FINAL REPORT FOR THE MANAGEMENT OF METASTATIC PROSTATE CANCER STUDY

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THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau
NEW ZEALAND

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WORD FROM THE PRINCIPAL INVESTIGATOR

This report is the synthesis of 2 years work from a multi-disciplinary team of clinicians and researchers. We explore the national and regional picture of metastatic prostate cancer in New Zealand men, including the use of pharmacological and chemotherapeutic agents. We have described the management of men with a metastatic diagnosis within the Midland Cancer Network region, including collecting their treatments, follow up, monitoring and outcomes. We hope this will improve the journey for men and their families.

I would like to thank all those who have helped us in our endeavors – including Auckland UniServices Ltd, our funders Janssen-Cilag Pharmaceuticals, our clinical and academic colleagues, the patients and partners who shared their personal experiences, Pathlab, Waikato, Bay of Plenty and Lakes district health boards, members of our governance and advisory groups.

We hope you find this report informative.

Sincerely,

Professor Ross Lawrenson

December 23, 2014

DEDICATION

We would like to dedicate this report to the participants who shared their stories. For some, these were in their final days. Thank you for your generosity with your time and conversation in helping to create a better experience for other New Zealand men dealing with prostate cancer.

Arohanui

BACKGROUND

DEVELOPING AN UNDERSTANDING OF METASTATIC PROSTATE CANCER

Prostate cancer is the most commonly diagnosed male cancer and the third most common cause of male cancer death in New Zealand. About 2900 men are diagnosed with prostate cancer and 590 New Zealand men die from prostate cancer every year (NZ Cancer Statistics). A review of 535 men newly diagnosed with prostate cancer suggested that 11% were diagnosed with metastatic disease at the time of diagnosis. Māori were more likely to have metastatic disease at diagnosis (19.3%) compared with NZ European (9.8%)[1].

For Māori men, prostate cancer ranks as the 2nd most common cause of cancer death after lung cancer[2]. For Māori, the age adjusted incidence in 2005 was 74.9 per 100,000 compared to 95 per 100,000 for the total population. Mortality due to prostate cancer was 25.5 per 100,000 for Māori compared to 17.3 per 100,000 for the total population[3]. Māori men are thus 20% less likely to be diagnosed with - but 65% more likely to die from prostate cancer than non-Māori men. As Māori are more likely to be diagnosed with advanced disease their outcomes will be worse than non-Māori. However, once inequity in stage of diagnosis is accounted for, Māori men are still more likely to die of their prostate cancer than non-Māori men. This large inequity from diagnosis to death occurs along the treatment pathway and is suggestive of differences in access to and quality of care. Prostate cancer has the second largest inequity in cancer survival between Māori and non-Māori after uterine cancer[2].

The treatment of metastatic disease includes use of androgen-deprivation therapy (ADT), radiotherapy and chemotherapy. Access to treatment depends on appropriate access to specialist care from urologists, radiation oncologists and medical oncologists[4].

There are no standardised New Zealand guidelines for the management of metastatic disease or the use of ADT. Treatment regimens may vary depending on various factors which may include: patient characteristics, such as age, comorbidities, domicile, tolerance to specific drug type and patient acceptance of treatment. Clinician preference, access to a medical oncologist, and access to subsided medication may also be factors in the treatment pathway for men with metastatic disease. Most prostate cancers are hormone sensitive and regress with ADT for a variable period of time, particularly if patients have non-metastatic disease on either continuous or intermittent therapy[5].

A proportion of men will go on to develop castrate resistant prostate cancer (CRPC). The definition of CRPC varies between studies and centres but is usually based on factors such as a rising PSA level whilst on ADT, symptomatic progression or changes to metastatic lesions on imaging. Generally, CRPC will develop in 10-20% of patients[6].

BACKGROUND

It has been shown that improvements in survival can be achieved by appropriately using different medications to treat castrate-resistant tumours. In New Zealand, chemotherapy was rarely used for men with prostate cancer but the introduction of Docetaxel as an approved treatment, and a number of new agents that have been brought to market overseas means that potentially great changes are likely in the management of metastatic prostate cancer. One of these new products is Abiraterone which inhibits testosterone production. The unsubsidized cost of this medication is prohibitive for many men. As Māori men tend to be from the lowest socio-economic quartile Janssen Pharmaceutical were interested in exploring the possibility of a tiered pricing structure to ensure disadvantaged men had more equitable access to a new and effective treatment.

The proposed study was designed to look at differences in the treatment of Māori and Pacific men compared with non-Māori/non-Pacific, and examine differences in outcome. The main outcomes of the study were to be:

1. A national overview of the epidemiology and pharmaceutical treatment of metastatic prostate cancer, including differences in pharmaceutical treatments by ethnicity;
2. A detailed understanding of pathways to diagnosis and of access to and through treatment, and quality of treatment for Māori, Pacific and Other New Zealand men with metastatic prostate cancer;
3. An in-depth understanding of the experiences of Māori and Pacific men living with metastatic prostate cancer;
4. An assessment of the health and economic costs of treatment for metastatic prostate cancer following diagnosis for Māori, Pacific and other NZ men;
5. An assessment of the need for tiered pharmaceutical pricing for medications used for treating metastatic prostate cancer.

BACKGROUND

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STRUCTURE OF STUDY

ADVISORY GROUPS

This project was developed with the assistance of multiple people and organisations. We worked with various external and internal groups to assist in our understanding, through advising and guiding our research process. The external groups included: Waikato DHB Kaumātua Kaunihera, Ministry of Health, Prostate Cancer Foundation, and the Cancer Society.

The identification and engagement of key stakeholders was seen as essential for the research project. We worked with three key advisory groups. The first was an Academic Steering Group (ASG) that included clinical academics dealing day to day with the issues of men with prostate cancer. The ASG included urologist, medical and radiation oncologists, specialist nurses and key academics. The ASG provided academic and clinical governance and assured the quality of the research team outputs.

The second advisory group was the Community Advisory Group (CAG), which was developed for the Midlands Prostate Cancer study, but also supported the on-going work. The CAG included representatives from the Prostate Foundation, the Cancer Society, the MCN and local self-help groups. This group was established to provide a consumer and community perspective to the research project. They provided advice on methods of consultation with end users, support with advice to men (referrals) and input into the study to ensure that the end user perspective is heard.

The third group was the Māori cancer advisory group, Hei Pa Harakeke. This was a generic cancer group formed by WDHB Te Puna Oranga and MCN to advise on all aspects of care for Māori patients with cancer – including men with prostate cancer.

<u>Governance Academic Steering Group Members:</u>

- Dr Leanne Tyrie (Kathleen Kilgour Center, Tauranga)
- Dr Peter Fong (Auckland DHB and UOA)
- Mr Michael Holmes (Waikato DHB)
- Dr Nina Scott: Ngāti Whatua, Waikato (Waikato DHB)
- Dr George Laking: Te Whakatōhea (Auckland DHB and UOA)
- Mrs Tiffany Schwass (Waikato DHB)

<u>Academic advisors to the project team were:</u>

- Associate Professor Alistair Stewart (UOA)
- Associate Professor Paul Rouse (UOA)

- Dr Richard Edlin (UOA)
- Dr Geraldine Leydon (University of Southampton, UK)

Consumer Advisory Group Members:

- Mr Graham Harbutt (Formerly Waikato Cancer Society)
- Mr Dene Ainsworth: Te Ātiawa (NZ Prostate Cancer Foundation)
- Mr Jack Porima: Ngati Hikairoa (Raukura Hauora O Tainui)
- Mr Jeffery Morse (Counsellor)
- Mr Rawiri Blundell: Ngati Porou ki uawa (Midland Cancer Network)
- Ms Margie Hamilton (Midland Cancer Network)
- Dr Nina Scott: Ngāti Whātua, Waikato (Waikato DHB)
- Mr Tamati Peni: Raukawa (Waikato DHB)

Research Team Members:

- Professor Ross Lawrenson (University of Auckland (UOA)) – Principal Investigator
- Dr Charis Brown - Project Manager
- Dr Zuzana Obertova - Cancer Epidemiology PhD Student
- Ms Chunhuan Lao - Health Economics PhD Student
- Dr Nina Scott: Ngāti Whātua, Waikato Equity Advisor

This project would not have been possible without the support and guidance of our governance and advisory groups. We extend our sincere thanks to members for their time and invaluable contribution to this project.

STUDY ONE

REVIEW OF THE INCIDENCE, OUTCOMES AND TREATMENT FOR METASTATIC PROSTATE CANCER IN NEW ZEALAND

AIM

The aim of this study was to ascertain the patterns of dispensing ADT, including anti-androgens and luteinizing hormone-releasing hormone (LHRH) analogues, and chemotherapeutic agents in New Zealand men within the first year after prostate cancer diagnosis.

METHODS

A nationwide audit of androgen deprivation therapy and chemotherapy treatment for prostate cancer was undertaken. A cohort of men diagnosed with prostate cancer between 1 January 2006 and 31 December 2011 was identified from the New Zealand Cancer Registry (NZCR[a]). For each patient data extracted from the NZCR included date of diagnosis, extent of disease at diagnosis, age at diagnosis, and ethnicity. The extent of cancer at diagnosis is coded in the NZCR as follows: B (localised), C (invasion of adjacent tissues or organs), D (invasion of regional lymph nodes), E (distant metastases), and F (unknown). For the purpose of our study, C and D extent were grouped under the category "regional spread".

Only about one-quarter of prostate cancer cases have an extent at diagnosis listed in the NZCR. Prostate cancer is similar to bladder and liver cancer with respect to the low recording of extent at diagnosis. Although the proportion of incident prostate cancer cases with known extent at diagnosis slightly improved from 25.7% to 28.1% between 2006 and 2010, for further research into prostate cancer on national level it will be essential to at least achieve proportions of known extent similar to colorectal and breast cancer, where more than 80% of cases have known extent recorded.[1] The New Zealand Cancer Control Council is currently reviewing the reporting of all cancers in an effort to improve the availability of data in the NZCR, including extent at diagnosis.[2]

Data for the cohort of men identified from the NZCR were linked to the Pharmaceutical Collection by a unique encrypted number derived from the National Health Index (NHI) number, which is individually assigned for every public health system user in New Zealand. The Pharmaceutical Collection is an administrative claims database that contains information from pharmacists on dispensing subsidised medications. For this study, data were extracted on androgen deprivation therapy, including anti-androgens

[a] http://www.health.govt.nz/nz-health-statistics/national-collections-and-surveys/collections/new-zealand-cancer-registry-nzcr

(flutamide, bicalutamide, cyproterone) and LHRH analogues (goserelin, leuprorelin), and also on chemotherapeutic agents (doxorubicin, epirubicin, paclitaxel, mitozantrone, docetaxel). The information included chemical ID, indicating the primary active chemical ingredient, and the therapeutic group level 1-3[b].

Men with prostate cancer morphology not consistent with adenocarcinoma (67), men with unknown ethnicity (1478) and those diagnosed at death (374) were excluded from the analysis. In addition, 17 men were excluded because their domicile was listed as "overseas".

The frequency of ADT and chemotherapy use in the first year after the initial diagnosis was analysed by patients' age (<60 years, 60-69 years, 70-79 years, 80+ years), ethnicity (Māori, Pacific and non-Māori/non-Pacific), and extent of disease at diagnosis. Differences between distributions were tested using the chi-square or Fisher exact test (when sub-group sample sizes were small). Probability (p) values < 0.05 were considered to be statistically significant.

RESULTS

The final study population included 15,947 men diagnosed with prostate cancer in New Zealand in the six years between 2006 and 2011. Table 1 summarises the demographic information (age and ethnicity) by extent of prostate cancer at diagnosis.

Most men were diagnosed between the ages of 60 and 79 years (68.2%). There were 908 (5.7%) Māori men, 445 (2.8%) Pacific men, and 14,594 (91.5%) non-Māori/non-Pacific men in the sample. The proportion of Māori men in the 2006 Census total NZ male population of 50+ years (since most prostate cancer cases occur in men aged 50+) was 7%, while Pacific males comprised 3%, and non-Māori/non-Pacific men 90%.

In total, 15.0% of men were recorded as having localised extent at diagnosis, 7.6% regional spread, 5.8% metastases, and 71.7% were recorded with unknown extent.

