CM, et al. New England Journal of Medicine. 2013: 369:603-10 **[5]** Gacci M, Corona G, Salvi M, et al. European urology. 2012: 61:994-1003 **[6]** Ahyai SA, Gilling P, Kaplan SA, et al. European urology. 2010: 58:384-97 **[7]** Tan A, Liao C, Mo Z, Cao Y. British Journal of Surgery. 2007: 94:1201-8 **[8]** Bachmann A, Tubaro A, Barber N, et al. European urology. 2014: 65:931-42 **[9]** Gilling P, Tan A, Anderson P. PD5-02 multicenter experience of a novel treatment for bph: Aquablation–image guided robot-assisted water jet ablation of the prostate. The Journal of Urology. 2015: 193:e92-e3