Contents

2. Editorial
   Prof Anthony J Costello

3. Melanoma in Men: Survival Disparity and Closing The Gap
   Dr Rithva Vyas

5. Risk Prediction Tools in Guiding The Management of Prostate Cancer
   A/Prof Monique J. Roobol

   Dr Edmond Kwan & Dr Ben Tran

9. A Synopsis of Recent Publications in Prostate Cancer
   Dr Homi Zargar

11. Helping Men Adhere to Sexual Rehabilitation following Prostate Cancer Surgery:
    Changing the Conversation
   Dr Christian J. Nelson

13. It’s Not Over Until It’s over: Finding Meaning in the Face of Mortality
    Max Rutherford

15. Extinguishing the Smoking Gun in Bladder Cancer
    A/Prof Peter Black

19. Helping Smokers Quit: Removing Barriers
    Dr Sarah White

21. Health Journalism
    Jill Margo

Editorial

Prostate cancer screening remains a hot topic. Most recently, the NHMRC Guideline for GPs on screening and prostate cancer have offered a mildly positive set of recommendations, which differs from uniformly negative messaging from many other groups both in Australia and internationally. Although NHMRC permit limited PSA testing they advise GPs that they can abandon the DRE. I disagree fairly strongly with this advice as many prostate cancers are detected by DRE. My 97 year-old GP father taught me as a medical student the importance of male DRE examination “there is a sovereign in every rectum” was his advice. In summary, for GPs my advice regarding PSA testing simply put is “Men over 40 who are interested in their prostate cancer risk should be offered a PSA test and a careful DRE.”

PSA alone is imperfect in screening and risk stratification. So, when it comes to specialist review, many urologists are now incorporating radiographic imaging of the prostate (multi-parametric MRI) prior to recommending a prostate biopsy. In this edition of The Manual, Associate Professor Roobol describes the value of risk stratification tools, which enable us to undertake multivariable analysis for individual patients in order to improve clinical decision-making in this complex area.

The introduction of genomics and cancer gene sequencing heralds a very exciting improvement in our ability to treat metastatic prostate cancer. Whereas before 2000 we had only castration as monotherapy for metastatic prostate cancer, we now have multiple new treatments with the ability to alter the natural lethal history of systemic cancer. We now see significant life extension in many patients using our new weaponry. In particular, in the area of systemic treatment for prostate cancer, we are seeing a changing role for chemotherapy, the evidence for which is reviewed in this edition.

President Obama announced recently “The MOONSHOT” against cancer. This billion dollar initiative looks to bring the stakeholders, oncologists, health insurers, pharmaceutical companies and banks together to incorporate Immunotherapy into the existing cancer therapy guided by genomic information in individual cancer patients. This concept, described as Precision Oncology or Personalised Medicine, will dramatically shape the way cancer care is delivered.

These issues will be discussed at the upcoming National Prostate Cancer Conference in late August 2016 at the Melbourne Convention Centre. Thirty international experts will join around 900 local urologists, oncologists, scientists, general practitioners, nurses and allied health practitioners in holistic discussions of all aspects of prostate cancer care.

While as clinicians we are committed to our own continuing education, it is essential that we realise our patients will also be seeking their own ‘education’. In this edition, Jill Margo provides us with an insight into the important area of health-journalism from the journalist’s perspective.

The new Prostate Cancer Clinic in North Melbourne next to The Royal Melbourne Hospital is expanding rapidly. The clinic offers rapid access for all men, regardless of health insurance status, to care for all aspects around risk assessment, diagnosis and treatment of prostate cancer. It provides a true one stop prostate shop, where patients can usually be seen within two weeks. Clinic staff include Urologists, Radiation Oncologists, Medical Oncologists, Nurses, Physiotherapists, Exercise Physiologists, Endocrinologists and Cardiologists. The Clinic is the first of its kind in this country and could serve as a template for similar clinics elsewhere.

In late 2016, a full imaging service will be in place with MRI, CT, US and PET scanning available. We also provide immediate access for cystoscopy and urodynamics evaluation. The centre runs in conjunction with the Department of Urology at The Royal Melbourne Hospital under my direct supervision. The clinic cares for men in a timely fashion to meet the unique needs of gender specific men’s health. Men have really been short-changed for years in the lack of provision of appropriate men’s health clinics. Please feel free to visit us and see the Clinic in action.

Prof Tony Costello
Melanoma in Men: Survival Disparity and Closing the Gap

Dr Ritva Vyas
Dermatologist

The lifetime risk of developing melanoma is higher in men (1.72%) compared to women (1.22%) [1]. Population based studies on melanoma have consistently demonstrated reduced survival in men, with women having an adjusted survival advantage of approximately 30% in stage I/II melanoma and 15-20% survival advantage in stage III/IV melanoma [2,3]. In Australian men, there is in fact a trend of increasing mortality from melanoma in excess of the increasing incidence. While gender related differences of survival in melanoma are well established, evidence-based verification of the underlying mechanisms remains challenging.

There are several gender specific physiologic differences in the skin, any number of which could influence the tumor microenvironment, including skin thickness and color, response to sex hormones, susceptibility to UV-induced immunosuppression and mechanisms of oxidative stress [1]. There are sex differences in the shaping of T-cell immunity to melanoma with higher numbers of tumor associated antigens (TAA) detected in women [4]. Estrogens exert their effects on skin via estrogen receptor beta and are known to improve epidermal thickness, wound healing, photo-aging and inflammatory disorders [5]. Hormonal influences on melanoma have been studied in the laboratory, and there is some suggestion that loss of estrogen receptor beta may play a part in melanoma progression.

There are significant clinico-pathological differences in the presentation of melanoma in men who present with thicker primary melanomas, with higher rates of ulceration, and metastases. The most common site of developing melanoma in men is on the dorsal trunk which can be a difficult area to self examine compared to women who are more likely to develop melanoma on the legs. Nodular melanoma, which is an aggressive subtype of cutaneous melanoma, occurs more often in men. Recurrence in men is more likely to be with metastases whereas women have more local recurrence and intrasternal metastases.

