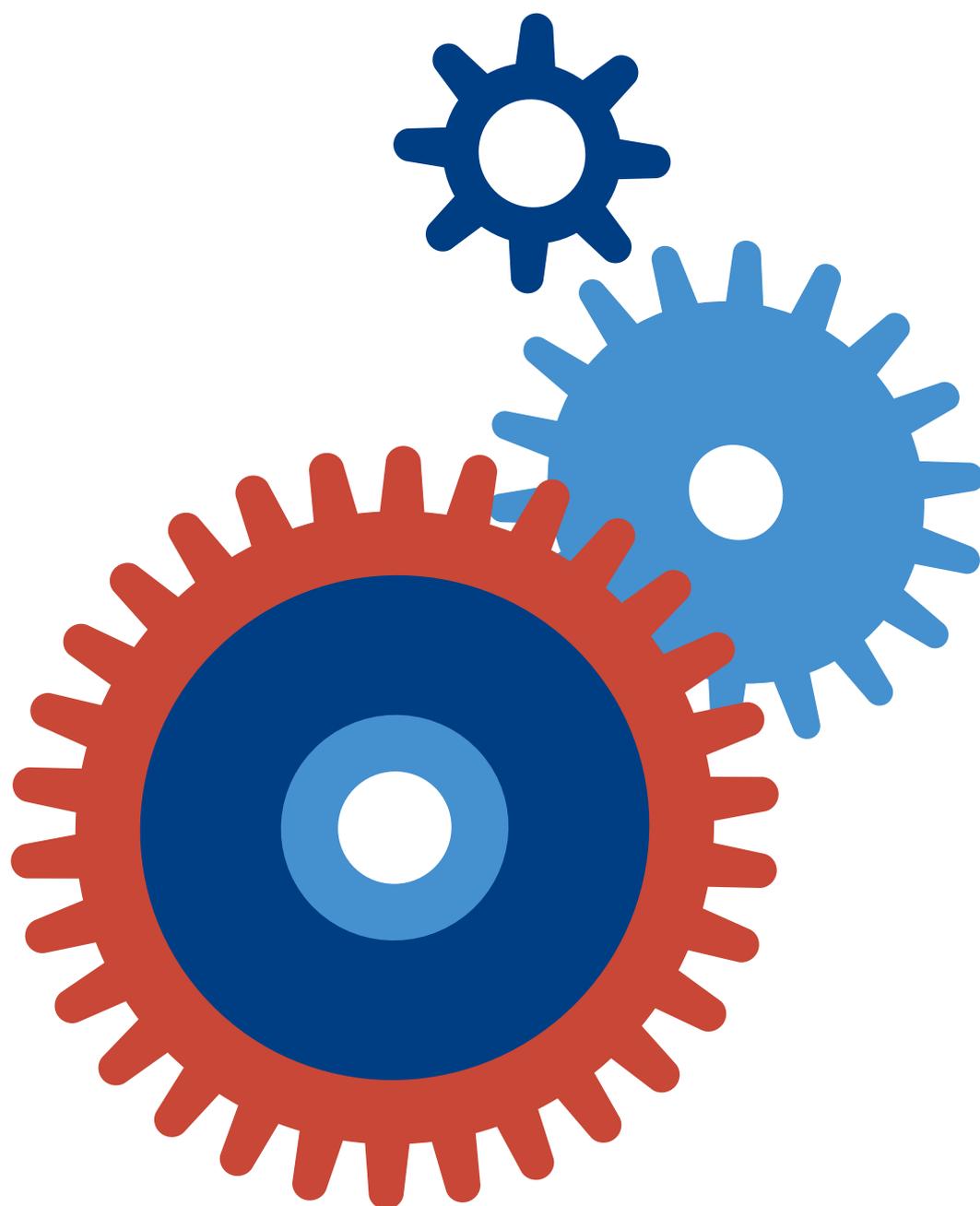


Prostate Cancer Management and Referral Guidance



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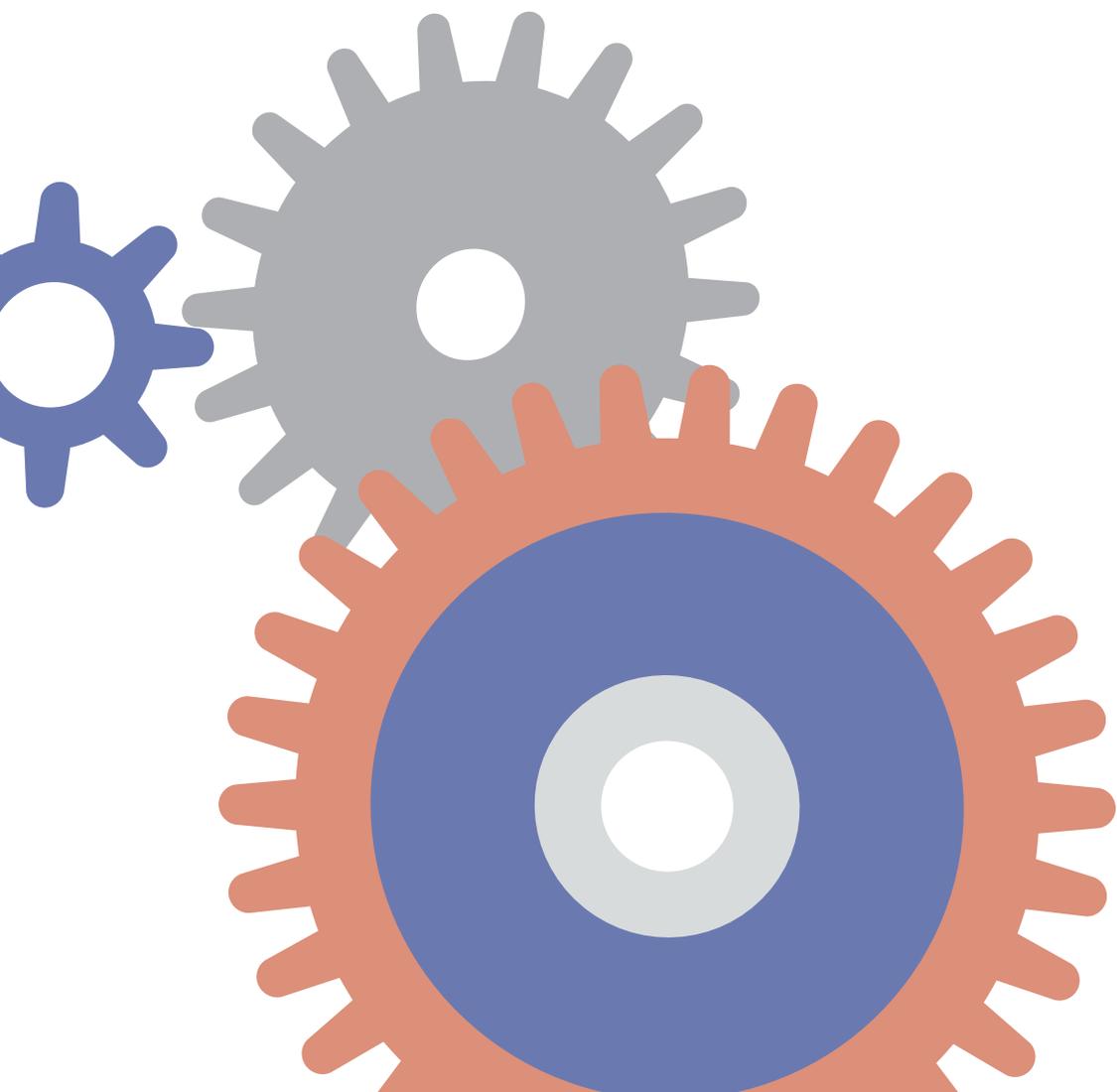
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Introduction

About this guidance

This guidance is to help primary care practitioners provide men and their family and whānau with consistent, culturally appropriate information on prostate cancer testing and treatment.