Table 1 Demographic characteristics of men diagnosed with prostate cancer by extent of disease at diagnosis*

Extent at diagnosis	Localised (N=2385)	Regional spread (N=1205)	Metastatic (N=925)	Unknown (N=11,432)	Total (N=15,947)
Age at diagnosis	n (%)	n (%)	n (%)	n (%)	n (%)

[b] http://www.pharmac.health.nz/tools-resources/pharmaceutical-schedule

<60 years	836 (35.1)	305 (25.3)	58 (6.3)	1711 (15.0)	2910 (18.2)
60-69 years	1251 (52.5)	606 (50.3)	166 (17.9)	4271 (37.4)	6294 (39.5)
70-79 years	279 (11.7)	243 (20.2)	275 (29.7)	3782 (33.1)	4579 (28.7)
80+ years	19 (0.8)	51 (4.2)	426 (46.1)	1668 (14.6)	2164 (13.6)
Ethnicity					
Māori	83 (3.5)	61 (5.1)	80 (8.6)	684 (6.0)	908 (5.7)
Pacific	24 (1.0)	25 (2.1)	46 (5.0)	350 (3.1)	445 (2.8)
non-Māori/non-Pacific	2278 (95.5)	1119 (92.9)	799 (86.4)	10398 (91.0)	14594 (91.5)

*excludes prostate cancer morphology not consistent with adenocarcinoma, men with unknown ethnicity, those diagnosed at death, or domicile listed as "overseas"

Androgen deprivation therapy (flutamide, bicalutamide, cyproterone, goserelin, leuprorelin) or chemotherapeutic agents (doxorubicin, epirubicin, paclitaxel, mitozantrone, docetaxel) were dispensed for 4978 (31.2%) men in the first year following their initial diagnosis. Chemotherapeutic agents were dispensed only for 24 men (0.2%). Most of the patients received doxorubicin (11), with docetaxel being the second most common agent used (5).

Within the first year post-diagnosis, pharmacologic ADT was dispensed for 47 men with localised prostate cancer at diagnosis (1.9% of all men with localised disease recorded in the NZCR), 266 men with regional spread (22.1%) and 664 men with distant metastases (71.8%). Due to the small number and proportion of men with localised disease who received ADT within one year post-diagnosis, further analysis focused on patients with regional and metastatic prostate cancer.

The reporting of pharmaceutical data by district health boards was voluntary until July 2008, which may have affected data linkage in the first years of the study. However, the frequency of ADT use in the first year after diagnosis was 70.2% for men diagnosed with distant metastases in 2006-2007 and 70.9% for those diagnosed in 2009-2010. Figure 1 shows the frequency of types of pharmacologic ADT by age group, and extent of disease at diagnosis (regional spread, distant metastases, and all extent (including localised, regional, distant and unknown extent).

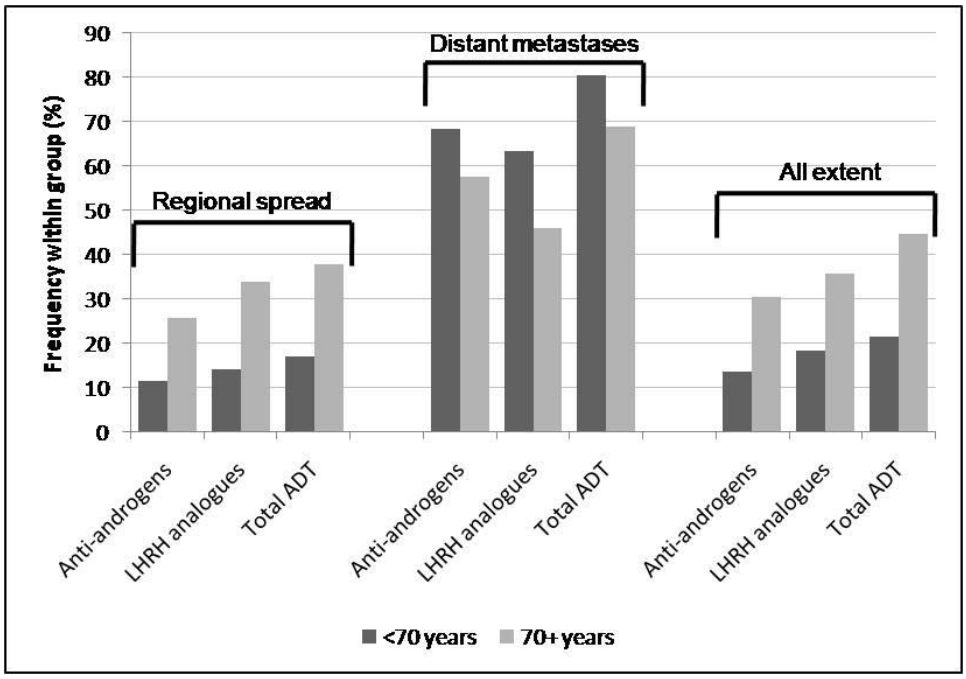

Figure 1 Frequency of types of pharmacologic ADT by age group and extent of disease at diagnosis (regional spread, distant metastases and all extent, including localised, regional spread, distant metastases and unknown).

In men with metastatic cancer, anti-androgens (60.1%) were used more commonly than LHRH analogues (50.1%; χ^2 p<0.0001). By contrast, overall (all extents), more patients received LHRH analogues (25.5%) than anti-androgens (20.6%; χ^2 p<0.0001) as did patients with regional spread (18.8% v. 14.8%; χ^2 p=0.008). Men diagnosed with metastatic cancer before the age of 70 were more likely to receive ADT than older men (80.4% v. 69.0%; χ^2 p=0.001).

ADT was less likely to be dispensed for non-Māori/non-Pacific men than for Māori and Pacific men (30.5% v. 38.5%; χ^2 p<0.0001, and v. 38.9%; χ^2 p<0.0001, respectively).

In men with advanced cancer, 53.2% (out of all men on ADT) received both anti-androgens and LHRH analogues within the first year post-diagnosis, followed by those who received anti-androgens only (25.8%) and those who received LHRH analogues only (21.0%). Table 2 shows the distribution of anti-androgens and LHRH analogues use individually and in combination in men with advanced disease.

Table 2 Proportion of types of ADT in men with advanced cancer by age and ethnicity.

Therapy	N	Anti-androgens n (%)	LHRH analogues n (%)	Anti-androgens plus LHRH analogues

				n (%)
Age at diagnosis				
<70 years	335	65 (19.4)	79 (23.6)	191 (57.0)
70+ years	595	175 (29.4)	116 (19.5)	304 (51.1)
Ethnicity				
Māori	77	20 (26.0)	9 (11.7)	48 (62.3)
Pacific	46	15 (32.6)	3 (6.5)	28 (60.9)
non-Māori/non-Pacific	807	205 (25.4)	183 (22.7)	419 (51.9)
Total	930	240 (25.8)	195 (21.0)	495 (53.2)

A significantly larger proportion of men older than 70 years at diagnosis received anti-androgens only compared with men younger than 70 (29.4% v. 19.4%; Fisher exact test p=0.001). Non-Māori/non-Pacific men were more likely to received LHRH analogues only compared with Māori and Pacific men (22.7% v. 11.7%; Fisher exact test p=0.03, and v. 6.5%; Fisher exact test p=0.009, respectively).

DISCUSSION

The aim of this study was to assess the frequency of use of ADT and chemotherapeutic agents for NZ men in the first year after cancer diagnosis, particularly for metastatic patients for whom ADT should be prescribed immediately.[3]

Seventy two percent of men recorded as having metastatic disease at diagnosis received pharmacologic ADT (anti-androgens and/or LHRH analogues). Whilst a small number of men with prostate cancer had an orchidectomy (2%), it seems that a quarter of men with advanced prostate cancer did not receive hormonal treatment. Since management guidelines for locally advanced and particularly metastatic prostate cancer clearly include use of androgen deprivation therapy as part of the treatment pathway[4,5], there is a need for improvement in this area in New Zealand. In comparison, in the USA 95% patients diagnosed between 1994 and 2002 with stage IV disease received either surgical or pharmacologic ADT, while 16% received chemotherapy.[6] Men with advanced prostate cancer were more likely prescribed both anti-androgens and LHRH analogues in the first year as opposed to anti-androgens or LHRH analogues alone.

In NZ men with advanced prostate cancer, chemotherapeutic agents were used very rarely in the first year post-diagnosis. Only five men received docetaxel and 11 men received doxorubicin. Some of the chemotherapeutic agents, such as docetaxel were first subsidised in 2011, so they would not appear in the Pharmaceutical Collection previously.

It seems that both pharmacologic ADT and chemotherapy is under-utilised in New Zealand patients with advanced prostate cancer. Data from other countries show that physician preference has an important influence on the use of ADT[7], as do the presence of subsidies[8], patient's age and tumour grade at diagnosis.[9] Thus the solution to improved dispensing is likely to involve a greater understanding of the barriers to prescribing from the physicians' perspective but also of patients' views on ADT use.

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STUDY TWO

THE MANAGEMENT AND COSTS OF METASTATIC PROSTATE CANCER IN A COHORT OF NEW ZEALAND MEN

AIM

As has been noted the New Zealand Cancer Registry Data rarely records the stage of diagnosis. Therefore, to understand the management of metastatic prostate cancer it would be useful to identify a population-based cohort where all men have been staged. This study based in the Midland Cancer Network (MCN) region aimed to describe men diagnosed with metastatic prostate cancer and reconstruct the management of their disease. We planned to investigate the outcomes for men and estimate the costs across the management pathway.

METHOD

Eligible patients

We identified patients diagnosed with prostate cancer in the Midland Cancer Network Region between 1 January 2009 and 31 December 2012 from the New Zealand Cancer Registry (NZCR). The NZCR is a population-based tumour registry whose primary function is to collect and store cancer incidence data. From this database, we received the National Health Index number (NHI) of each man registered with prostate cancer during the requested period. The NHI number is a unique identifier that is assigned to every person who uses health and disability support services in New Zealand. In addition to the NHI, we received the recorded ethnicity, place of residence and date of birth for each of these men.

Approximately 75%-80% of prostate cancers are un-staged on the national register (NZCR). To correctly identify men who were metastatic within our cohort, we sought access to public and private hospital and specialist medical files for each identified patient. Every man was staged through a clinical file review where we recorded necessary staging information from both the diagnosis and treatment phases. Recorded data included: Prostate-specific antigen tests (PSA), digital rectal examination (DRE) scores, primary and secondary Gleason scores, imaging results and clinical staging. For patients whose clinical or pathological reports did not specify the cancer extent, their records were examined by an urologist to identify the cancer extent at diagnosis. Patients whose cancer extent at diagnosis could not be identified were excluded. We included patients who had metastatic disease in 2009-2012 in this study.

Treatment pattern and survival

Dates of all tests and treatments were recorded to ensure accuracy of diagnosis date. The date of death was extracted from the Mortality Collection (MORT) which classifies the underlying cause of death for all deaths registered in New Zealand. The medication type and dispensing date were extracted from the national Pharmaceutical Information Database (PHARMS). PHARMS records claim and payment information from pharmacists for all subsidised dispensed medications. PSA values and dates were provided by Pathlab; a pathology service that provides medical testing within the Midland region. PSA at diagnosis included the PSA test nearest to the diagnosis date, i.e., within 3 months. We identified the role of the physician who prescribed ADT and/or chemotherapeutic agents from the clinical files, and added this information to the PHARMS dataset. The censored date in the PHARMS dataset was 31 December 2012. Overall this was the censor date for the study.

We examined the characteristics of the eligible patients, including age, ethnicity (Māori/Pacific, non-Māori/non-Pacific), and PSA level. The approaches to ADT in New Zealand included orchiectomy, anti-androgens (flutamide, bicalutamide and cyproterone) and luteinizing hormone-releasing hormone (LHRH) agonists (goserelin, leuprorelin). The pattern of ADT for metastatic cancer was examined, including the characteristics of men treated with ADT, the time from the metastatic diagnosis to the first ADT prescription, and the identification of clinicians who initiated prescribing ADT. We also characterised patients who had an orchiectomy or radiotherapy to treat metastatic complications and those who subsequently had chemotherapy (doxorubicin, epirubicin, paclitaxel, mitozantrone, docetaxel).

We believe the outcomes for men treated with ADT is of interest in understanding the use of ADT survival was measured in months, from the date of metastatic diagnosis to the date of death. Men were censored if they were alive by the date of 31 December 2012. The all-cause survival of patients with metastatic cancer was estimated by the Cox proportional hazards model with adjustment for patients' age and ADT use.

Cost estimation

To identify hospital events and pharmaceutical information for eligible patients, we linked our dataset with the National Non-Admitted Patient Collection (NNPAC), National Minimum Dataset (NMDS) and the PHARMS through patients' NHI numbers. NNPAC collects national records for outpatient and emergency department events (we identified them as outpatient events in this study) and NMDS includes clinical data for inpatients and day patients (inpatient events). The pharmaceuticals used for metastatic prostate cancer included anti-androgen therapies, LHRH analogs,

bisphosphonate (alendronate sodium, etidronate disodium, zoledronic acid and pamidronate disodium), chemotherapeutic agents, antidepressants (amitriptyline, citalopram hydrobromide, dothiepin hydrochloride, doxepin hydrochloride, fluoxetine hydrochloride, moclobemide, paroxetine hydrochloride and venlafaxine), urinary agents (finasteride, oxybutynin, solifenacin succinate and tamsulosin hydrochloride) and alpha adrenoceptor blockers (doxazosin mesylate and terazosin hydrochloride). Bisphosphonate is used for patients who are under the risk of having fractures after ADT. Urinary agents and alpha adrenoceptor blockers are used to treat urinary problems.