In several studies, gender has been found to be an independent predictor of survival even after adjusting for various clinical and pathological factors including age, thickness, mitotic rate, ulceration and site. There may be several sociological and behavioral factors that increase risk of melanoma in men. Although basic skin health knowledge is similar between genders, lower numbers of men practice sun protection and adhere to screening recommendations [6]. Men are less likely to self-detect their melanomas and make fewer visits to health-care providers which may lead to thicker melanomas at time of diagnosis. A Swedish study found that in all age groups of men there was a later stage at diagnosis and worse survival in men who lived alone versus men living with a partner [7].

Strategies to optimise melanoma outcomes in men should encompass prevention, diagnosis, management and future research. Preventative and educational initiatives on sun protection and melanoma awareness should be tailored to reach the target audience so they can have maximal impact. This is exemplified by the campaign against tanning beds targeted at changing behaviors in young women.

As the major determinant of survival is depth of invasion, strides towards early detection of melanoma will be key. It has been estimated that reducing sex inequalities in stage at diagnosis would result in a 5% reduction in deaths within 5 years of a melanoma diagnosis [8].

Skin self-examination has been shown to increase the detection of thin melanoma [9]. A case-control study in the United States for reduced risk of melanoma mortality (OR 0.37, 95% CI = 0.16-0.84) in people who examined their own skin [10].

In high risk patients will benefit from education on skin self-examination and performing self-examination at regular intervals with interval period determined by their individual risk.

Descriptive studies have demonstrated that melanomas detected during a screening examination are thinner than those that present in other ways, however currently there is insufficient evidence to recommend population-based, whole-body skin cancer screening. In a large skin cancer screening study undertaken in the United States, the overall yield of melanoma was 1.5 per 1000 screenings compared with a yield of 2.6 per 1000 screenings among men age >= 50 years. The yield was improved further for men age >= 50 years who reported either a changing mole (6.6 per 1000 screenings) or skin types I and II (burns easily, never tans, or tans only with difficulty) (3.8 per 1000 screenings) [11]. Therefore it seems that consideration should be given to opportunistic whole-body skin cancer screening for men over the age of 50, especially if they have additional risk factors.

Dermoscopy has been shown to increase the accuracy of melanoma diagnosis as compared to benign pigmented lesions in the hands of expert users and is rapidly becoming the standard of care for assessment of pigmented lesions. Total body photography can also aid in early melanoma detection in selected patients including those with history of melanoma, multiple melanocytic naevi and atypical melanocytic naevi. For all patients, once melanoma diagnosis is confirmed by histology, timely and coordinated clinical care is provided preferably in a multidisciplinary care setting. Optimal cutaneous management after definitive treatment of primary melanoma should include education, surveillance for melanoma recurrence, detection of subsequent melanomas, detection of non-melanoma skin cancers and in patients with advanced melanoma management, of cutaneous side effects of systemic therapy.

Prospective studies with selected screening and its effects on mortality are needed to provide the level of evidence required for formulation of clinical practice guidelines. Research should continue toward new technologies that can potentially aid in early melanoma detection including reflectance confocal microscopy, multispectral digital dermoscopy and infrared imaging among others. As the search for biomarkers in melanoma continues, sex-stratification in biomarker studies could potentially add valuable information [12]. Future clinical drug trials should be designed to detect differences in response rates between genders. Insights into gene expression profiling, epigenetics and the tumor microenvironment may further uncover sex differences in melanoma and aid in developing more directed therapies.

References

In figure 1, the relation between PSA level and probability of finding PCa on TRUS guided biopsy is shown. Here we see that with increasing the PSA cut-off level the percentage of benign prostate biopsies (i.e. no PCa detected at this point in time, hence an unnecessary biopsy) is decreasing. However, the percentage of biopsy detectable prostate cancers that are not being detected also increases in an almost similar rate. The latter could be regarded as positive if it concerned only potentially indolent prostate cancer but unfortunately that is not the case. By increasing the PSA cut-off level to prompt prostate biopsy also potentially life threatening prostate cancers are being missed. This fact has driven researchers to find ways to increase the predictive capability of the serum PSA test by adding more relevant clinical information into decision making.

When more information (often called predictors like e.g. age or outcome of the digital rectal examination (DRE)) is available when deciding to perform a prostate biopsy, it is not workable to define different thresholds values for all individual predictors. The predictive information of each of the predictors is bundled into a probability (risk) score that is calculated using risk prediction tools or nomograms. The probability scores can subsequently be used to define a certain threshold value that prompts further action when surpassed.

A perfect risk stratification tool allows us to distinguish those men without PCa from those with a potentially indolent or a potentially aggressive PCa. Figure 2 shows the hypothetical result of perfect risk stratification (1), a risk stratification based on PSA (2) and finally a risk stratification based on a multivariate prediction tool (3).

This so-called multivariate risk based approach has proven to be superior in prostate cancer detection as compared to decision making on the basis of the result of a PSA test (or combination with outcome of DRE) [5]. In table 1, we see the effect of the number of unnecessary prostate biopsies avoided and prostate cancer diagnoses missed with raising the PSA cut-off value, versus adding a risk based cut-off value as calculated using the Rotterdam Prostate Cancer Risk Calculator, to the commonly applied PSA cut-off value of 3.0 ng/ml [6]. While number of avoided biopsies is comparable there is a remarkable difference in PCa diagnosed.

This is just one example of a multivariate prediction tool for prostate biopsy outcome. There are many more tools developed [7] and while e.g. the EAU guidelines and the Melbourne Consensus Statement recommend the use of these tools in decision making they understandably refrain from recommending one particular tool [8,9].

Despite numerous publications showing risk prediction tools outperform decision making, as compared to the PSA test alone, they are not frequently used in daily clinical practice for different reasons. The basic "problem" is that there are many tools available, that they originate from different, population-based, or clinical cohorts and are not often compared head-to-head, or when this is done, they perform very differently. This all affects trustworthiness and as such seriously hampers clinical implementation.