The guidance includes an algorithm to help primary care practitioners have an informed discussion with men who present with prostate-related concerns. Explanatory notes provide more detailed information on each of the steps involved.

This guidance has been endorsed by:

- The Royal New Zealand College of General Practitioners
- The Prostate Cancer Foundation of New Zealand
- The Urological Society of Australia and New Zealand
- The New Zealand Urological Nurses Society
- The New Zealand Society of Pathologists.

Need for this guidance

New Zealand men currently receive conflicting advice about prostate cancer testing and treatment. Some men may benefit from early diagnosis and treatment, but have limited opportunity to access appropriate health services.

Unlike other cancers, prostate cancer often grows slowly. With routine prostate specific antigen (PSA) testing, many men can be diagnosed with a cancer that is not going to progress during their lifetime. Such a diagnosis may increase men's exposure to unnecessary treatment-related harms. On the other hand, some men will still develop aggressive and potentially life-threatening prostate cancer. These men may benefit from prompt diagnosis and treatment.

Development process for this guidance

This guidance was developed by the Primary Care Sub-group of the Prostate Cancer Working Group.¹ The Prostate Cancer Working Group supports and advises the Ministry of Health to implement the Prostate Cancer Awareness and Quality Improvement Programme (AQIP),² which aims to improve prostate cancer care for New Zealand men by:

- giving men better and more equitable access to information about prostate cancer testing and treatment
- supporting primary care practitioners to manage men presenting with prostate-related concerns
- removing barriers that restrict men's access to diagnostic and treatment services
- giving men consistent care and equitable outcomes across the entire care pathway.

¹ For more information on the Prostate Cancer Working Group, visit: www.health.govt.nz/our-work/diseases-and-conditions/cancer-programme/prostate-cancer-programme/prostate-cancer-working-group

² For more information on the AQIP, visit: www.health.govt.nz/publication/prostate-cancer-awareness-and-quality-improvement-programme-improving-outcomes-men-prostate-cancer

This guidance is largely based on the recommendations of the Prostate Cancer Taskforce.³ However, other publications were also considered, including the National Institute of Clinical Excellence's guidance on prostate cancer: diagnosis and treatment (Carter et al 2013), the European Randomised Study of Screening for Prostate Cancer (Schröder et al 2014) and the guidance on prostate cancer diagnosis and treatment produced by a number of other jurisdictions.

The Primary Care Sub-group acknowledges the evidence around prostate cancer testing and treatment continues to evolve. This guidance will be revised every two years, with subsequent versions published on the Ministry of Health's website (www.health.govt.nz).

It was sent out to numerous stakeholders for comment before publication, including:

- district health boards
- primary health organisations
- relevant professional colleges
- non-governmental organisations, such as the Prostate Cancer Foundation and the Cancer Society.

It is part of a suite of resources being developed under the AQIP. Other resources that will be developed over the next two years include:

- an electronic decision support tool to help men's decision-making around prostate cancer testing and treatment
- guidance on the use of active surveillance
- guidance on the pathologic diagnosis and staging of prostate cancer
- guidance on managing men with advanced or metastatic prostate cancer
- patient information for men and their family and whānau.