Table 3 Phase time distributed to different phases[c].

Patient died during the follow-up period	Length of phase time	Diagnostic phase	Treatment phase	Death phase
Yes	≤ 3 months	/	/	All the follow-up time
	(3,6] months	The follow-up time excluding the last three months	/	The last three months prior to patient's death
	> 6 months	The first three months after the metastatic diagnosis	The time between the diagnostic and death phase	The last three months prior to patient's death
No	≤ 3 months	All the follow-up time	/	/
	> 3 months	The first three months after the metastatic diagnosis	The follow-up time excluding the first three months	/

The follow-up time was measured from the date of metastatic diagnosis to the date of death or the censor date. We divided the treatment pathway into three phases: diagnostic phase, treatment phase and death phase[1]. The death phase was the last three months prior to patient's death. The diagnostic phase was the first three months after the metastatic diagnosis. The treatment phase consisted of the time from the end of the diagnostic phase to the beginning of the death phase. The follow-up time was first distributed to the death phase, then to the diagnostic phase and finally to the treatment phase. The detailed principles of how to distribute patients' follow-up time are shown in Table 3. Though there are other ways of breaking down patients' follow-up time[2], the three-phases method was the most suitable one for our study because the follow-up time for these patients varied greatly.

[c] Note: Eight patients died during the period from 1 January 2013 to 31 March 2013 (within 3 months from the censor date for this study). For these eight patients, the last 3 months prior to patients' death (excluding the time in 2013) were distributed to the death phase. Since we have survival data till 6 months after the censor date in the three datasets, there was no follow-up time that should be recorded at the death phase was distributed to the treatment phase.

The estimated costs excluded goods and services tax (GST) and were valued in 2012/13 New Zealand dollars (NZ$). The costs were not discounted in this study, because discounting would lead to difficulties in assessing the costs during the three phases. Half of the patients in our cohort died within 12 months. Not discounting the costs incurred in the following years (after the first year of metastatic diagnosis) would not bias the results significantly.

Although we considered events in oncology, urology and palliative care (OUP) are more relevant to metastatic prostate cancer, it is difficult to identify in all cases which hospital events were associated with metastatic prostate cancer (and its complications) and which events are unrelated. Therefore, we did two cost estimations: 1) the overall healthcare costs; 2) the costs associated with the management of prostate cancer - pharmaceuticals and events in oncology, urology and palliative care (POUP) costs. Only the events in public hospitals and subsidised pharmaceuticals were included in the estimation. The pharmaceutical costs in this study included the drug cost, mark-up and dispensing fees[3]. Events in private hospitals and general practices, and patients' contributions in pharmaceutical costs were not considered. The inpatient costs were estimated by multiplying the accumulated cost weights for all events with the purchase unit price (NZ$ 4,614.36 in 2012/13). The cost weights which provide resource utilisation information are calculated by the Ministry of Health for each DRG code using the Weighted Inlier Equivalent Separation (WIES) method, and a purchase unit price is set each year[4]. We linked the outpatient events with the unit cost of each event (in 2012/13) through the purchase unit codes and computed the aggregate outpatient costs. The unit costs for outpatient events were provided by the Waikato District Health Board. The pharmaceuticals identified were all fully subsidised in 2012/13. Therefore, the subsidies which were available in Pharmaceutical Schedule[5] were equal to the drug cost. Pharmaceutical mark-up is 4% of the drug cost when it is below NZ$150 or 5% of the drug cost when it exceeds NZ$150[3]. We used a NZ$5.30 dispensing fee for all pharmaceuticals, as recommended by PHARMAC[6].

The medical costs and the POUP costs during the three phases were estimated by age group (<60, 60-69, 70-79, 80+) and ethnicity (Māori/Pacific, non-Māori/non-Pacific). The differences in the medical costs and the POUP costs among different subgroups were examined by Kruskal-Wallis test and Mann-Whitney U test. The Jonckheere-Terpstra test was used to identify whether there was any trend in the costs among the four age groups.

The medical costs and the POUP costs during the treatment phase were log-transformed (natural logarithm) to examine their correlation with phase time and age

group (<80, 80+) by ordinary least-squares regression. The reason why we used the two age groups (<80, 80+) instead of the four age groups (<60, 60-69, 70-79, 80+) was that the pearson correlation showed that the difference in the costs during the treatment phase between the two age groups (<80, 80) was more significant (p<0.001).

RESULTS

Characteristics of the eligible men

Two thousand, one hundred and twenty seven men had a diagnosis of prostate cancer in the Midland Cancer Network region during the period between 2009 and 2012. Māori and Pacific men accounted for 9.1% (193/2127) of these registrations. Among these men, 234/2127 (11%) were found to have metastatic prostate cancer in 2009-2012 - 26/193 (13.5%) of Māori/Pacific men and 208/1934 (10.8%) of non-Māori/non-Pacific men. The characteristics of the eligible patients are shown in Table 4. The mean age of the patients was 75 years at metastatic diagnosis. The mean age of the Māori/Pacific (72 years) men was lower compared to non-Māori/non-Pacific (76 years). The proportion of Māori/Pacific men diagnosed with metastatic cancer at the age of < 70 years old was 38.5% compared with 28.8% for non-Māori/non-Pacific.

Table 4 Characteristics of eligible men.

	Māori/Pacific (26)	non-Māori/non-Pacific (208)	Total (234)
Age			
<60	2 (7.7%)	15 (7.2%)	17 (7.3%)
60-69	8 (30.8%)	45 (21.6%)	53 (22.6%)
70-79	7 (26.9%)	66 (31.7%)	73 (31.2%)
80+	9 (34.6%)	82 (39.4%)	91 (38.9%)
PSA level within 3 months before or after the metastatic diagnosis			
<10	2 (9.1%)	22 (15.2%)	24 (14.4%)
10~20	1 (4.5%)	10 (6.9%)	11 (6.6%)
20~100	6 (27.3%)	36 (24.8%)	42 (25.1%)
100~1000	8 (36.3%)	57 (39.3%)	65 (39.0%)
≥1000	5 (22.7%)	20 (13.8%)	25 (15.0%)
No PSA test	4	63	67

The PSA level at metastatic diagnosis is shown in Table 5. Of the PSA values at metastatic diagnosis, 79.1% were ≥20 ng/ml, 54.4% were ≥100 ng/ml, and 15.0%

were ≥1000 ng/ml. Māori/Pacific men with metastatic cancer were more likely to have a PSA level of ≥1000 ng/ml (22.7%) and less likely to have a PSA result of <20 ng/ml (13.6%) compared with non-Māori/non-Pacific (13.8% and 22.1%, respectively).

Table 5 Characteristics of patients treated.

	Number of patients	Radiotherapy	ADT	Chemotherapy
Ethnicity				
Māori/ Pacific	26	13 (50.0%)	21 (80.8%)	0
non-Māori/non-Pacific	208	82 (39.4%)	173 (83.2%)	5 (2.4%)
Age				
<60	17	12 (70.6%)	16 (94.1%)	1 (5.9%)
60-69	53	27 (50.9%)	48 (90.6%)	2 (3.8%)
70-79	73	26 (35.6%)	62 (84.9%)	2 (2.7%)
80+	91	30 (33.0%)	68 (74.7%)	0
Total	234	95 (40.6%)	194 (82.9%)	5 (2.1%)

Treatment for patients with metastatic prostate cancer

After the metastatic diagnosis, 194/234 (82.9%) of patients received anti-androgens or LHRH agonists. Two patients subsequently underwent orchiectomy after pharmacological ADT. Five men had chemotherapy (all were treated with docetaxel). To treat the complications caused by the metastatic cancer, 104/234 (44.4%) had radiotherapy. Among the 21 patients whose follow-up time was less than one month (either because of death or being censored), only seven (33.3%) received ADT. The characteristics of patients on different treatments are displayed in Table 5. Māori/Pacific men were no less likely to have radiotherapy (RR: 1.27 (95%CI: 0.83-1.93)) or to receive ADT (RR: 1.14 (95%CI: 0.49-2.66)), compared to non-Māori/non-Pacific men. The possibility of having radiotherapy decreased with age, from 70.6% for men aged <60 to 33.0% for men aged 80+. A similar pattern was found for men on ADT, from 94.1% for men aged <60 to 74.7% for men aged 80+. The two men who received an orchiectomy were both over 70 years at the time of treatment. The five patients who had chemotherapy were all non-Māori/non-Pacific men aged less than 80 years.

Table 6 The first ADT after the metastatic diagnosis, by department prescribed.

Department	Bicalutamide	Cyproterone acetate	Flutamide	Goserelin acetate	Leuprorelin	Combined androgen blockade	Total (n)
Oncology	2 (6.5%)	5 (16.1%)	2 (6.5%)	11 (35.5%)	0	11 (35.5%)	31
Urology	8 (5.8%)	40 (28.8%)	39 (28.1%)	11 (7.9%)	26 (18.7%)	15 (10.8%)	139
Others	1 (6.3%)	7 (43.8%)	3 (18.8%)	0	3 (18.8%)	2(12.5%)	16
Unknown	1 (12.5%)	2 (25.0%)	3 (37.5%)	1 (12.5%)	1 (12.5%)	0	8
Total	12 (6.2%)	54 (27.8%)	47 (24.2%)	23 (11.9%)	30 (15.5%)	28 (14.4%)	194

The pharmacological ADT type first prescribed after metastatic diagnosis and what type of clinician prescribed the first pharmacological ADT is presented in Table 6. Of the 194 patients on ADT, the most common first prescription was cyproterone acetate (27.8%). The proportions of other drugs prescribed first for metastatic prostate cancer patients included: flutamide (24.2%), leuprorelin (15.5%), goserelin (11.9%), combined androgen blockade (CAB) (14.4%) and bicalutamide (6.2%). The first pharmacological ADT course was predominantly prescribed by urologists (74.7%). Urologists were more likely to prescribe anti-androgens as the first pharmacological ADT (62.6%), whilst oncologists were more likely to prescribe LHRH agonists and CAB (71.0%). The timeframe from diagnosis to first pharmacological ADT was relatively short with most patients (72.2%) starting their first course of pharmacological ADT within 4 weeks. Of the 194 men with pharmacological ADT, 73.7% (143/194) switched to a different medication at some stage while only five (2.4%) were treated with docetaxel.

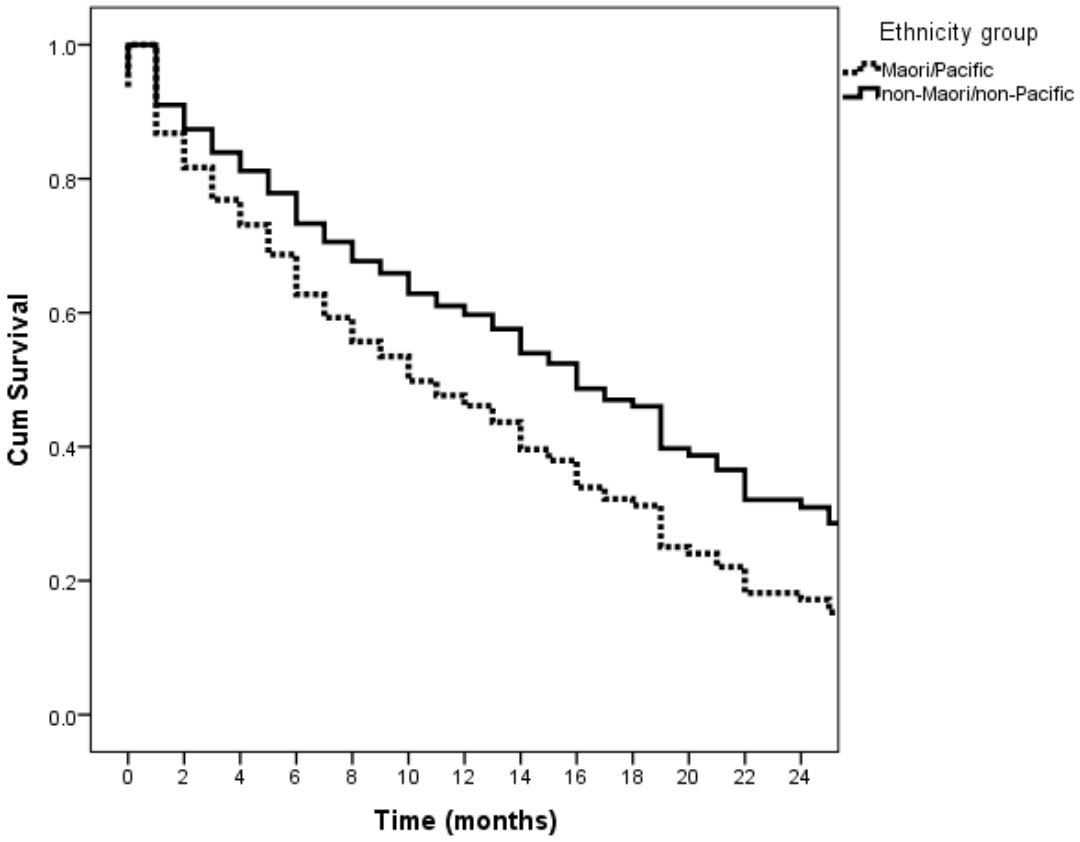
The number of PSA tests for men treated with pharmacological ADT in 12 months after the metastatic diagnosis is shown in Table 7. No PSA test was recorded for 46 (24%) patients, whilst 80 (41%) had three or more tests. Thirty men were recorded as having a serum testosterone measured.