Why, despite uncertainties regarding which prediction tool to use, is it still advisable to take into account a multivariate risk assessment? If we at look and review meta-analysis on the performance of these tools, there is one observation and one remark that are crucial. First of all, as said before, despite the fact that the different tools provide different risk outcomes when applied to one patient, they all outperform a decision to proceed to biopsy on the basis of a PSA test alone [5]. Obviously and justly, all clinicians would reply that they never base the decision to biopsy on the outcome of a PSA test alone. They know their patient, also take into account other factors and make a decision based on their clinical expertise. This is daily clinical practice and totally acceptable. However, there are patients that fall in the so-called ‘grey area’ where a clinician can have doubts on whether to proceed to biopsy or not. It is exactly in those men, that an objective risk assessment, often based on the biopsy results of thousands of men, can be of help in making the correct decision.

So in conclusion, while head-to-head comparisons of available risk prediction tools in representative patient cohorts around the world are definitely needed, this should not hamper their current use in daily clinical practice. Risk prediction must be conceived justly, all clinicians would reply that they never base the decision to biopsy on the outcome of a PSA test alone. They know their patient, also take into account other factors and make a decision based on their clinical expertise. This is daily clinical practice and totally acceptable. However, there are patients that fall in the so-called ‘grey area’ where a clinician can have doubts on whether to proceed to biopsy or not. It is exactly in those men, that an objective risk assessment, often based on the biopsy results of thousands of men, can be of help in making the correct decision.

References
Chemotherapy in Prostate Cancer: Now “The Beginning”, No Longer “The End”

Dr Edmond Kwan & Dr Ben Tran
Department of Medical Oncology, The Royal Melbourne Hospital

Many years ago, the use of chemotherapy in advanced prostate cancer (PCa) was limited to those with symptomatic, castration-resistant disease. Whilst effective in improving symptoms and quality of life, as well as prolonging overall survival, it was used as a last line treatment; subsequently, patients viewed chemotherapy in PCa as “The End”. Advances in the past few years have dramatically altered this perception. Chemotherapy is now used earlier and it is important that we remove the stigma of “The End”.

The treatment landscape for advanced PCa has changed significantly in recent years. Not so long ago, the only treatment available was surgical castration (i.e. bilateral orchidectomy) or chemical castration, through the use of Androgen Deprivation Therapy (ADT). Cytotoxic chemotherapy was only effective if patients were no longer sensitive to ADT or hormones. The mechanism of action of ADT is to bring tumour levels of testosterone down to castrate levels by either removing the source of androgens (e.g. by castration) or interfering with the production of androgens (e.g. with anti-androgens such as flutamide or finasteride). This treatment is generally well tolerated and has a low risk of serious adverse effects.

Docetaxel became available to metastatic castration-resistant PCa patients on the Pharmaceutical Benefits Scheme (PBS) in Australia in 2007. At this time, it was only considered suitable for chemotherapy, offer 6 cycles of concurrent upfront docetaxel. When doing so, it is important to counsel patients appropriately and make the distinction that the use of chemotherapy for PCa is now “The Beginning” and no longer “The End”.

Two pivotal studies were published together in the New England Journal of Medicine, TAX327 and SWOG-99-19. Both studies demonstrated that docetaxel chemotherapy improved overall survival. Both studies compared docetaxel chemotherapy to mitoxantrone chemotherapy, which was the standard of care at the time. Patients were treated until disease progression or unacceptable toxicity, with a maximum of 10 cycles of docetaxel allowed in TAX327, and 12 cycles in SWOG-99-19 [1,2]. In clinical practice, it would be rare to exceed 10 cycles of docetaxel chemotherapy, due to either disease progression or intolerable cumulative toxicity such as fatigue or neuropathy.

Based upon TAX327 and SWOG-99-19, the regimen and schedule that moved forward was docetaxel 75mg/m² given every three weeks (like other chemotherapy agents, docetaxel dose is calculated using body surface area, which takes into account height and weight). At this dose and schedule, docetaxel is very tolerable. The common side effects reported by the trials (and consistent with clinical practice) include hair loss, fatigue, neutropenia, mucositis, neuropathy and diarrhoea; the rates of serious toxicity are relatively low. Quality of life was assessed in TAX327, where it was demonstrated that the use of docetaxel in patients with metastatic castration-resistant PCa led to significant improvements in quality life, in particular improvements in weight loss, appetite, pain, physical comfort and bowel/gut function. The survival advantages associated with docetaxel use in this metastatic castration-resistant population were observed in both studies. In SWOG-99-19, there was a 20% improvement in overall survival (HR 0.80, p=0.02), whereas in the TAX327 study, there was a 24% improvement (HR 0.76, p=0.009), equating to an approximate three-month overall survival advantage over mitoxantrone [1,2].

Docetaxel was well tolerated in TAX327 and SWOG-99-19, and quality of life was improved in patients treated with docetaxel. Quality of life outcomes were measured using the EORTC QLQ-C30 questionnaire. In TAX327, the HRQoL advantage in all domains was significant, whereas in SWOG-99-19, the advantage in fatigue, nausea/vomiting and bowel/genitourinary function was significant, but not in physical function or role function. The survival advantage associated with docetaxel use in these studies was maintained in both patients with pain at baseline and those without at baseline. Further, as the trials progressed, clinicians were able to optimise quality of life in their patients. Given this practice of delaying chemotherapy, the initiation of docetaxel in patients with metastatic castration-resistant PCa was often viewed as “The End” and this stigma continues today.

From 2011 onwards, several new drugs have become available for PCa, all of which improve survival and quality of life. These include novel hormonal agents, abiraterone acetate and enzalutamide, and the novel chemotherapy agent, cabazitaxel. In Australia, the PBS limits the use of these agents to patients who have previously had docetaxel chemotherapy (or are deemed to be inappropriate for chemotherapy). Subsequently, docetaxel is being used earlier. Analectedly, there are increasing numbers of asymptomatic patients being treated with docetaxel, the rationale being to ensure that upon disease progression, patients are well enough to receive subsequent lines of therapy.