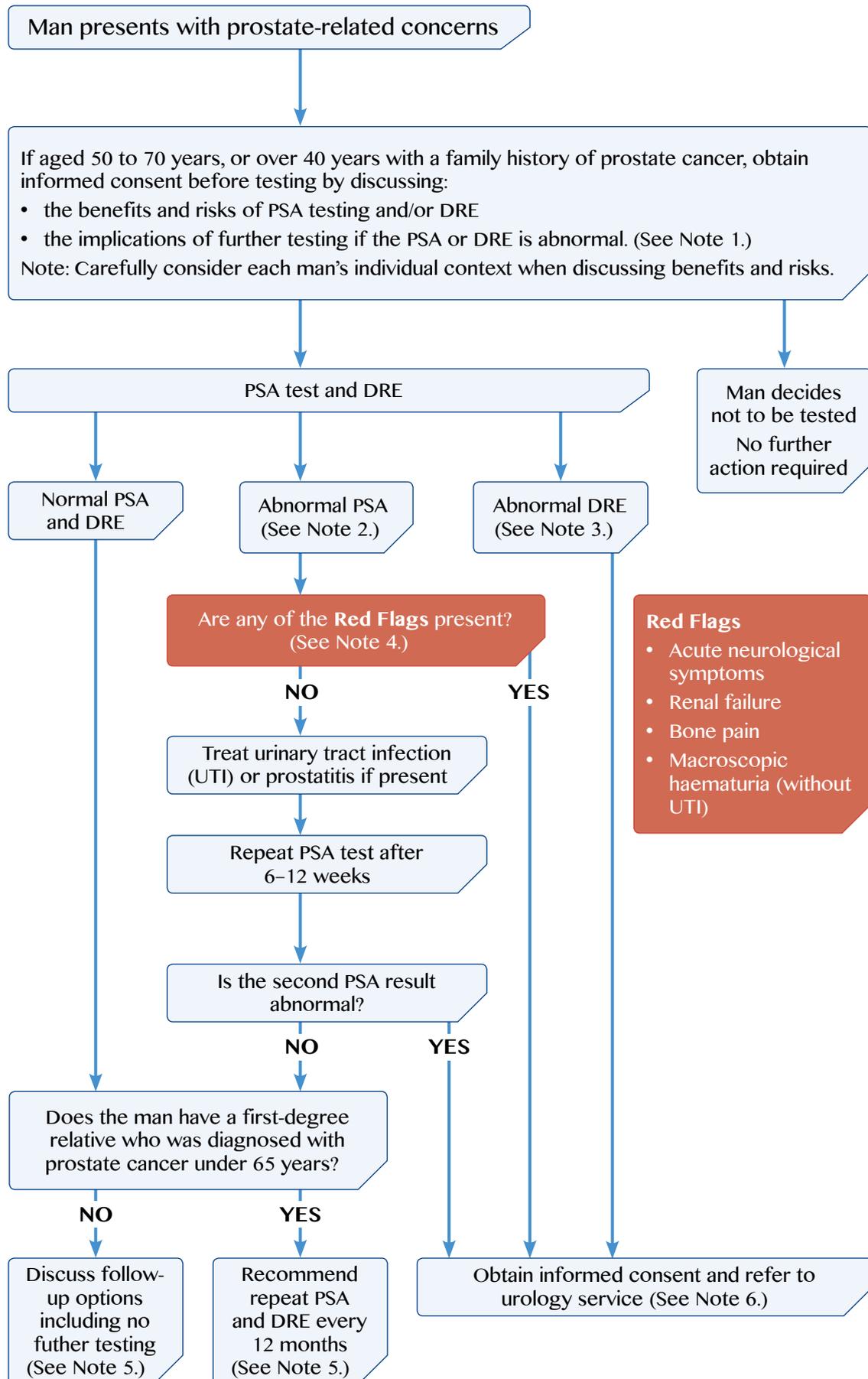
Integrating this guidance into routine clinical practice

District health boards and primary health organisations are responsible for integrating this guidance into their clinical pathways for prostate cancer in a way that reflects the particular needs of their patients and communities.

When using this guidance, primary care practitioners should be conscious of the disparities that exist in prostate cancer outcomes for different men, such as for Māori men or men who live in rural areas. For example, Māori men are less likely to be diagnosed with prostate cancer than non-Māori men, but are 37 percent more likely to die from the disease (Ministry of Health 2014). The reasons behind these disparities are not well understood. However, in part, they appear to be related to differences in the access that different groups of men have to appropriate information and diagnostic and treatment services.