Table 7 Number of PSA tests for patients on ADT in 12 months after the metastatic diagnosis.

Follow-up time	0	1	2	3	4+	Total
1-90 days	16	7	3	0	0	26
91-180 days	7	8	5	3	2	25
181-270 days	7	3	2	4	6	22
271-360 days	0	2	5	5	7	19
>360 days	16	14	19	11	42	102
Total	46	34	34	23	57	194

Survival in men with metastatic prostate cancer

Figure 2 All-cause survival by ethnicity by Cox proportional hazards model.



We found 134/234 men had deceased by 31 December 2012. The all-cause survival curve by ethnicity from the Cox proportional hazards model is displayed in Figure 2 and shows that survival for non-Māori/non-Pacific was superior. Māori/Pacific patients had 1.49-fold (95% CI: 0.89-2.49) risk of death in comparison with non-Māori/non-Pacific patients after adjustment for patient's age and ADT use. Patients who did not receive ADT were 4.29-times (95% CI: 2.73-6.75) more likely to die than patients who were on ADT after adjustment for patient's age and ethnicity. Older patients were more likely to die than younger patients were (hazard ratio: 1.04, 95% CI: 1.02-1.06) after adjustment for ethnicity and ADT use.

Costs of metastatic prostate cancer

After each patient's pathway had been divided into the three phases, 197 patients had phase time during the diagnostic phase, 162 patients during the treatment phase and 141 patients during the death phase (Table 8). The average phase time was 82 days

during the diagnostic phase, 406 days during the treatment phase and 75 days during the death phase.

Table 8 Average costs during the three phases by age group and ethnicity.

	Number of patients	Average phase time (days)	Average medical costs	Average POUP costs
By age group				
Diagnostic phase				
All patients	197	82	$5,576	$2,427
<60	17	85	$4,188	$3,020
60-69	47	88	$5,758	$3,192
70-79	66	82	$4,341	$2,443
80+	67	77	$7,016	$1,724
p value*			0.282	0.003
p value†			0.383	0.002
Treatment phase				
All patients	162	406	$13,428	$7,130
<60	15	619	$18,560	$14,805
60-69	42	434	$14,067	$8,953
70-79	54	431	$15,482	$7,439
80+	51	292	$9,219	$3,044
p value*			0.21	<0.001
p value†			0.011	<0.001
Death phase				
All patients	141	75	$10,558	$4,305
<60	5	78	$15,867	$13,403
60-69	21	80	$17,027	$9,282
70-79	47	81	$10,314	$4,182
80+	68	70	$8,339	$2,184
p value*			0.001	<0.001
p value†			<0.001	<0.001
By ethnicity				
Diagnostic phase				
All patients	197	82	$5,576	$2,427
Māori/Pacific	23	78	$5,398	$1,132
Non-Māori/Non-Pacific	174	83	$5,599	$2,598
p value‡			0.079	0.065
Treatment phase				
All patients	162	406	$13,428	$7,130
Māori/Pacific	18	374	$10,369	$7,516
Non-Māori/Non-Pacific	144	410	$13,811	$7,081
p value‡			0.464	0.831
Death phase				
All patients	141	75	$10,558	$4,305
Māori/Pacific	17	76	$9,871	$4,278

Non-Māori/Non-Pacific	124	75	$10,653	$4,309
p value‡			0.582	0.773

Medical costs: the overall healthcare costs; POUP costs: the costs of pharmaceuticals and events in OUP
* Kruskal-Wallis test †Jonckheere-Terpstra test ‡Mann-Whitney U test

The average medical costs for these men were $5,576 (average POUP costs: $2,427) during the diagnostic phase, $13,428 (average POUP costs: $7,130) during the treatment phase and $10,558 (average POUP costs: $4,305) during the death phase (Table 8). The POUP costs during the three phases decreased with age: from $3,020 for men aged <60 to $1,724 for men aged 80+ during the diagnostic phase (p=0.002); from $14,805 for men aged <60 to $3,044 for men aged 80+ during the treatment phase (p<0.001); and from $13,403 for men aged <60 to $2,184 for men aged 80+ during the death phase (p<0.001). The medical costs during the death phase also decrease with age, from $15,867 for men aged <60 to $8,339 for men aged 80+ (p<0.001). There was no significant difference in either the medical costs or the POUP costs between Māori/Pacific men and non-Māori/non-Pacific men.

The proportion of each cost element in POUP costs is shown in Figure 3. Overall, the inpatient costs accounted for the largest proportion (46.4%) in POUP costs, followed by the outpatient costs (32.1%) and pharmaceutical costs (21.5%). The proportion of each cost element in POUP costs differed in the three phases. The proportion of inpatient costs in POUP costs was highest during the death phase (76.6%), and lowest during the diagnostic phase (31.1%). The percentage of pharmaceutical costs in POUP costs experienced the reversed pattern: lowest during the death phase (7.3%), and highest during the treatment phase (29.0%). ADT cost comprised 95.3% (anti-androgens: 6.8%; LHRH analogs: 88.5%) of total pharmaceutical costs. Docetaxel was the only chemotherapeutic agent identified in the PHARMS for these patients. It only accounted for 2.5% of the total pharmaceutical costs.

Figure 3 The proportion of each cost element in POUP costs.

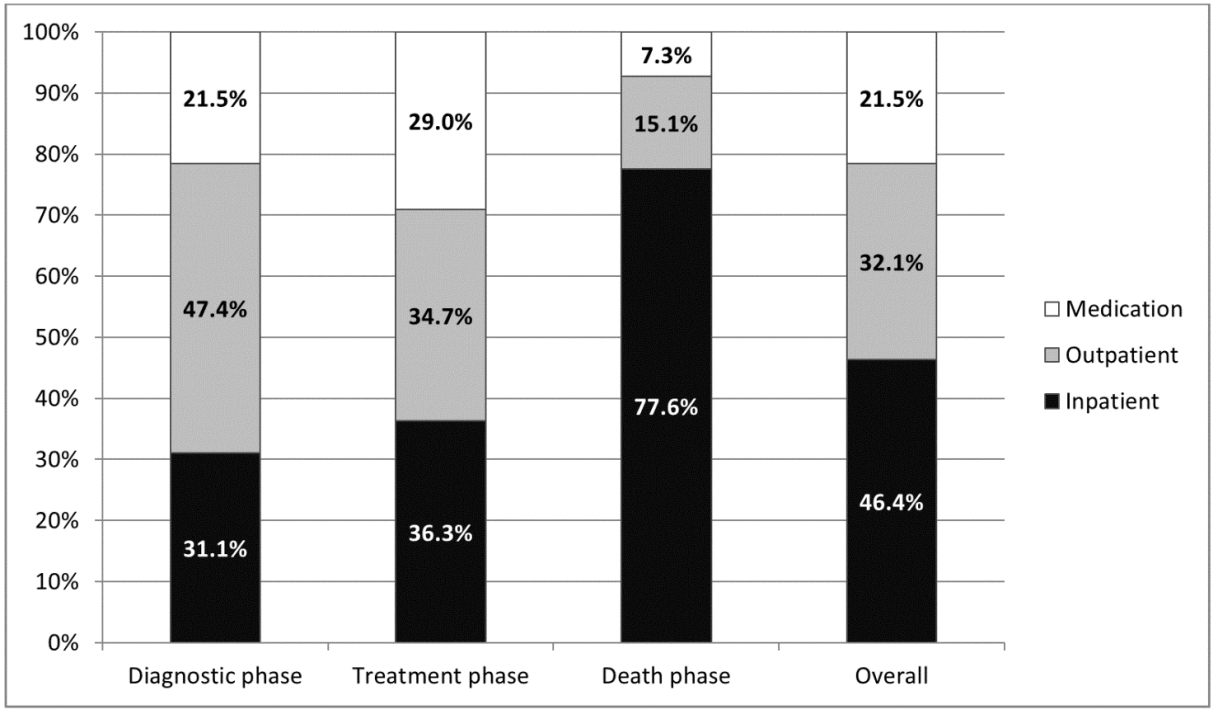
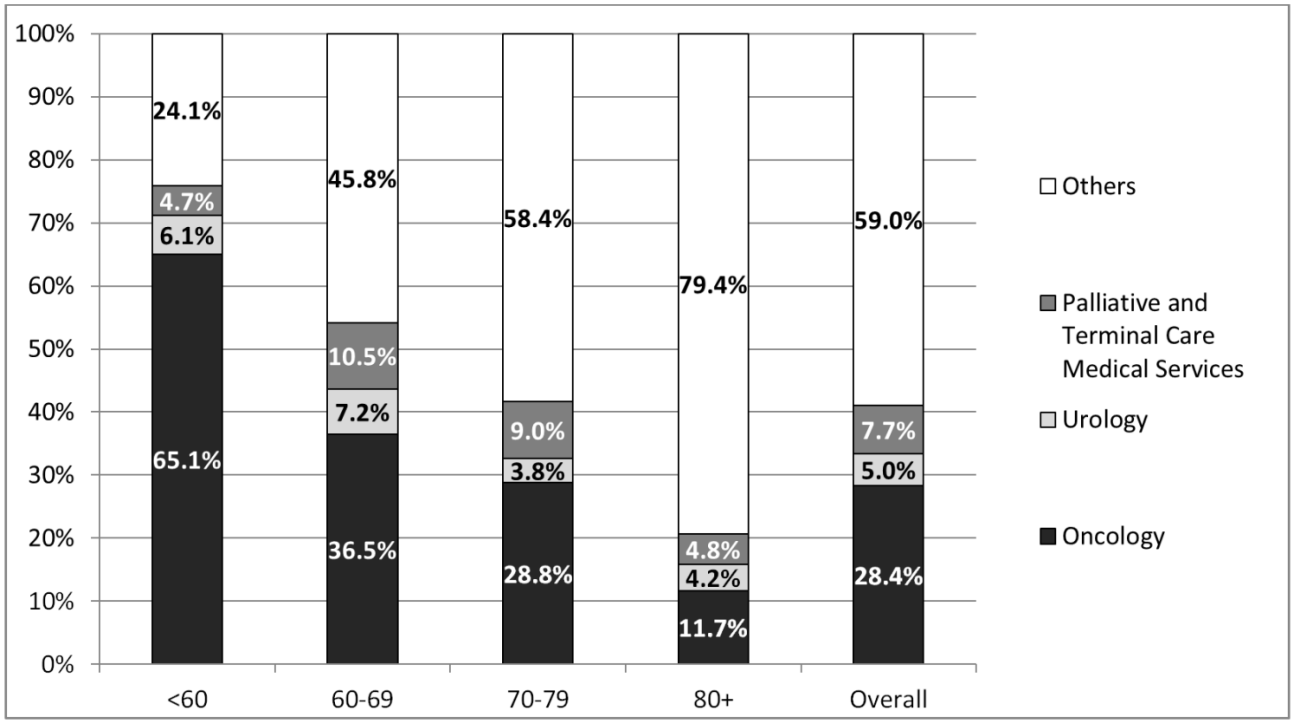


Figure 4 displays the proportion of cost in different health specialties in total hospital costs. Approximately 28.4% of the hospital costs incurred in oncology, 5% was associated with the services in urology, and 7.7% was for palliative and terminal care services. The proportion of oncology cost in total hospital costs decreased with age, from 65.1% for men aged <60 to 11.7% for men aged 80+. In contrast, the percentage of hospital costs in other specialities (other than oncology, urology and palliative care) in total hospital costs increased with age, from 24.1% for men aged <60 to 79.4% for men aged 80+.

Figure 4 The proportion of hospital costs incurred in each health specialty in total hospital costs by age group.



The results from the ordinary least-squares regression model were transformed into formulas to predict the medical costs and the POUP costs during the treatment phase (Table 9). The medical costs and the POUP costs during the treatment phase for men aged <80 would be twice and three times, respectively, the costs for men aged 80+, when the phase time is the same. The medical costs would double every 231 days and the POUP costs would double every 173 days.

Table 9 Formulas to predict the costs during the treatment phase.