The biggest paradigm shift for advanced PCa occurred in 2014, when results from the CHAR2T3ED study were presented at the American Society of Clinical Oncology Annual Meeting. The CHAR2T3ED study examined the role of upfront docetaxel chemotherapy together with ADT (so called “chemo-hormonal” approach) in patients with metastatic, hormone-naïve prostate cancer. This study demonstrated that the upfront use of docetaxel chemotherapy, for 6 cycles only, provided a 39% improvement in overall survival, a dramatic benefit of nearly 14 months (HR 0.61, p<0.001), best seen in patients with high volume metastatic disease. These results were later confirmed by the STAMPEDE study, which also studied the use of upfront docetaxel chemotherapy, together with ADT for patients with newly diagnosed metastatic hormone naïve PCa. STAMPEDE demonstrated a 22% improvement in overall survival (HR 0.78, p=0.006). Both studies have since been published and also confirm that the use of docetaxel in this patient population is very tolerable, with a similar toxicity profile to that seen in TAX327 and SWOG-99-19 [4,5]. However, not all patients will be appropriate for upfront combined chemo-hormonal therapy; in elderly and frail patients, the benefits for upfront docetaxel may be outweighed by potential risks. Subsequently, for patients with metastatic PCa, the new standard of care is to offer ADT to everyone, and in patients who are considered suitable for chemotherapy, offer 6 cycles of concurrent upfront docetaxel. When doing so, it is important to counsel patients appropriately and make the distinction that the use of chemotherapy for PCa is now “The Beginning” and no longer “The End”.

References

The role of PSA screening for detection of prostate cancer (PCa) remains an extensively debated issue. In the first quarter of 2016, The National Comprehensive Cancer Network (NCCN) Prostate Cancer Early Detection Guidelines Panel, called for a tailored approach for PCa Screening [1]. While conceding that the two ends of the PSA-screening spectrum, with one advocating unrestricted PSA screening in contrast to blanket cessation of all testing, both fail to acknowledge the biologic diversity of PCa, the guidelines panel put forward a judicious, personalized approach to population screening utilizing PSA testing.

The panel proposed that in well-informed men aged 50 to 75 years, PSA testing at 1 to 4 years’ interval can reduce PCa related mortality for the population screening utilizing PSA testing. Interval prostate biopsies are the cornerstones of any AS protocol, however the need for repeat biopsy has been often cited as one of the drawbacks of AS strategy. Bokhorst et al recently reported on the complications associated with prostate biopsy in a cohort of men in the Prostate cancer Research International Active Surveillance (PRISAb) study [2]. Overall, the rate of infection post biopsy was low at 2.5% with only 55 infection episodes after 2184 biopsies in 1164 men. The majority of biopsies were obtained via the rectal route (84%) with fluoroquinolones as antibiotic prophylaxis of choice (86%). There was no difference in the rates of infection between transrectal (2.7%) and transperineal biopsies (2.1%). Overall, 23% of men experienced at least one complication related to their first diagnostic biopsy. On multivariable analysis, the number of previous biopsies was not associated with any increased risk of post-biopsy infection.

In the setting of metastatic PCa, two landmark trials have highlighted the benefits of early chemotherapy [3-5]. In the CHARTED trial (n=790), men with hormone sensitive metastatic PCa were randomized to treatment with androgen deprivation (ADT) alone versus ADT plus six cycles of docetaxel (Doc) chemotherapy. The median overall survival for the combination arm (57.6 mo) was significantly longer than observed with ADT alone (44 mo)(HR 0.81, 95% CI 0.47-0.80; p < 0.001). The study also demonstrated that the addition of Doc at the commencement of ADT improved the time to castration resistant PCa, and cancer-specific survival. After stratification, according to the metastatic burden of the disease, the benefit of Doc was only observed in patients with high volume metastatic disease, however, the study was not powered to detect this.

In the STAMPEDE trial (n=2962), men with high-risk, locally advanced, metastatic or recurrent prostate cancer commencing first-line, long-term hormone therapy were randomized with 2:1:1:1 ratio to standard of care only (SOC-only; control), standard of care and zoledronic acid (SOC + ZA), standard of care and docetaxel (SOC + Doc), or standard of care with both zoledronic acid and docetaxel (SOC + ZA + Doc). There was no evidence of any survival advantage in SOC + ZA arm when compared with SOC-only group (HR 0.94, 95% CI 0.79–1.11; p=0.450). In contrast, survival advantages were observed in both of the Doc containing treatment arms with 22% (HR 0.78, 95% CI 0.60–0.93; P=0.006) and 18% (HR 0.82, 95% CI 0.69–0.97; p=0.022) reduction in the risk of death for SOC + Doc and SOC + ZA + Doc arms respectively, compared to control arm. The median follow up time for the study was 43 (IQR 30-93) mo. Furthermore, the authors reported that the addition of Doc to standard of care therapy improved the median survival by 10 months, as well as improvements in prostate-cancer-specific survival, failure-free survival, and skeletal-related events. These benefits were also observed in the SOC + ZA + Doc arm. A higher proportion of patients receiving Doc therapy reported grade 3 or higher adverse events (52%) during the first 6 months on trial compared to the rest of the cohort, but for the 1998 patients with adverse event data around 1 year after randomization, no difference in the proportions of grade 3 or higher toxic effects were observed (around 10% for all arms).

Both these trials provide irrefutable evidence that upfront Doc chemotherapy improves survival in patients with metastatic PCa. In the non-metastatic setting, data needs to be further matured before reaching any conclusions.

STRIVE, a randomized, double-blind phase II study, compared the efficacy and safety of bicalutamide, and enzalutamide, in men with castrate resistant PCa (CRPC) [6]. The study randomized 396 men with nonmetastatic or metastatic CRPC to either drug while men continued with their primary ADT. Men in the enzalutamide arm experienced a 76% reduction (HR 0.24, 95% CI, 0.18-0.32; P <0.001) in the rate of progression or death compared to men receiving bicalutamide with a significantly longer median progression free survival time (19.4 vs. 5.7 mo). The favorable effects of enzalutamide were detected in both non-metastatic and metastatic settings. Long-term data from a single arm study has confirmed the safety and efficacy of enzalutamide monotherapy in men with hormone-naive PCa, demonstrating long-term declines in PSA, with a minimal influence on the total-body bone mineral density [7]. Previous studies have demonstrated the therapeutic benefits of enzalutamide post chemotherapy and in chemo naïve men with CRPC [8,9].

Detection of androgen receptor splice variant 7 (AR-V7) in circulating tumor cells from men with CRPC has been demonstrated to correlate with a more favorable response to therapy with taxanes than with enzalutamide and may serve as a biomarker in CRPC aiding in selection of men for appropriate treatment [10].