³ For more information on the recommendations of the Prostate Cancer Taskforce, visit: www.health.govt.nz/publication/diagnosis-and-management-prostate-cancer-new-zealand-men-recommendations-prostate-cancer-taskforce

Algorithm for supporting men with prostate-related concerns



Note 1: Preliminary considerations for men considering prostate cancer testing

1.1. Age

If men are considering being tested, they need to know there is no clear evidence on what age men should begin prostate cancer testing. The best recommendation is for primary care practitioners to discuss the benefits and risks of prostate cancer testing with men aged between 50 and 70 years and men aged over 40 years who have a family history of prostate cancer, as they are the most likely to benefit (Andriole et al 2009; Schröder et al 2009).

There is no strong evidence to suggest that testing men over the age of 70 years reduces mortality from prostate cancer in this age group. Generally men aged over 70 years, who have a normal-feeling prostate on digital rectal examination (DRE) and who have had 'normal' PSA tests in the past, should be advised they are not likely to benefit from any further PSA testing.

Some men aged over 70 years who have a family history of prostate cancer or who have had a previously raised PSA level may benefit from further monitoring if they are otherwise well and have a life expectancy of more than 10 years (Hugosson et al 2010).

1.2. Family history

A man is defined as having a family history of prostate cancer if he has at least one first-degree relative (father or brother) who was diagnosed with prostate cancer. Men with a family history of prostate cancer are twice as likely to develop the disease than men without a family history. If a man has two or more first-degree relatives who were diagnosed with prostate cancer under the age of 65 years, then his risk increases by 5–11 times (Steinberg et al 1990).

A small group of men with prostate cancer (about 9 percent) will have the true hereditary form of the disease, which is defined as three or more affected relatives or at least two relatives who have developed prostate cancer before the age of 55 years (Steinberg et al 1990; Bratt 2002). Patients with hereditary prostate cancer usually develop the disease six to seven years earlier than other men, but have about the same chance of developing a more aggressive form of the disease (Carter et al 1992; Grönberg et al 1996).

1.3. Ethnicity

Inequalities in prostate cancer outcomes are significant in New Zealand. The most notable inequalities are between Māori and non-Māori men. In 2011, Māori men were about 18 percent less likely to be diagnosed with prostate cancer than non-Māori men, but were 37 percent more likely to die from the disease once diagnosed (taking age and stage into account) (Ministry of Health 2014).

The reasons behind these inequalities are not yet well understood (Lamb et al 2008). However, they appear to be related to differences in Māori men's access to appropriate information and to diagnostic and treatment services. Primary care practitioners should work to understand any barriers that exist for Māori men in terms of accessing such services (for example, difficulty getting to a laboratory or outpatient appointment due to work commitments, family needs or transport difficulties). Where possible, primary care practitioners should try to address any individual or system-level barriers, so their patients fully understand why they may need further diagnostic work.