Costs	Age group	Formula
Medical costs	<80	$C=1312\times e^{0.003T}$
	80+	$C=619\times e^{0.003T}$
POUP costs	<80	$C=431\times e^{0.004T}$
	80+	$C=146\times e^{0.004T}$

C: costs
T: phase time during the treatment phase
Medical costs: the overall healthcare costs;
POUP costs: the costs of pharmaceuticals and events in OUP

DISCUSSION

Characteristics of men with metastatic prostate cancer

We found in this sample 11% of men presented with metastatic prostate cancer. This is a greater proportion than has been found to have Stage IV disease in a USA study using the SEER data (6.4%)[7] or a similar study from Spain (4%)[8]. Both these countries have a high utilisation of PSA testing and therefore an increasing proportion of men with low risk prostate cancer at diagnosis. The prevalence of 11% is significantly lower than the proportion found in Scandinavia where PSA testing is less widespread[9].

While the mean age of men diagnosed with prostate cancer in NZ is 68 years (during 2010), the mean age of men presenting with metastatic cancer is 75. We identified 17 out of 2127 men aged < 60 years (0.8%) who presented with metastatic disease. This is a small but important group of men who would have a substantial life expectancy if not for their cancer. We noted (as have other studies) that Māori/Pacific men were more likely to present with metastatic disease and generally had higher PSA levels at diagnosis[10].

Treatment and Management

We had found that most of the men diagnosed with metastatic disease (83%) are treated with ADT. We do not have the reasons for why 17% of men were not treated with ADT. Some of these men might have developed CRPC before the metastatic diagnosis. We have shown that increasing age reduces the likelihood of pharmacological ADT being initiated. Only one-third of men who died within the first month post-metastatic diagnosis had begun treatment. A study from the US has suggested that only 11% of stage 4 prostate cancer patients were not treated compared with a quarter of stage 4 lung or kidney cancer patients who are not treated[11]. Our results show fewer men receive treatment than in the USA but age and prognosis seem to be important indicators of reduced likelihood of active treatment. It is also noteworthy that the use of radiotherapy presumably for the treatment of bony metastases and pain seems to reduce with increasing age in our cohort.

While pharmacological ADT is commonly used to treat NZ men with metastatic prostate cancer a number of treatments seem to be used as first line. Orchiectomy which was a common first line treatment is now rarely used in the Midland Cancer Network Region of New Zealand although it is still used in the Southern Cancer Network Region[12] and is a recommended option by UK NICE 2014[13]. Androgen antagonists such as cyproterone or flutamide are commonly used as first line treatment especially by urologists. In contrast, radiation oncologists use LHRH more frequently, while a small proportion of patients are started on combined androgen

blockade. The evidence for the use of these different agents is now dated and could be considered as unreliable[14,15].

There seems to be little demonstrable difference between cyproterone and flutamide with regards to survival and side effects although toxicity is said to be more pronounced with flutamide[16]. Bicalutamide is preferred by some as it is longer acting[17] and for those who are willing to accept the adverse impact on overall survival and gynaecomastia in the hope of retaining sexual function it may be used as monotherapy[13]. LHRH antagonists are longer acting and equally effective as anti-androgens[18] – indeed they are considered marginally superior by NICE. In certain conditions such as in the presence of bony metastases, anti-androgens may be given for a short period to reduce the risk of flare that can be caused by LHRH antagonists. One of the issues in the use of various LHRH antagonists is cost and there is a suggestion that leuprorelin as a Depo treatment is the most cost effective LHRH formulation[19].

Combined androgen blockade has been suggested as more effective than monotherapy but is not recommended as first line therapy by NICE 2014. Overall, there is little to choose between the different treatments with regard to improved life expectancy, so costs and patient tolerability become very relevant. It also seems that physician preference is a factor with notable differences between the treatments used by urologists compared with radiation oncologists. However, it may be due to the differences in the patient mix (different characteristics) seen by different specialists.

We have shown that chemotherapy is rarely used with only 2.4% of patients being offered docetaxel[12]. Chemotherapeutic agents are usually used as second or third line treatments in the presence of CRPC. The definition of CRPC is not specific but is usually characterised by rising PSA levels, the development of further metastasis or increasing symptoms. In a review of studies looking at the prevalence of CRPC, it was shown between 9.5% and 53% of men who had undergone medical or surgical castration had CRPC[20]. It should be noted that many of these studies were on men treated for localised or locally advanced disease. However, it is well recognised that many men treated with ADT will progress to CRCP. It would seem to be reasonable that these men are monitored with PSA and when indicated imaging such as CT or bone scans. When men with prostate cancer develop evidence of hormone-refractory disease it is suggested that their treatment options should be discussed by the urological cancer multidisciplinary team. Those with CRCP could be considered for review by a medical oncologist and either more intensive ADT therapy[21] or chemotherapy[22]. We have noted that 24% of men treated with ADT did not appear to be monitored with PSA. We also noted a significant proportion of men switched ADT therapies although we do not have

the reason for switching but it is likely to be linked to tolerability and effectiveness. We did not find evidence of other biomarkers (other than PSA test) being used to monitor treatment although 30 men did have testosterone levels measured. There does seem to be scope for guidelines in the monitoring of men on ADT with both bio markers and imaging in order to identify early evidence of CRPC and to ensure the most effective treatments are offered. It appeared that medical oncologists are rarely involved in the management of men with advanced prostate cancer. Our data showed that only 1% of the pharmacological ADT agents were prescribed by medical oncologists.

Survival

Our study of survival of men presenting with metastases has shown poor survival of this group of men. We have shown that only 50% of these men will survive 12 months and 30% 2 years. These findings are considerably worse than data from overseas – in the UK 80% of patients with metastatic prostate cancer survive one year and 60% 2 years[23]. Survival is poorer for older men and those with high PSA levels at diagnosis. The poorer prognosis in older men is likely due to not only the presence of age related comorbidities but also the decreasing use of ADT and radiotherapy for treatment in older men. We have also shown that those treated with ADT have better survival. This is probably a reflection of prescribing bias where patients who have a very poor prognosis are less likely to be offered active treatment. Survival is worse for Māori/Pacific men compared with non-Māori/non-Pacific despite their younger age. Māori/Pacific men tend to present with higher PSA levels and higher grade of disease.

Costs

The average medical costs for these men were $5,576 (average POUP costs: $2,427) during the diagnostic phase, $13,428 (average POUP costs: $7,130) during the treatment phase and $10,558 (average POUP costs: $4,305) during the death phase. This study showed that the average medical costs and the average POUP costs during the death phase were about twice the costs during the diagnostic phase where the average phase time was similar. It might be ascribed to the expensive medical services for end-stage patients, e.g., palliative radiotherapy and inpatient hospitalisation. Changes in the treatment pattern for metastatic prostate cancer will alter the estimated results. The financial impact of new treatment options can be measured by comparing the costs of new treatments with the costs of the base-case scenario.

The inpatient costs accounted for the largest proportion (46.4%) in POUP costs, followed by the outpatient costs (32.1%) and pharmaceutical costs (21.5%). The composition of costs was different from that in a Netherland study where only 3% of the costs were for outpatient services and 84% of the costs were for treatment and

hospital stay[24]. The Netherland study was based on data in the 1990s. The differences in the results between the Netherland study and our study may be ascribed to the evolving management pattern for metastatic prostate cancer.

The POUP costs decreased with age during the three phases. We found that the proportion of OUP costs in total hospital costs also decreased with age, especially the oncology cost, from 65.1% for men under the age of 60 to 11.7% for men aged 80 or over. If patients mainly received treatments for metastatic prostate cancer and its complications in the OUP departments, younger patients received more treatments for metastatic prostate cancer than older patients.

Chemotherapy was rarely used for metastatic prostate cancer in New Zealand, though its effect in survival for patients with CRPC has been proven[25]. If chemotherapy is more commonly used for metastatic prostate cancer, the treatment phase where the cost per patient day was the lowest would be prolonged. Though chemotherapy is expensive, the additional cost added to the cost per patient day will be absorbed over a longer time period. Wider use of chemotherapy in treating CRPC is unlikely to increase the average daily cost significantly.

Strengths and weakness

As mentioned the staging of prostate cancer is rarely available in the NZCR. There would have been fewer patients eligible for this study if we had only included patients whose cancer stage was metastatic in the NZCR. One of the strengths of our study was that the clinical records of men were examined to identify the cancer stage and date of diagnosis. More patients diagnosed with metastatic prostate cancer in 2009-2012 were identified, with complete data on metastatic disease recorded directly from clinical records. These data have been linked to prescribing, mortality data and coting data. A weakness is that the study has been carried out in a region of New Zealand that may not be representative of other regions. However, we have shown elsewhere that the differences between regions are not large[10,26].

CONCLUSION

Overall we note that metastatic disease is still commonly diagnosed at presentation in New Zealand and that the survival in these patients is substantially worse that would be expected from overseas comparisons. The incidence of metastatic disease is greater in Māori as its mortality compared to non-Māori. The use of different formulations of ADT is noteworthy as is the lack of consistency of monitoring for CRPC. There seems to be a strong case for the development of New Zealand guidelines on the management of metastatic disease including the use of first line treatments and the need for ongoing

monitoring for the development of CRPC. We also believe there is a need for consistent action in the assessment of men who develop CRPC with assessment by a multidisciplinary team and improved access to chemotherapeutic agents. It would seem probable that better management of this group of patients could offer substantial improvements in outcomes.

The management costs for patients with metastatic prostate cancer varied by phase, with the death phase being the most expensive. The costs of treating metastatic prostate cancer decreased with age. Wider use of chemotherapy is likely to increase the overall pharmaceutical costs but is unlikely to increase the average daily cost significantly.

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STUDY THREE

TALKING ABOUT METASTATIC PROSTATE CANCER: HOW DO MEN FARE?

BACKGROUND

Prostate Cancer is predominantly characterized as a slow-growing cancer, mainly affecting older men. Most New Zealand men (75%) who are diagnosed with prostate cancer will have an early stage cancer detected, which can be successfully treated. However, approximately 12-13% of men diagnosed with prostate cancer annually will be found to have a late stage cancer or metastatic disease, which is incurable. Māori men are 20% less likely to be diagnosed with prostate cancer but if diagnosed are twice as likely to be found to have a late stage diagnosis.[1,3]

Recent research has identified a need for further insight into the experiences of New Zealand (NZ) men with metastatic prostate cancer at diagnosis[1]. Prostate cancer patients have acknowledged that receiving a prostate cancer diagnosis has an immediate and in some cases long-term emotional and psychological impact on themselves and their family[1]. Research has shown that men can be impacted for many years post their original diagnosis and /or treatment. Issues identified along the prostate cancer pathway have included; access to culturally appropriate health information and care[1,5], variation in care and outcome by ethnicity[3,4], and inadequate advice/follow-up[1,5].

Previous research has identified that men with a prostate cancer diagnosis have a low level of knowledge regarding their condition[6]. This has meant that engagement of men in the decisions about their care has sometimes been hampered. Information has been highlighted as a key factor to improving engagement in decision making and enabling men to understand their diagnosis, condition and self-care. However, there are significant gaps in understanding the needs of NZ men with a late stage diagnosis and their need for specific care, tailored to extending and ensuring the maintenance of quality of life. In NZ, survival after a metastatic prostate cancer diagnosis is bleak with 50% survival after 12 months reducing to 20% at 24 months[2]. This variability can continue throughout the journey and can create uncertainty about treatment received and future prognosis.

Aim

It was our intention to understand how men experienced their prostate cancer journey, from learning about their metastatic diagnosis to grasping their condition, the treatments they were on and their future prognosis. Of key interest was the information that men received along the pathway, their access and use of supportive care services and anticipated use of specialist services as the need developed.

METHODS

Men in this study were recruited from the same cohort of men identified for study two of the project. During 2009-2012 there were 2,127 men identified in the Midland Cancer Network

(MCN) region: Waikato, Bay of Plenty and Lakes District Health Boards as having a prostate cancer (C61) diagnosis at original registration on the New Zealand Cancer Register (NZCR). The NZCR is a national register of all cancer registrations in NZ. Through a clinical note review and specialist assisted restaging of each patient's medical history 234 of these men were identified as being metastatic at original registration[2]. Men were included in this study if they were 40 years and over; had proven metastatic prostate disease; and were domiciled in the MCN region at diagnosis. While recruitment focused on Māori and Pacific men, due to high mortality, non-Māori/non-Pacific men were also included in the study.

Men were approached in the first instance by the District Health Board Urogenital Cancer Specialist Nurse who wrote to men on behalf of the researchers, providing an information sheet and consent form. Responses were directed back to the researcher and contact was made with men to participate in the interview. Most meetings took place at the patient's home. If family members were present they were invited to take part in the interview. All interviews with Māori men had two researchers present, one of whom was Māori.

An unstructured interview format was used along with a topic guide to prompt discussion. Key topics were identified prior to beginning interviews. Topics covered the information and care received by men. Interviews explored understanding of the diagnosis, current health needs, gaps in care, communication and information and future progression (Table 1). Of interest was the patient's clarity on their diagnosis, prognosis, sources of information, knowledge about accessing and use of supportive care, if their needs were being met and if they knew how to remedy any issues as they arose.