These trials provide strong evidence for alterations of our longstanding practices in men with advanced PCa. Further data on the first choice of therapy at the commencement of ADT, the selection of men for chemotherapy or the best sequence of agents are needed.

References
Helping Men Adhere to Sexual Rehabilitation following Prostate Cancer Surgery: Changing the Conversation

Dr Christian J. Nelson
Memorial Sloan Kettering Cancer Center
Department of Psychiatry and Behavioral Sciences
New York

It is well understood that erectile dysfunction is common following radical prostatectomy. Almost all men, approximately 85%, will report difficulty with erections to some extent following surgery [1, 2]. The importance of this to men cannot be underscored. Many men will report significant distress related to erectile dysfunction (ED), and it is now well established that ED is associated with depressive symptoms [3, 4]. The rate of depression in men with ED has been reported to be as high as 56%, and the relationship between ED and depression has been demonstrated in large, well-designed, population based studies of aging men in the US, Finland, Brazil, Japan, and Malaysia [5]. Some assume as men grow older they will be less concerned about sexual functioning; however, these studies have been conducted in men between the ages of 40 to 70 years old, and have all controlled for age in their analyses. When focusing on prostate cancer, some authors have argued that ED distress is mitigated as patients focus on the life-threatening nature of their illness [6]. Nevertheless, data confirms the presence of depressive symptoms, ED bother, and loss of masculine identity following prostate cancer treatment [4].

Penile Rehabilitation

With the high incidence of ED following prostate cancer surgery, coupled with ED’s large psychological toll, “penile rehabilitation” programs have been developed to help men recover their erectile function following prostate cancer surgery. These programs instruct men to achieve medication assisted erections 2 to 3 times a week (with or without the use of sexual activity) immediately following radical prostatectomy for 18 to 24 months. The premise is that consistent erections will put oxygen rich blood into the penis tissue thereby sustaining tissue health while the cavernous nerves heal. This process increases the chance that men will recover erections. Penile injections have become a cornerstone of many rehabilitation programs, as PDE5Is are ineffective immediately post radical prostatectomy. This type of penile rehabilitation strategy has demonstrated effectiveness with 52-67% of men who use have used a rehabilitation strategy returning to natural erections compared to 10-20% of men returning to natural erections who did not participate in a penile rehabilitation program [7, 8]. As a result, penile rehabilitation programs are now considered the “best practice” for helping men with sexual functioning following surgery, and 89% of Sexual Medicine professionals are utilizing some type of penile rehabilitation with these men [9].

Avoidance of the Use of ED Treatments and Penile Rehabilitation

Despite the importance of rehabilitation, many men avoid using ED treatments and quickly drop out of rehabilitation programs [10]. The literature indicates that compliance with ED treatments is poor. Data shows that 50% to 80% of men discontinue use of ED treatment (i.e. oral medication, injections, and vacuum devices) within a year of starting these interventions [2, 11]. In men with prostate cancer, only 27% continue therapy for a year [10]. When focusing on erectile rehabilitation, pilot data indicates that only 10% of men use penile injections at the suggested rate for rehabilitation of two times per week [12]. Considering the importance of rehabilitation, the difficulty sustaining treatment can negatively impact men’s recovery of erections following surgery.

Our qualitative research with 30 men who had participated in an erectile rehabilitation program indicated that many men fall into a “cycle of avoidance” when using these programs. The cycle starts with men thinking about their ED and the need to use any ED treatments. Thinking about ED leads to unfavorable thoughts and predictions. Examples include: “I am not a real man,” “my wife/partner will leave if I cannot perform,” or “I will not be able to finish.” These negative thoughts induce anxiety, fear, and low confidence related to using ED treatments and, entering into a sexual situation, and as one man stated, “its fear, I am afraid to try anything (sexually).” Avoiding penile rehabilitation strategies and sexual situations becomes an effective and powerful short-term strategy to reduce the anxiety and fear associated with these situations. However, this only leads to short-term psychological relief, and in the long run it leads to a failure to engage in rehabilitation. This long-term failure can then lead to increased frustration and disappointment.

Changing the Conversation with Men about Penile Rehabilitation

Using a framework from Acceptance and Commitment Therapy and the feedback during our qualitative interviews, our group has developed and initially tested a way of talking to men to help reduce avoidance to penile rehabilitation (see Table 1) [12]. As a first step, it is important to shift the focus away from the problem (e.g. ED and using injections) to why rehabilitation is important to the man. Men who were successful with using penile rehabilitation focused on the importance of sexuality and intimacy in their lives, and viewed “getting back to a whole man” as a meaningful goal. Next, it is important to acknowledge that anxiety and fear are a normal part of the process, and men should accept that they may be nervous and anxious when they think about sexual situations or penile rehabilitation. When men experience this anxiety it is helpful to think about the long-term benefit of rehabilitation. It can be important to highlight that these feelings of anxiety and fear are common and can lead to avoidance, and to discuss their willingness to tolerate short-term distress to allow them to achieve their long-term goals. Men who were successful kept their “eye on the prize” and saw the process of rehabilitation as “getting back to the life I want.” They noted a willingness to go through the “hassle” of using injections while possibly enduring some emotional let-down if failures occurred so that they would not “deteriorate” and come to feeling like a “man again.” Also, it may be helpful to discuss and highlight any possible benefits they will use to avoid rehabilitation (e.g. forget, too busy), and to help them understand the idea that this is normal and as one man stated, “It’s fear, I am afraid to try anything (sexually).” Avoiding penile rehabilitation may then become an effective and powerful short-term strategy to reduce the anxiety and fear associated with these situations. Men who were successful with rehabilitation focused on the long-term benefit when they focused themselves finding excuses. Lastly, it is important to have men make a specific commitment to the number of injections they will use a week.

Changing the Conversation with Men about Penile Rehabilitation

Explore and Focus on Importance of Sexuality

Acknowledge Short-term Anxiety

Focus on Long-term Goals as Opposed to Short-term Anxiety

Discuss/highlight Barriers

• Ask what will get in the way
• Predict they will find excuses to avoid treatment

Ask for a Commitment to Injection Target

References

Finding Meaning in the Face of Mortality

Sigmund Freud is quoted as saying that the principle ingredients of a good life are work and love. Provided we don’t interpret this too literally, it remains as true for those approaching the end of life, as it is for those whose lives are just beginning.