1.4. Other demographic and lifestyle factors

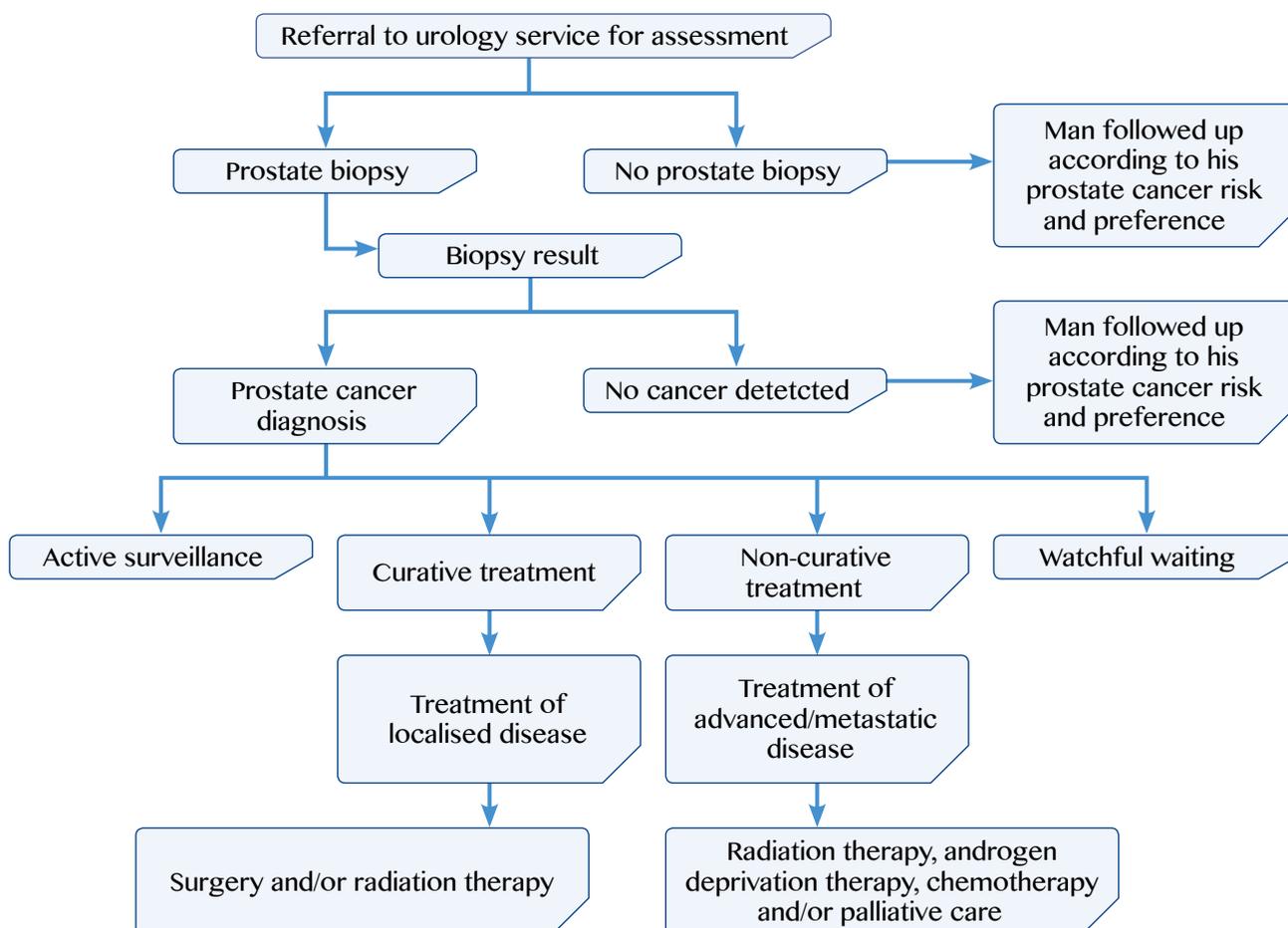
Men who live in rural or low-decile communities may have restricted access to diagnostic or treatment services, meaning that they may be more likely to have poorer prostate cancer outcomes than men who do not live in such communities. Research shows a disparity in PSA testing across New Zealand, with a higher proportion of men being tested in decile 1 communities compared with decile 10 (Gray et al 2005). It is not known if this higher rate of testing results in better outcomes, or not. However, it suggests a significant disparity in access to health services between men who live in low-decile communities and those in higher-decile communities.

There is conflicting evidence whether obesity, smoking, diet, prostatitis or sexually transmitted infections can increase a man’s risk of developing prostate cancer (Health Science Center San Antonio 2006; Cancer Research UK 2014; American Cancer Society 2015a, 2015b). In general, these men should be managed in the same way as any other man presenting to their primary care practitioner with prostate-related concerns.

1.5. Obtaining informed consent for prostate cancer testing

Primary care practitioners must obtain informed consent (which can be verbal consent) before doing a PSA test and/or DRE. The decision to have a PSA test and/or DRE is entirely the man’s, but it is the primary care practitioner’s responsibility to make sure the man understands the benefits and risks before he makes his decision. This includes making sure the man understands the benefits and risks of the PSA test and DRE, and the benefits and risks of the procedures he could undergo if he has an abnormal PSA or DRE or is diagnosed with prostate cancer (see Figure 1).