Table 10: Summary topic guide for discussion prompts

Topic Area	Prompt
Communication and information	Knowledge about: • Advanced prostate cancer • Services and access-Who do they contact if in trouble? • ADT/chemo - Information received-who from? Side effects? Medication holiday? • Symptom management, death
Current health status	Concerns regarding your condition How will these be addressed Keeping healthy Knowledge about current health status
Gaps in care	Experience with treatment What is important to the patient – re: their disease Patient support needs Carer knowledge and support

Future progression	Service support Symptom treatment Palliative/End of life care

Interviews were recorded using a Dictaphone and transcribed verbatim. Interviews were then analysed using NVivo 10 (QSR International) to code, organise and manage data into themes. Data were coded inductively and sections reviewed by the research team. An iterative process continued involving reading, coding, re-reading, re-coding until clear themes developed. We continued to recruit and interview men until we had reached saturation, where no further themes emerged.

RESULTS

During 2014 we interviewed 12 men, 4 Māori and 8 non-Māori diagnosed between the period 2009 to 2012 and domiciled within MCN. Participants were aged between 59 and 87 years (Table 2). Eight men were diagnosed either in 2011 or 2012. Most men had at least 1 family member as a support person in their care. All but 1 man was on currently or had been on previously Androgen Deprivation Therapy (ADT) as treatment for their cancer. Participants were at various stages of the metastatic disease continuum. Six men still had a high level of mobility and could work to support themselves/family. There were differences in the level of end-of life care need required by men.

Table 11: Characteristics of men interviewed

	Māori	Non-Māori	Total
Age at diagnosis			
<70 years	3/4 (75%)	5/8 (62.5%)	8/12 (66.7%)
70+years	1/4 (25%)	3/8 (37.5%)	4/12 (33.3%)
Year of diagnosis			
2009 and 2010	-	4/8 (50%)	4/12 (33.3%)
2011 and 2012	4/4 (100%)	4/8 (50%)	8/12 (66.7%)
Key support person			
Wife	2/4 (50%)	7/8 (87.5%)	9/12 (75%)
Other family	1/4 (25%)	1/8 (12.5%)	2/12 (16.7%)
Health Professional	1/4 (25%)	-	1/12 (8.3%)
Androgen deprivation therapy (ADT)			
Yes	4/4 (100%)	7/8 (87.5%)	11/12 (91.7%)
No	-	1/8 (12.5%)	1/12 (8.3%)

Themes

When recounting individual prostate cancer journeys participants would relay their current experience with the trauma of learning of their diagnosis, the experiences they had with health and supportive care services and the concerns they had for the future. Very slowly feelings of self-blame, anger at health care professionals, guilt and vulnerability about where they were, the limitations in their future plans and the burden that they now posed to their respective families came to be expressed. To make sense of their journeys findings were ordered in time sequence, from the point of learning about the diagnosis, to understanding the condition, to current awareness of health and supportive care and finally to thoughts of the future (Figure 1). Findings were limited to reporting on information and communication, current knowledge,

knowledge gaps, awareness and use of support services, future intended support service use and questions.

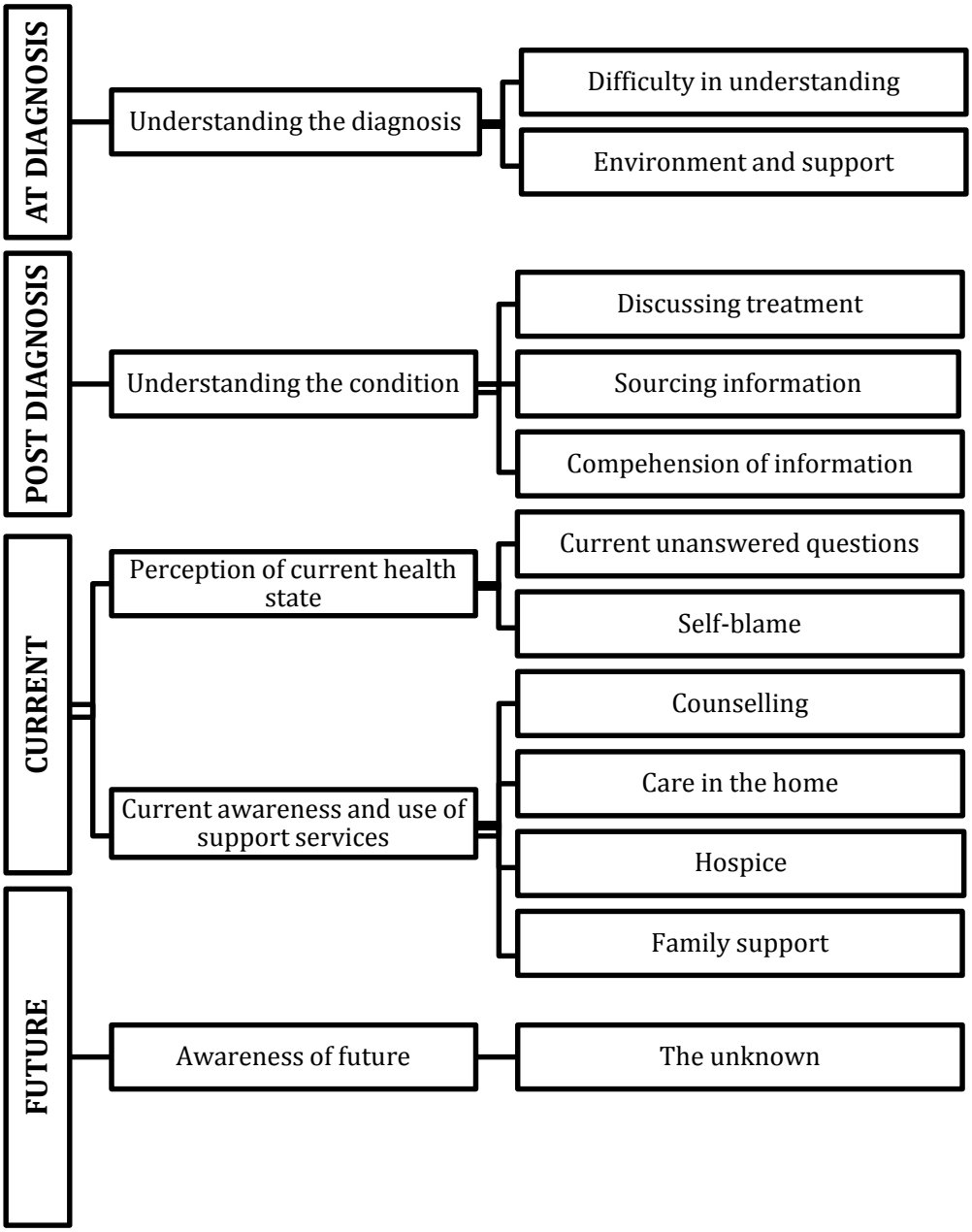

Figure 5: Table of themes

STUDY THREE

1. AT DIAGNOSIS

UNDERSTANDING THE DIAGNOSIS

All men recalled their experience of learning of their prostate cancer diagnosis during the course of their interview. Some men had not known that they had a health issue until they had become symptomatic, while others described a series of failures within the system which had resulted in delays in their diagnosis and/or treatment. Pivotal in the 'understanding process' was the conversation/s between specialist and patient. For some men the information was successfully relayed in a comprehensible and meaningful way:

> *He [the urologist] communicated very well because he brought things to a level that I think we both understood.* ***P10***

> *[The urologist] didn't hold back on information and I was accepting of whatever he said. Whatever we wanted to know he told us.* ***P12***

Difficulty in understanding

Most men they found that they had not clearly understood the information relayed to them, putting them on the back foot later in the cancer pathway for knowledge around their condition and for taking an active role in the decision making around their care. Right from the start of the prostate cancer journey men described difficulties in understanding their initial prostate cancer diagnosis:

> *I didn't really comprehend it – they said I had prostate cancer and I thought I never had prostate cancer… it doesn't hit you like that…* ***P6***

> *…it didn't really sink in.* ***Wife of P7***
> *No, it didn't sink in at all.* ***P7***

Some men described a feeling of "shutting down". This meant that their ability to engage meaningfully in the comprehension of the pathway forward and in gaining further insight into their condition was impeded:

> *I saw his mouth open and close but didn't hear what was coming out... Once he said you've got cancer you know I don't know whether I shut off and trust me I shut off … I didn't know what to say.* ***P9***

> *It was just straight out "You've got prostate cancer" and get that big C word and that's it, it's all over …You say the big C word and then you shut down.* ***P3***

Receiving a metastatic diagnosis was a double setback and later created other complexities in the comprehension of their condition. The delivery of the message by clinicians varied and the way the message was received and absorbed differed. Unsurprisingly some men described a fatalistic feeling of 'it's all over' once they had learned of their diagnosis:

> *It was a shock because I was pretty fit at the time and we certainly… even thought we were both over 60 [years old] we weren't really thinking of death at that stage…* ***P12***

> *…when I came home I thought, oh well, that's it because they didn't say that you'll come back for radiation or treatment…* ***P6***

> *…it's difficult if I didn't have Stage 4 at least it's not sort of, you know, it'd be easier to work with …and because this thing is incurable …then you know that creates another issue to get to grips with... So I think the knowledge that you've got the Stage 4 one is the killer I think.****P9***

> *[the specialist] said, "You've got a really advanced cancer in your prostate. By now, you've probably had it for years – it will, without doubt be through all your bones". Well that didn't cheer me up or anything."****P4***

For one wife learning that her husband had prostate cancer and that it was at a severely advanced stage, was by chance. Her husband was not aware of his condition either. She learnt of his diagnosis when she read the hospital discharge papers that her husband had received after he had arrived home from a stay in hospital:

> *…it was the discharge papers from the hospital that had it written on it. I had no idea. … it said that "his ribs, and in his spine" and that's the only information that we had and I hadn't really discussed it with [my husband]…* ***Wife of P1***

Assumptions played a part in some of the confusion felt by men. Participant three (P3) believed that there was an expectation that he already knew about his condition: "*…he talked like… I should have known about these things, but I didn't".* Other men also felt and discussed the presence of assumptions but this was predominantly at later stages of their cancer treatment.

ENVIRONMENT AND SUPPORT

The physical environment of the specialist offices affected the way some men recalled the experience of receiving their diagnosis. Some men graphically described the environment and used terms like, 'ugly', 'impersonal', 'drabby' and 'morbid'. The environment men were in when hearing their cancer diagnosis was important, with some men acknowledging that if it had been more pleasant it may have helped them to feel better.

> *When I went down to that department, a drabby looking place, ugly seats and everything just impersonal, - from the people that were on the counters were impersonal …you'd think that there'd be a more professional outlook. If this place was better looking I would have felt better, dunno.* ***P3***

> *… you walk in there sometimes and you wonder about the wallpaper… you wonder where the coffin's sitting around the corner.* ***P6***

> *Oh, like walking into a funeral directors – it's quiet, there's not many people walking around. … Yeah, and you're thinking to yourself, gee, they're either really sick or passed*

away. And I said to [wife], fancy having such a morbid place. …Yeah, but it's like you go there to die sort of thing. ***P6***

Participant three described a need for having someone, like a support person, as essential to talk with both during and after receiving the diagnosis. He said that this person could have been a family member, or a specialist nurse but discussion and time to ask questions directly after the time with the specialist would have helped him through the diagnosis process:

They needed to change the way that I went in. They needed to tell me you know, like – we have your thing – could you come in and then you know, bring someone with you or something, you know? ***P3***

Later Participant three (P3) developed a supportive relationship with the urogenital specialist nurse who supported him with the gaps in his knowledge and access to care:

P: Yeah, yeah. So she kept in touch with me to make sure my appointments were done and that they were doing what they were supposed to be doing and that was really, really good. It made that journey from there, better. Better right through and she rung and said leave my number on there and if anything crops up and give her a ring and so that's cool.P3

2. POST-DIAGNOSIS

UNDERSTANDING THE CONDITION

Discussing treatment

While communication was important when letting men know that they had prostate cancer, it became even more important during the next steps as men and their families embarked on a journey into the unknown. Available treatments to supress cancer growth and for symptom management were discussed with the patient either by a urologist or an oncologist:

… there were five options put out on the table towards me. ***P11***

… I remember was I was told all the different treatments I could have – you know, surgery or radiation or this that or the other. ***P8***

*… it wasn't until [the oncologist]started spelling it out and the girls in the radiation unit. They were very, very [helpful] …they discussed things freely and openly.****P7***

Sourcing information

Men discussed the ways that they gained knowledge and considered how helpful those methods were in their understanding of their condition. Most participants mentioned that the specialist had provided at least some written material that they could refer to when at home. But there was a strong desire to find out more about the disease, particularly to 'fill-in' the

gaps left lingering after meetings with specialists, health professionals and those that arose outside of scheduled appointments.