The mental health of children is frequently gauged by the quality of their attachments, and their capacity for immersive play. Similarly, the mental health of adults approaching the end of life is intimately linked to the quality of their relationships and their willingness to engage with whatever life throws at them.

The musician David Bowie (pictured right) spent the last year of his life working on an album released just a week before his death from liver cancer. During the same time period, he also overcame his fear of flying to tour incognito around the suburbs of his youth with his wife and fifteen-year-old daughter.

The neurologist, Oliver Sacks, who also died last year, wrote the following after learning that his liver cancer had become terminal: “I want and hope in the time that remains to deepen my friendships, to say farewell to those I love, to write more, to travel if I have the strength, to achieve new levels of understanding and insight [1].”

Not all of us will end our days recording best-selling albums or writing the New York Times, but such examples orient us to the fact that the last few years of life may hold more potential than we imagine.

In the not-too-distant past, interventions directed at cancer patients laboured under the unintended weight of premonitions of death not too far removed, but over the past decade the focus has shifted towards an emphasis on wellness, and interventions intended to enhance the quality of life. This article will preview two such examples before discussing the aspirations of dignity therapy of Dr Chochinov, both recognize the fact that, as if they no longer have anything meaningful to contribute, they still have: the company of family and friends, the beauty of nature, the enjoyment of music or art, or an interest in sport or politics.

On the day that my father-in-law died (a decade after being diagnosed with throat cancer), the Sydney Swans achieved a significant AFL victory. Not long after the game, Fitz suffered a heart attack and was transported to hospital still wearing the Sydney Swans beanie that he had been wearing all afternoon despite the intense heat. He died just a couple of days later but the circumstances of his death gave some comfort to those who knew about his lifelong passion for sport, and for whom the beanie remains a significant keepsake.

In the final session of the Memorial Sloan-Kettering course, group members present a “legacy project” which documents their life experience and the meanings they would like to pass on to others. This final session mirrors the work of Dr Harvey Max Chochinov from the Manitoba Palliative Care Research Unit (Winnipeg, Canada) who has pioneered a range of interventions intended to maintain the dignity of patients nearing the end of life.

Dignity Therapy

Dr Chochinov’s “Dignity Therapy” [4] is designed “to assist people dealing with the imminent end of their lives” and includes a range of interventions, one of which is detailed below.

This particular intervention is built around a 30 to 60-minute session during which therapists ask a series of open-ended questions that encourage patients to talk about their lives and what’s mattered most to them. The conversation is recorded, transcribed, edited and then returned within a few days to the patient, who is given the opportunity to read the transcript and make changes before a final version is produced. Many choose to share the document with family and friends.

According to the researcher’s website: “The first clinical trial using Dignity Therapy has overwhelmingly affirmed the value of this method for both patients and families” and since then this intervention has been replicated at other palliative care centres around the world [5].

The meaning-centred psychotherapy of Dr Breitbart, and the dignity therapy of Dr Chochinov, both recognize the fact that, no less than anyone else, patients approaching the end of life are not just patients experiencing a disease; but patients facing the end of a caring relationship. Opportunities such as the ones listed above help them to escape the veil of isolation that all too frequently shrouds the lives of the dying and provides them with an opportunity to share something of significance with the people they leave behind.

Staying Well

There is a growing body of evidence to suggest that lifestyle changes can have a significant impact on one’s quality of life and can equally lessen the burdens of sickness and old age. Here we will touch briefly on the benefits of exercise and mindfulness meditation, but other factors - including diet, the quality of one’s relationships, spirituality and contact with nature - may be of equal importance.

The benefits of exercise for the general population are very well documented but there is also mounting evidence to suggest that regular exercise can be of benefit even to those undergoing treatment interventions such as hormone therapy and/or chemotherapy for late-stage cancer [6].

There is also considerable evidence to support the use of mindfulness meditation for people diagnosed with cancer, with further evidence to support its use in men with prostate cancer. The benefits, according to Cancer Research UK, include: less pain and fatigue; better quality sleep; fewer disturbances of mood; improved memory and concentration; reduced stress; and increased feelings of wellbeing [7].

Conclusion

The “end of life” is a vague and inclusive term that might equally be used to describe anything from the time remaining post diagnosis (which could amount to decades) to the last few hours of life.

When the Nobel Prize winning scientist Francis Crick was told that his colon cancer had returned he said, “Whatever has a beginning must have an ending.” When he died, at eighty-eight, he was still fully engaged in his most creative work [1].

It often takes an illness to convince us of what’s important in life, to recognize that however long we may have there will always be opportunities to: deepen friendships, embrace the people we love, appreciate the beauty of nature, “and achieve new levels of understanding and insight [1].”

References

Bladder cancer is a smoker’s cancer. After lung cancer, it is the second most common smoking-related malignancy. Only lung, oral and head and neck cancers have a higher relative risk associated with smoking [1]. The most recent epidemiologic studies indicate a fourfold excess risk of bladder cancer in smokers compared to individuals who never smoked, and a twofold increase in former smokers versus never smokers [2].

For both men and women, approximately half of all cases of bladder cancer are attributed to smoking [2, 3]. Although smoking rates peaked in the 1970s for men and in the 1980s for women in the United States [4], the incidence of bladder cancer has remained stable for the past 30 years [5]. The reasons for this remain unclear, although the association between smoking and bladder cancer has become stronger in more recent studies and one hypothesis states that the concentration of some carcinogens in cigarette smoke may have increased despite reductions in concentrations of tar and nicotine [2].

Smoking is not only associated with the development of bladder cancer, but also with its prognosis. This is true especially in the context of non-muscle invasive bladder cancer [6], which makes up 75% of all cases. Patients who are current smokers and who have smoked the highest number of cigarettes have the highest risk of recurrence. An association to bladder cancer progression is suspected but not well established. Similar, but less robust associations, have been observed with muscle invasive bladder cancer after radical cystectomy [7] and with upper tract urothelial carcinoma [8]. These epidemiologic findings are consistent with the molecular mechanisms by which smoking exerts its carcinogenic effects, including DNA mutation, chromosome 9 alteration and immunomodulation.