Figure 1: Prostate cancer care pathway following referral to a urology service



How primary care practitioners present this information will vary depending on each man's needs and level of health literacy. The information that they should provide is included in section 1.6.

Men should be invited to bring a support person with them to their appointment with their primary care practitioner. This person could be their partner, a close friend or a member of their extended family or whānau.

1.6. The benefits and risks of prostate cancer testing and treatment

The role of primary care practitioners is to provide men and their family and whānau with clear and balanced information about the benefits and risks of prostate cancer testing, so that they can make an informed decision on whether or not to proceed. The information that men need to make an informed decision is included in sections 1.6.1. to 1.6.5 below. How primary care practitioners provide this information may need to change depending on each man's individual needs.

1.6.1. Benefits of prostate cancer testing

- Men and their family and whānau can be reassured that prostate cancer is unlikely to be present if the man's PSA and DRE are normal.
- If testing indicates that prostate cancer is present, it is likely to be early stage, meaning that the chance of cure is greater (Albertson et al 2005; Cooperberg et al 2010).
- If a man is found to have localised, low-risk prostate cancer, he has the option of entering an active surveillance programme.⁴ This will allow him to delay or avoid potential treatment-related harms.

1.6.2. Risks of prostate cancer testing

- PSA testing and DRE can produce false positives due to calcifications in the prostate, prostatitis, urinary tract infection, benign prostatic hypertrophy, recent ejaculation or cycling.
- PSA testing can also produce false negatives when the prostate cancer releases no or little PSA.

1.6.3. Risks of prostate biopsy

- An abnormal PSA test does not confirm that a man has prostate cancer. However, it does indicate the need for further diagnostic testing; usually a prostate biopsy.
- Risks associated with prostate biopsy include:
 - false negatives (where the biopsy misses the prostate cancer)
 - infection / systemic sepsis (Loeb et al 2013)
 - transient haematuria
 - transient haemospermia
 - transient rectal bleeding.

⁴ For more information on active surveillance, visit:
www.health.govt.nz/publication/guidance-using-active-surveillance-manage-men-low-risk-prostate-cancer

1.6.4. Risks of active surveillance

- Men on active surveillance are more likely to die from another cause than from their prostate cancer, but some men on active surveillance will still develop more aggressive disease and may require curative treatment.
- Men on active surveillance require regular monitoring. This mostly relies on the findings of repeat prostate biopsies, PSA tests, DREs and occasionally MRIs.
- Some men find active surveillance psychologically stressful. Around 20–30 percent of men on active surveillance decide to exit the programme in favour of curative treatment or watchful waiting.

1.6.5. Benefits of curative treatment

- Curative treatment is successful:
 - in most men with early and moderately advanced disease (70–85 percent relapse-free survival at 10 or more years after treatment)
 - in many men with locally advanced disease (50–60 percent relapse-free survival at 10 or more years after treatment).
- Outcomes from curative treatment are also affected by co-morbidities, such as diabetes, obesity, cardiovascular disease and respiratory problems.

1.6.6. Risks of curative treatment

- Curative treatment of any cancer carries a risk of adverse events, including failure to stop the spread of the disease.
- The curative options for prostate cancer – radical prostatectomy, external beam radiation therapy, high dose rate brachytherapy and low dose rate brachytherapy (seeds) – differ in their adverse effect profiles.
- Some radiation oncology and urology services do not offer high dose rate brachytherapy and low dose rate brachytherapy.
- All curative treatments have a risk of erectile dysfunction, although erectile dysfunction is not uncommon in men aged over 50 years without prostate cancer (Weber et al 2013).
- Radical prostatectomy carries the additional risk of urinary incontinence.

1.6.6.1. Risks of radical prostatectomy

- Early risks associated with a surgical procedure, such as wound infections.
- Later risks include urinary incontinence and erectile dysfunction (Wilt et al 2012; Wallis et al 2015).
- Wound infections generally resolve themselves quickly with antibiotic treatment, but urinary incontinence and erectile dysfunction may continue indefinitely.