Most of the men interviewed identified two main methods of finding out more information about prostate cancer and subsequent treatments. This was by pamphlet and booklets provided by a health professional, and sourcing information from the Internet. Men and their partners were offered a variety of different paper-based resources to help with understanding their condition. Men found these of varying use:

> *Oh, they gave me the information on what prostate cancer is because it's all up on the wall. Take some of these.* ***P3***

> *We had the book …and I think we probably learnt about the different treatment regimes [online]. I think we read that probably from the start.****P12***

Timing of the information provided was also acknowledged as being important:

> *…so the Cancer Society gave me those 2 books which I read up on and I took what I needed out of it I guess and the information I think was there with the pamphlets when I started to read them. I didn't read them initially, no, but when I did read them yes, I understood* ***P9***

The Internet provided fast and easy access to a significant amount of literature on the disease and its treatments:

> *I didn't, we didn't understand Gleason score so we started to do some research on it… We had a lot of information off the internet.* ***P12***

> *…he would mention Zoladex so I knew he was on some sort of treatment, yeah, this is Google, Dr Google you can do a little bit of research, yeah.* ***P11***

Family members sometimes supported men in finding out more about the condition and looked to find solutions for better living, symptom control and new medications. Wives in particular were interested in finding out more so they could support their husband through understanding more:

> *We read everything we could on cancer – well she did and she'd say oh you should read this and I didn't want to read some of it, you know, but I did, but she was digging out information on cancer all the time, everywhere.* ***P4***

> *I found out on the Internet just going into different sites; prostate cancer sites, and reading up about Gleason scores and things.* ***Wife of P10***

Comprehension of information

There were however, some significant issues once men started reading more widely. The level of information and the quantity was daunting. Men identified difficulty in trying to filter out what was relevant to their stage from all sources of information.

> *No, I don't go on there (Internet) – I think I've got enough problems now just having the prostate than trying to figure out, trying to start reading about it and getting worse so I just go with what's happening and see what happens in the end.* ***P3***

> *Confusing because you're not a specialist, you know, you're reading about your own body and praying that it's not gonna be your turn.* ***P11***

The terminology used hindered comprehension of the disease by patient and family members. While some information had been of use, there were limitations were apparent for men and their wives as they sought information specific to the extent of cancer.

> *...[the booklet] it's not broken down into what an average practical person can understand. It's more when you start reading the book the medical thing it's more confusing – it makes you say, well O.K. where is [my husband] in all of this.* ***Wife of P2***

> *Just information based on the prostate cancer; not specific. ...at that stage yeah I knew at that time I had stage 4...* ***There wasn't a booklet that was specific about stage 4****...* ***P9***

There was also an awareness of the absence of information about the journey through the health system. Participants three and six identified that the process of navigation and knowing what to expect was difficult. There was no preparation or awareness of next steps:

> *I've seen a lot of pamphlets out there with diagnosis and what goes on but they don't tell you the journey? You know the journey from the time you get diagnosed from the doctor – then you go up to the hospital – all that I didn't know about – you know I just go up for an appointment.* ***P3***

> *...I sort of lost my way a bit... When you have your treatment and stuff and when you come off all that jargon, that's it and I need to know because my levels have gone up again.* ***P6***

3. CURRENT

PERCEPTION OF CURRENT HEALTH STATE

Initially, when men described their current health state there were revelations about their most recent PSA levels and what the outcome of a previous specialist appointment had been. As they worked through their last encounter with a health professional and relayed biomarker results their discussion moved to disclosure of physiological changes that had occurred, such as symptoms that had appeared and that they felt were unresolved. Every participant in the study had at least one question regarding their current condition; some had multiple unanswered questions and concerns.

Questions ranged from understanding changes in biomarker levels, to physical symptoms to

side effects of the treatment. The development of a symptom was fused with participant expression of fear and anxiety; words to this effect were scattered throughout discussions of their cancer. There were also unresolved questions about what issues meant to their current health state and what was going to be done to address these issues:

> *…I've gone from nothing to now 2.97[PSA]... It shot up to there and I don't know whether that's good, bad or indifferent, you know.* ***P6***

> *No, I'm just scared … the other day and had a talk to a Doctor… and she said to me that I need a scan cos I'm worried that cos I've got a very sore lower back and I had cancer in the spine in the lower neck in the middle of the spine and in the lobes.* ***P6***

> *The biggest issue at the moment is knowing; "I don't know what's going on!"* ***P6***

> *My only concern at the moment is with the creeping up again and nobody pushing any panic button. I go along next week and it's up to 10 – what the hell's happening?* ***P7***

> *I don't want to be told after this test next week that it's gone to 10. I don't want that. I want to know now and if it's increasing what's the reason? I don't know. Haven't got a clue…* ***P7***

> *I'm still on Zoladex, yeah, stayed on the Zoladex. I'll stay on that by the sound of things. I guess I'm in the wait and see progress now. I was offered chemotherapy, I have no symptoms, I have no pain, so why make me crook has been the big question.* ***P11***

Men even asked questions of the researcher/s to find answers to their concerns:

> *But you know, I said, I know I had some cancer in my spine, just below the neck and I said I'm just a bit scared that it's …starting to grow. Well, I don't know what it does… you don't know do you?* ***P6***

> *How do I know about my lymph glands? Does PSA pick that up?* ***P7***

Participant six noted that when he had sought answers to his questions there were delays in accessing the help that he required. In this instance he described the need for a scan to understand the growth of his cancer and the increase in PSA levels and pain. He felt that there was a lack of action by 'someone' who was supposed to be looking after him:

> *…I went to [urologist] yesterday and … I said to him, I said I really need another scan and [urologist] said, you do. You do need another scan. Everybody says you do but does it happen? …They're all interested but where are they? Like somebody needs a bomb under them don't they? P6*

Another question participants had was about the "time" issue. Some wanted to know what the life expectancy of their condition was. This was rarely and reluctantly answered by specialists:

Well the only thing that pops into mind and it's not a question I really want an answer to – is the time? The time element. ***Wife of P1***

Initially when he first diagnosed this …he gave us/me a rough time line of two years. He was very reluctant to give a time line but he said we want to talk averages. I had a life expectancy of two years. …He didn't want to give a timeframe at all. …but I sort of said – are we talking ten years or we're talking six months sort of thing. It would be useful to know and probably with the level of metasticies and the level and the Gleason score he said on an average you could be looking at two years, something like that but he said it could be longer. ***P12***

Self-blame

When issues arose and participants described situations where they felt that they had not received optimal care there was a process of participant self-blame and/or minimisation. The events that occurred may have been serious and the delays unacceptable but participants often took the burden of the responsibility for outcomes not proceeding as they should have or at least minimised the role of the health professional in the situation.

*…I think I'm, well, I am the problem.****P3***

…I didn't ask the questions correctly, I think. You know that was my fault. I don't think I was able to understand or comprehend it, I don't think. ***P9***

I don't listen very well even though I'm a good listener sometimes. I don't listen to what that particular person's saying as a result of I mean possibly not wanting to listen to it perhaps at that point or perhaps trying to get to grips with what he just said... ***P9***

Participant one (P1) had missed out on receiving ADT treatment for over 12months before a health professional noticed this during an acute presentation to hospital. Rather than blaming the clinic, for the oversight, the husband and wife described the errors as a series of "hiccups" that they felt was ultimately their fault:

*There's been a lot of hiccups along the way.****P1***
…it was probably our fault for changing doctors. ***Wife of P1***

Some men had gone through experiences that left them questioning the decisions made regarding their treatment and empowered them to be more active in the decision making around their care. This was important in improving their own health outcomes and ensuring that steps on their health care pathway were not over looked:

Well I'm gonna ask more questions now because of my lack of knowledge of what was wrong and my acceptance of the treatment and in respect to the people that were doing it. ***P7***

I was just dumbfounded as to how this could be and you know so as far as getting the pamphlet was concerned they gave me information that was required; I didn't ask the questions because I didn't think I needed to ask the questions. I don't think I thought that it was bad as what it was. ***P9***

CURRENT AWARENESS AND USE OF HEALTH AND COMMUNITY BASED SUPPORT

Of all of the gaps in the knowledge men had around their prostate cancer the variance that stands out the most between men was the level of knowledge about supportive care. In most cases level of knowledge was tied to the level of need, that is, men with more advanced disease had a higher level of need for services that could provide support; therefore, they had gained an increased level of knowledge around the services available. But a more progressive cancer did not always mean improved access to supportive care. This is where the advocacy of family members became significant in addressing supportive care from service providers, and highlighted the significant advantages that men with help from family had over those that did not.

Organisational support varied. Participants recounted contrasting experiences with many of the health care services they used, including general practice, hospital, and community based supportive care. In particular, three sectors of community based support services were considered within participant interviews: counselling, care in the home and hospice.

Counselling

During the course of the interview, as men disclosed more about the impact that their condition had and was having on their lives, discussion about access to and use of counselling came up. Counselling was seen as potentially having value but only two of the twelve men in the study were offered counselling, both of whom took it up. Most men described a desire to participate in counselling and felt that this would have helped with their understanding, acceptance of the condition and support the changes to their relationship. Resoundingly men acknowledged that they would have accessed counselling if they had known that it was available:

I really do think that anyone that's got prostate cancer or anything like that needs counselling. ***P3***

I would have done, yes, yes. I would have done. ***P8***

Well I should have, I should have just done something about it and I haven't. ***P9***

The impact of prostate cancer was unavoidably apparent in the relationship of the husband and wife. There was an awareness of a need to talk about the condition and its effects, but this was not always discussed openly. Issues that may have been able to be addressed with the help of a counsellor were neglected, sometimes causing more distress, even two years after diagnosis:

[Counselling] may have helped us talk a little bit more about it. [My wife] thinks I clam up about it. She thinks I don't want to talk about it. It's not the case. I don't want to, I suppose, make it seem more of an impact than it need be. She will probably disagree and say you know we probably could talk more about it than we do and that might help. ***P10***

[Addresses wife]: Do you think I need to see someone about it? You keep saying I don't open up, I don't talk about it? ***P10***

Yeah, for me and my Mrs it was a big life change. I suppose I can tell you, we haven't really talked about it. That's the worst part about it we haven't really talked about it. She knows about it and but we haven't had a good talk about it because it's me I can't handle it. I should have got counselling eh? ***P3***

Men also spoke about suffering from depression, either directly because of the cancer, or indirectly through the changes that it necessitated in their life:

*Nah, never been offered... I went a bit, was a bit depressed mainly because, well my job was on the line for a while... P****11***

No, I don't need it now, I don't need it now, yeah, but I had to going through my depression and everything. I had to vent off to someone I could relate to, someone I could feel comfortable with and then I could say, this, this and this has been happening to me, - can I vent off to you about it? ***P2***

Care within the home

One of the most substantial issues men and their wives had as the cancer progressed beyond the reach of any treatment regime to pain and symptom relief was the access to supportive care that allowed them to be within their own home, particularly in the end stages of life. Care within the home required the coordination of support services like: occupational therapy to assess ability to perform daily activities; home help, in the form of cleaning, cooking, showering aid; and, resource accessibility and funding (primarily through the DHB). It was the synchronisation of these three systems that participants, particularly those highest at need (P1 and P2) described as failing them during this time of need and leaving them feeling concerned about the level of quality of life and burden placed on family members:

...in the last three days they've [OT] been backwards and forwards, backwards and forwards, yeah, yeah, cos they've had meetings with the staff here and with the doctors and all that just to get a plan in place. But the plan in place doesn't exactly [meet] my needs, immediate needs you know. My doctor said they're not going to send me home with nothing in place. [But there are] no ramps, not too concerned about the shower, showering, just my mobility from when they drop me off from the ambulance and wheel myself into my home ...I can see myself bedridden for a while. ***P2***

Home help was available but it was limited:

> *Five days a week and Saturday and Sunday mornings. Just mornings that's for food preparation and personal cares. With personal cares all he used to do was just watch me having a shower and watch that I didn't fall over and trip on the mat, yeah. It was more like a safety issue. Just watch me. But I could walk around the house you know with my walking frame or now with my walking stick I could walk around the house.* ***P2***

> *I was only getting Monday and Friday for an hour for housework at that time but I said, "As [my husband] is getting heavier and I'm having trouble with my leg and my back …I just felt I needed help with his personal care and so we do have that now but they still don't know how to take [urinary aid] off or put them on. …we have a young fella that comes, vacuums and does the shower and everything and I'm teaching him how to take it off but men are a bit rougher than females.* ***Wife of P1***

In addition to Participant one's wife noticing that the level of skill for the home help was inconsistent and "a bit rough" Participant two's wife also noticed that the support her husband received was falling short of the level of care that he required to be adequately supported in the home:

> *The services they call in – the people aren't qualified, …they just come in and they just not qualified… caregivers for this situation, so I've had to take over their duties for five months which is damaging my health…* ***Wife of P2***

The money required for Participant two to go home and enable him to have the best quality of life, with mobility ramps and wheelchair accessible showering was unlikely to occur without private funding. Participant two's wife was particularly distressed at the thought that her husband was going to be housebound for the duration of his life. She strongly felt that those in charge of assisting her and her husband were missing the point:

> *….this is what is churning in here is that everybody that comes through that door that's with this hospital has condemned you before you've even gone home.*

> *We don't want any freebies. We're not looking for that. What we're doing is and we don't want to mortgage ourselves up to the hilt to make his life easier and I'm not gonna put anybody in debt for that. We discussed that and he's not going into a rest home or a facility. So all we're looking for is that he doesn't become housebound.*

> *[when] he mentioned palliative terminal advanced cancer. People go to skip, skip, skip, skip to death. They don't see what you've got to live in between that time so you can have good quality and reflect back on your life and stuff like that. They don't want to throw money into somebody that's gonna die. They don't.* ***Wife of P2***

Hospice

Hospice is the palliative care service provider intended to support people with life limiting conditions. Either the specialist or general practitioner (GP) referred seven of the twelve men

to hospice. There were some common misconceptions about the work of hospice, and the role that it played in the on-going care of men. One of the issues appeared to be an inherent suspicion or uncertainty of hospice, it's purpose and when it was most relevant in the end of life care for men. The most common association was that hospice was a place to die:

> *My fear was that they wanted me to go into the Hospice. I knew they had beds there and I wouldn't get out of the place. I would die there. …I was actually horrified when they turned up here cos I thought you had Hospice when you're dying. The last one I wanted to see was a Hospice person here…* ***P12***

> *It's just that I've only ever heard of people going in [to Hospice] as the last resort over their life?* ***Wife of P1***

When men were contacted by hospice there was a sense that they were not ready to die. Generally, men and their partners felt that contact meant someone knew something about their condition that they didn't

> *I got referred to Hospice about 2 months later… it came out of the blue to be honest, you know, cos I was thinking you know why they contacted me? And the question my wife and I were thinking was what is [it] you know? We know what Hospice is, so what does this mean? Do they know something that I don't know? That's what was going through my head to be honest.* ***P9***

In one particular instance, a hospice nurse had informed one man that his referral to hospice meant that he had a specific timeframe of life remaining. This came as quite a surprise to him:

> *it came out of the blue to be honest, you know, cos I was thinking you know why they contacted me? And the question my wife and I were thinking was what is you know, we know what Hospice is so what does this mean? Do they know something that I don't know? …I was talking to the Hospice Nurse and she said well, generally, you've got between 0 and 12 months [to live]. So, after… I got the phone call from Hospice, [my daughter] and I went to Hospice to have a yarn to them, and they took us through …and we were thinking, - why are we here? You know, we have no need to be here. To be told, …that the Hospice is only on board if you've got that length of time...* ***P9***

The transition from acute care to community based palliative care through Hospice was sometimes problematic for participants as it was perceived by men as a sign they are nearing death. However, once initial contact had been established and the relationship with hospice grew, some men felt that the connection was beneficial.

> *She's been the constant one for the last 3 or 4 months. [Nurse] from Hospice she comes out every 2 weeks, she's like clockwork.* ***P6***

> *It's like that [receptionist] she's so easy to talk to and pleasant and you go to the counter and the people there are pleasant – well that makes a big difference.* ***P7***

Despite the benefit of an association with Hospice and an awareness that he would eventually need to participate in Hospice, Participant four identified that he preferred to maintain connection to his GP:

> *I'll probably go to my GP straight away. He's a real good guy and then I don't know if it would be any use going to hospital. I'd have to go to the hospice I imagine because that's what the Oncologist told me. He said, I can't do anymore but then I don't know what they would do, you know, I don't.* ***P4***

Family Support

Although the primary source of support for most men was their wife/partner, the wider family were acknowledged as a significant resource when available. For those men with a supportive and engaged family many of the concerns that arose were dealt with by someone other than the patient. Family assisted in seeking answers to questions as they arose.

> *…my family, …they're on the waka too, they're on the waka with me, you know. Whatever I go through, they're gonna be there in a supportive role, they're gonna be there, no matter what. …So to me it's all about that family, you know, that's important.* ***P2***

> *…when I went to see the Specialist she came with me …eventually my kids found out and they just went crazy. It was hard on them so we went to a cancer meeting …once a month on Tuesdays. We went to that and that's how we found out what it was and what was happening... Once we got to handle it was kind of relaxed. After that it was just a matter of getting the treatment done. …having family I think is the biggest secret.* ***P5***

> *We didn't know anything about it but [my wife] was terrific – she's a great person, she found out so much stuff – she got more into finding out information than I did.* ***P4***

Men also utilised assistance from health professionals within the family to gain insight into their condition and find support in accessing and navigating the services required:

> *My wife's a registered nurse so that helps. My Mum's a nurse as well so we had a reasonable amount of knowledge, my older sister's a social worker so I had lots of information there and I'm a fourth generation Rotorua with very good support from lots of people.* ***P11***

FUTURE

AWARENESS OF FUTURE

The Unknown: Unanswered questions about future condition

During the interview as men discussed what they knew about their condition and their current health state, there was generally a progression to deliberating on the future. For most men,

there was a sense of anxiety about the unknown future. There was an equal quantity of questions about their future condition as there were about their current health state. Understanding the warning signs of advancing cancer was of significant concern for some, as well as access to support and types of treatment available. Once more men described difficulties in understanding information received and also in knowing if the information that they had was relevant to their condition – now and in the future. For some men this was an on-going waiting game with an uncertain future:

> *What happens at the end? What am I gonna look forward to? That's where fear comes.* ***P3***

> *…will there be more radiation or is he gonna be just sent home to pass away?* ***Wife of P2***

> *…Will my bones become soft or crumbly …those spots are they the right spots? …still got to go answer those questions...* ***P11***

> *It would be good to know that there's symptoms that's going to happen and to look for it. I don't know what to look for. …You're at home by yourself what then – my hand might be twitching like this and you think is that part of it or what?* ***P3***

Participant three had a heightened anxiety around his condition as he was unclear about what would happen once his treatment finished. During a consultation the specialist identified that he could be on a particular types of ADT for approximately 18 months. Participant three had not known what would happen after 18 months had lapsed and at the time of the interview he was at 17months. Even though he had presented to a health professional to get the ADT injected every three months during this period he had not felt able to ask this question to alleviate his concerns:

> *[the specialist] reckoned I can only be on it [type of ADT] for 18 months and after 18 months they have to stop. Be 18 months this Christmas… All I've got is 18 months of injections and what happens after 18 months I don't know. What are the things to look out for? P3*

In addition to the unresolved and in many cases, unspoken concerns about the future that men had, there was also confusion about whether or not it would be good to know the answers to these concerns. Participant three flip, flopped between wanting to know and not wanting to know:

> *…I really I don't know whether I want to know or not. Just let it happen. It's part and parcel of the disease eh?* ***P3***

> *I don't know if it will be good for me to hear it or good for me not to hear it and just let it happen. But I would like to know where I am now and what the symptoms are going to happen. I have to hear. I want to know what it's gonna be when it gets to its worst and*

> *when it begins to start its worst – I want to know what the symptoms are so I can go to the next stage of treatment or something like that.* ***P3***

Men were asked about their plan for the future. This included questions around their intended use of services that could support them if their health deteriorated and if they had any intention to learn about what providers offered prior to the need arising. There was some discord around the intention of understanding or partaking in support services offered. Some men had no idea about what was on offer, nor a plan of what to do:

> *My worst part about it is when I do find something what do I do?* ***P3***

> *I just don't figure on having a problem.* ***P4***

Participant nine was more pragmatic about the potential for using services at some point in the future:

> *I've got [Hospice] phone number you know, and she's got mine, so I've got that pattern there I guess.* ***P9***

> *I'd have to revisit that so again, I don't take it in as well as I should. Perhaps I'm just parking it until such time as it's needed perhaps?* ***P9***

DISCUSSION

The difficulty that patients face in understanding their cancer journey is well-known and can be linked to the information provided and comprehended[6]. For men with a metastatic diagnosis there are particular health and information needs, specific to their stage of the disease, that require attention. Prognosis for men with castrate-resistant prostate cancer (hormone-resistance) is poor, with survival of 9-13months[7]. Information and communication along the metastatic pathway is pivotal and the timing of imparting this information is just as important as the message that it imparts. Without clear knowledge of their current and future pathway men and their families can suffer from anxiety, causing undue stress at an already distressing time.

Patients have identified that receiving a prostate cancer diagnosis has an immediate and in some cases long-term emotional and psychological impact on themselves and their family. Men described that there is, at times, significant variability in the information they received and the pathway of care. While there were some families who were able to support men by seeking out the information that they needed, questions and health information needs changed at times quite rapidly, with the progression of the cancer and duration on specific medications. This required on-going support to alleviate concerns about the unknown future.

Men highlighted the need for more information, increased support, understandable future planning, and identified these needs as existing even many years after their diagnosis. Clear communication and appropriately, targeted information that is adapted to health literacy level

and progression of disease is an important tool in assisting patients through the cancer experience.

When there are supportive family involved in patient care, family can be the bridge between health care professionals and the patient. The wife in particular plays a substantial role in the advocacy of men's need, often identifying the gaps in care first. Information needs to be available and clear for families to assist the patient adequately. This needs to be stage specific and outline what happens after treatment types, symptoms to expect with progression and develop a critical awareness of hormone-resistance as the cancer evolves. Patients and family can then decide if chemotherapeutic agents are suitable.

CONCLUSION

Simple changes can facilitate dramatic change for the patient experience. Men and their family should be better supported to ensure that their needs are met. Support, primarily through better communication and stage specific information should be available to partners and family so they are better equipped to support their loved-one and can avoid the stress of an unknown future. Through better communication, addressing even the most significant need can be improved. Time, tailoring messages and having a plan in place at each stage of the journey that patients and family can grasp can reduce the trauma of a cancer diagnosis and alleviate the uncertainty associated with the 'unknown' future.

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SUMMARY

We would like to acknowledge the contribution of men with metastatic prostate cancer to this study – both those known and unknown to the researchers. We have come to understand how devastating a diagnosis of metastatic prostate cancer is to not only the men but also their partners and families. We believe this study has provided some evidence of the difficulties men face, but also the opportunity to live well with disease and the role of the health services in helping to optimise outcomes for men with this disease.

We have shown that 11% of men with prostate cancer in our region present with metastatic disease. Māori men are about twice as likely to have metastatic disease at diagnosis as non-Māori. Most men presenting with metastatic disease are older than 70 and indeed 50% are greater than 80 years, however there is a group of younger men, including Māori men who present with advanced disease.

We found that the availability of androgen deprivation therapy is almost universal in younger men, but no doubt due to age or the presence of co-morbidities many older men do not receive ADT and indeed are also less likely to receive palliative radiotherapy. We did not find differences in access to ADT for Māori men. Docetaxel became widely available in 2011 after Pharmac began funding this new treatment for men with castrate resistant prostate cancer (CRPC). We found out the initiators and on-going management of ADT therapy varied considerably – and there did not seem to be a coherent approach to the diagnosis and management of CRPC. Consequently, only approximately 2% of men with advanced prostate cancer were treated with chemotherapy (docetaxel). Again younger men were much more likely to receive treatment. However, Māori men in our study were not treated with chemotherapy.

Mortality for metastatic disease was high with a 2 and 5 year survival that was considerably worse than outcomes quoted in the U.K. Outcomes for Māori men with advanced prostate cancer were even worse. While this is likely to be due to later diagnosis and the presence of more advanced disease at diagnosis – the lack of use of chemotherapy for Māori men may be a factor in the poor outcomes for these men.

Our qualitative research has raised a number of important issues. Firstly men and their families/whanau noted a lack of information about prognosis, treatment options, on-going monitoring and likely complications of treatment. This led to some distress which would seem to be avoidable. We also note that while men acknowledged they had reached a stage where their disease was terminal – that the support from the health services rather than intensifying – left some men with a sense of abandonment.

SUMMARY

We believe that terminal care is about optimising the last weeks and months of life and that health services should be aiming to help men and their families reach their objectives within the limitations of their disease. It would seem that while some services (both specialist and GP) provide excellent support – for some men the quality of palliative care seemed from their point of view to be lacking. It may be that further research is needed as to how to improve palliative care in this group of men. Having said this, as well as improving quality of life, the range of new treatments can extend the number of months lived – hence if quality of life is not compromised medication such as abiraterone would appear to offer real benefits. It is important that the ethnic disparities in the use of docetaxel are not repeated in the introduction of abiraterone to market – and that strategies, such as a fixed pricing structures, intended to reduce inequities are central to this. This is of particular importance for Māori men.

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