An influence of second-hand smoke on the incidence of bladder cancer has not been definitively established in epidemiologic studies, which offer conflicting evidence. It seems likely, however, that second-hand smoke should raise the risk of bladder cancer since it is clear that it contributes to lung cancer and it is well known that there is no threshold dose of smoking that is required to cause cancer.

Smoking cessation has a positive impact on the natural history of bladder cancer [9]. Firstly, smoking cessation reduces the risk of developing bladder cancer. Individuals who have stopped smoking for ≥10 years have a lower incidence of bladder cancer compared to those who quit for <10 years or who still smoked [2]. In general, the longer the time between smoking and diagnosis, the better the outcome will be [6].

Secondly, patients with non-muscle invasive bladder cancer have a lower risk of recurrence if they quit smoking compared to patients who continue to smoke [6, 9]. Unfortunately there is no prospective evidence to confirm that smoking cessation definitively affects outcome. The impact on muscle-invasive bladder cancer is less clear.

Finally, additional smoking-related cancers are common in patients with bladder cancer, and the risk of development decreases following smoking cessation [10].

The diagnosis of bladder cancer should therefore be inextricably linked to a smoking cessation program. Urologist and general practitioners managing these patients should concentrate on smoking cessation as an important component of the treatment strategy. One recent study demonstrated in a cohort of Californian patients with newly diagnosed non-muscle invasive bladder cancer that smoking cessation was almost five times more likely amongst active smokers (17% of patients) than in a comparable cohort in the general population (48% vs. 10%, P<0.001) [11]. This highlights the opportunity to convert a new bladder cancer diagnosis into a “teachable moment” [12].

While the diagnosis itself was reported in the study from California to be the key reason for quitting, advice from both the urologist and the general practitioner was also cited as an important impetus for quitting. The public awareness of smoking as a risk factor for bladder cancer lags behind other common smoking-related cancers [13]. Patient education and support in the process of cessation are absolutely essential, and these are the combined responsibility of the patients’ urologist and general practitioner. The diagnosis of bladder cancer results in regular office visits and procedures with the urologist, which offer important opportunities to reinforce counseling on smoking cessation.

The long natural history of non-muscle invasive bladder cancer serves to underscore the value of smoking cessation. Disease specific survival at 5 years exceeds 90%. At the same time, recurrences are frequent with a 5 year risk of recurrence between 50% and 80%, and a rate of progression to muscle invasive bladder cancer of up to 30%.

In summary, mounting evidence suggests that smoking status and cumulative lifetime exposure affect bladder cancer incidence, recurrence and progression, while smoking cessation may reduce these effects. It is critical for physicians treating patients with bladder cancer to make smoking cessation an integral component of the therapeutic plan.

References
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Presented by Australian Prostate Cancer Research in conjunction with the Asia-Pacific Prostate Cancer Conference

We warmly welcome you to join us for a day of updates and interactive sessions aimed at General Practitioners from all backgrounds.

Come away from this update with useful tips you can apply to everyday practice to better support and manage your patients.

Speakers from a variety of disciplines will present current trends and research.

Topics and sessions include:
- Erectile Dysfunction
- Cardiovascular Update
- Prostate Cancer
- Depression
- Osteoporosis
- Metabolic Syndrome

Dr Jane Crowe & Dr Ed Vergara

Program Convenors

Target Audience
This program is suitable for all General Practitioners regardless of their experience or where they practice.

Date
Saturday 3 September 2016
8:30am – 4:30pm

Location
Melbourne Convention & Exhibition Centre

Delivery
Face to Face, 6 hours of interactive education

RACGP
40 – Category 1 QI and CPD Points (Application in progress)

Cost
Complimentary to General Practitioners
Please register at: www.prostatecancerconference.org.au

A confirmation will be provided by registering and a final attendance email with further details will be forwarded 2 weeks prior to the event.

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Helping Smokers Quit: Removing Barriers

Dr. Sarah White
Quit Victoria,
Cancer Council Victoria

Smoking tobacco is the leading risk factor for preventable, premature mortality in men. A key cause of both coronary heart disease (CHD) and lung cancer, smoking in every age group in Australia. Smoking is also a key risk factor for many other diseases including 18 discrete types of cancer, stroke, type 2 diabetes, reduced circulation, chronic pulmonary obstructive disorders, dental decay, erectile dysfunction and reduced fertility (male and female). Smoking also has a direct impact on a variety of medical procedures and treatments. People who smoke prior to surgery have increased wound injection rates, worsened wound healing, increased anaesthetic complications and increased post-operative pain. People who smoke while undergoing cancer treatments have poorer outcomes and worse side-effects. And it’s worth noting that non-smokers exposed to second-hand smoke over a long period or in concentrated form, i.e. in a workplace or at home, have health risks that are not dissimilar to people who actually smoke.

So why do relatively few health professionals actively help their patients stop smoking?

Published studies of attitudes [1] and extensive feedback from health professionals have identified several barriers to addressing patient smoking. Some health professionals consider conversations about smoking time-consuming, ineffective or unpalatable. Others report lacking confidence in their ability to tackle the issue and/or in their knowledge of information on smoking cessation.

Population surveys show the vast majority (>80%) of smokers want to quit, and most expect health professionals to advise them to quit. Therefore, advising people to quit is highly unlikely to provoke hostility if done in a professional, non-confrontational manner. The worst that can be thrown up is that it is the patient’s “choice”. There’s no need to start an argument on addiction versus choice, just be as clear as advice to quit is health advice, not lifestyle advice.

And, yes, these conversations are effective.

Brief advice from a health professional significantly increases the chance that a patient will quit. In fact, an estimated one in every 33 conversations will lead to a patient quitting [2]. Low odds but high impact when one considers the health benefits for the patient and the people around them.

Which brings us to “how to do brief advice” and consultation time. The Smoking Cessation Guidelines for Australian General Practitioners, based on extensive reviews of evidence [3], are incorporated into The Royal Australian College of General Practitioners (RACGP) clinical guidelines for smoking cessation [4]. The guidelines use the “5As” – Ask (about smoking), Advise to quit, Assess (readiness to quit and nicotine dependence), Assist (with an offer of pharmacotherapy and/or behavioural support and/or referral to more intensive, proactive support), and Arrange (follow-up for progress and encouragement).

There is an alternative to the 5As; a shortened version that should take no more than a couple of minutes.

Ask if the person is a smoker. If the answer is no, affirm their decision or congratulate them for quitting. If the answer is yes, move on to Advise.

Advise smokers that quitting is the best thing they can do for their health. If possible, relate their smoking back to the medical issue at hand or to any previous history to personalise the advice.

Asking and advising alone can have an impact, but—ideally—active assistance should be offered. Providing active assistance according to RACGP guidelines will take some time as it involves providing behavioural support. However, active assistance can also be provided by referring the patient to a specialist service, and this should take relatively little time.

Refer: You can—with the patient’s consent—refer them to a local tobacco treatment specialist or, more simply, to the Quitline in your state or territory.

Quitline is an evidence-based telephone counselling service staffed by specially-trained allied health professionals. Quitline will make at least one proactive personal call to the patient to help them develop a personal plan for identifying and managing triggers to smoke and barriers to quitting, and provide motivational interviewing and advice on using pharmacotherapies. You can strongly recommend the patient call the Quitline (on 13 7848) themselves. However, clinical trials show that a referral followed by a proactive call is more effective than the patient making the call. Most Quitlines accept referral by fax or email (Google “Quitline” in your state/territory for referral information).

Smoking is a chronic, relapsing condition, so it’s critical to ask—at every visit—whether patients identified as smokers have reconsidered their smoking, whether they’ve tried to quit and how they’re preventing relapse if they have tried. Most people who try to quit will try multiple times; the important thing is to keep encouraging them to do so. If a patient has been unable to quit “cold turkey”, the most common method, then prescribing nicotine replacement therapy might be a next step (remembering that patches are subsidised on the PBS). If a patient has tried but relapsed, reinforce that there is no such thing as a “failed” quit attempt. Every attempt helps that patient understand more about their smoking.

It’s worth touching on “who still smokes”. The daily smoking prevalence has fallen to just 12.8% across Australia. High cigarette taxes, extensive smokefree legislation, plain packaging, and graphic media campaigns and health warnings have all contributed to a fall in prevalence and in smoking being socially denigrated.

Population groups in which smoking rates remain high include people with socioeconomic disadvantage, Aboriginal and Torres Strait Islander people, people with mental illness and with substance use disorders. It seems that people with complex needs also have difficulty quitting. Consider the profound physical, social and financial costs for these groups, and is a significant factor behind the life expectancy gap between Indigenous and non-Indigenous Australians and between people with and without mental illness.

Finally, there are several resources for health professionals to learn more about helping smokers quit. Apart from the RACGP guidelines, Start the Conversation (starttheconversation.org.au) was developed by a health service and has short videos from health professionals and provides resources and information on multiple aspects of smoking and smoking cessation. Two out of three Australian smokers will die from a smoking-related illness if they do not quit. Ask-Advise-Refer: it’s simple, it’s fast, it works, and it’s the best thing you can do for your patients.

References
Health Journalism

Jill Margo has been reporting on prostate cancer since 1993, when she began the first men’s health column in The Sydney Morning Herald. A few years later she took the column to The Australian and since 2000, it has appeared in The Australian Financial Review.

When I began writing about prostate cancer it was almost virgin territory. It was hardly mentioned in the lay press and there was low awareness of the disease in the community.

Today, readers know considerably more and want a different sort of reporting on this cancer. They don’t expect every story to feature a major advance and are interested in incremental improvements. For men fearing or facing prostate cancer, every little bit helps.

Articles about prostate cancer usually rate well for two reasons.
First, much of the male demographic of The Australian Financial Review is at risk of this cancer.
Second, the way this cancer intersects with masculinity is a concern. The spectre of compromised potency and continence hangs over most of these articles.

From my experience, our readers prefer nuanced rather than black and white reporting. They prefer a realistic appraisal of a development with all its uncertainties rather than simple overstatement that makes headline news. Our analytics show many read deep into a story and tackle the complexities it may present.

What to report

Unless there is an obvious news angle, my choice of what to report is often driven by an instinct developed over many years. I look for material that: can make men’s journey through this disease easier; can throw new light; might question the orthodoxy; may have long term ramifications or may expose untoward self-interest.

Where do I get information?

With so much new information coming online, the challenge for me is deciding what to report. Published research varies greatly in quality and it’s as easy to miss something significant as it is to be lured by empty ‘click bait’.

I usually trawl through journal summary services, press releases from journals and institutions, news wires and foreign newspapers, looking for something new.

If I find something interesting, I’ll dig around and read about its history, see what others are saying about it or I will call someone whose opinion I value.

Sometimes, readers email me with ideas or call with requests for a particular article to be written. Occasionally I get a tip off or am offered an early run on a story.

In the past 15 years, the ranks of public relations consultancies have swelled while the ranks of mainstream journalists have shrunk. This means many of the PR pitches and offerings don’t find a receptive audience.

Once I have selected a topic, I try to get some formal comment and find myself having to guard against the convenience of using the same expert voices repeatedly.

It’s always pleasing to find what we call “good talent”, people who can explain something simply, comment succinctly and are accessible. Events, such as conferences and launches, can be good places to meet fresh talent.

These days, most interviews are conducted over the phone although more can usually be gained face-to-face. The benefit is not only for the story in hand, but for ongoing contact. Whenever I can, I make the effort to meet the person.

Journals in transition

The internet has changed journalism. The move from print to digital has seen a dramatic drop in revenue which has meant diminishing employment for journalists. There are fewer specialist reporters and fewer senior reporters. This means complex health stories are often let go, or assigned to journalists who have other demands and no special interest in the subject.

There is an upside to the digital change because space online is almost unrestricted. A story that doesn’t make the paper because of space constraints can make it online and can then be promoted through social media. If it’s a really worthwhile piece, it may eventually end up in the paper too – but many say newspapers are on the road to extinction.

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