1.6.6.2. Risks of radiation therapy

- Early risks during and for up to several months after radiation therapy include fatigue, acute prostatitis, urethritis, cystitis, and proctitis.
- The later risks of radiation therapy include erectile dysfunction, rectal bleeding and lower urinary tract symptoms.

Note 2: Prostate specific antigen (PSA) testing

2.1. General information about PSA

PSA is produced by the epithelial cells of the prostate. PSA is organ-specific rather than cancer-specific, meaning that PSA levels may be elevated in the presence of non-malignant prostate conditions, such as benign prostatic hypertrophy or prostatitis (Stamey et al 1987).

Other factors may also produce a temporary increase in men's PSA levels. For this reason, men should ideally not have a PSA test within two days of having a DRE or within three days of ejaculation or cycling (National Health and Medical Research Council 2013). If a man consents to having a PSA test as well as a DRE, the PSA test should always be done first.

2.2. The relationship between age, PSA level and prostate cancer

Generally the higher a man's PSA level, the more likely it is that he has prostate cancer (Heidenreich 2008). However, some men will have prostate cancer even in the absence of a raised PSA (Thompson et al 2004).

Increased PSA levels can be transient, which is why men should always have a repeat PSA test after 6–12 weeks to confirm the result. The exceptions to this are if a man has a raised PSA level and an abnormal DRE or if a man has a raised PSA level and one of the red flags shown in the algorithm on page 3 (see Note 4 for more information on the red flags).

Whether a man's PSA result is considered clinically significant or not depends on his age. This is because the benefits of early diagnosis reduce with increasing age. At 70 years old, a man diagnosed with prostate cancer has a 50 percent chance of his prostate cancer becoming symptomatic during his lifetime, but by the time he reaches 75 years of age this risk reduces to 33 percent (Lamb et al 2007).

Table 1 identifies what an abnormal PSA level is, by age. If a man's PSA level is between 4.0 µg/L and 10.0 µg/L, there is a 40 percent chance of detecting prostate cancer on prostate biopsy (Leinert et al 2009). If a man's PSA level is between 10.0 µg/L and 20.0 µg/L, there is a 67 percent chance of detecting prostate cancer. A PSA level of more than 20.0 µg/L means that prostate cancer is highly likely to be present and metastases can sometimes be seen on bone or computed tomography (CT) scans. Values over 10 µg/L are rarely the result of benign prostatic hypertrophy, but prostatitis can cause significant and rapid rises in PSA levels.

Table 1: Definitions for an abnormal PSA level, by age

Age group	Abnormal PSA level (µg/L)
Men aged ≤ 70 years	≥ 4.0
Men aged 71–75 years	≥ 10.0
Men aged ≥ 76 years	≥ 20.0

Note 3: Digital rectal examination (DRE)

Most prostate cancers are located in the peripheral zone of the prostate gland and some can be detected on DRE (Horwich et al 2001).

Prostate cancer may present as a hard, discrete nodule or with asymmetry of the prostate gland. An enlarged prostate gland is not a good indicator for prostate cancer if the man's PSA result is normal, as the prostate gland generally increases in size as men age.

A man with an abnormal DRE should be referred to a urology service. An abnormal DRE indicates the need for a prostate biopsy, as it can be predictive of more aggressive prostate cancer (Katie et al 2007; Gosselaar et al 2008).

Some men may be reluctant to have a DRE. For Māori and Pasifika men, there may also be a cultural barrier to the procedure. Primary care practitioners should inform these men that not every prostate cancer increases PSA and there is a chance that they will still have prostate cancer even if their PSA result is normal. Around 20 percent of prostate cancers are diagnosed from an abnormal DRE when the PSA level is normal.

If a man declines a DRE, even after he has been given the above information, it is acceptable to refer him to a urology service based on two clearly abnormal PSA results.

Note 4: Red flags that may indicate advanced or metastatic prostate cancer

If a man has a clearly abnormal PSA result and any of the conditions described in Table 2, he does not need to have a second PSA test before being referred to a urology or radiation oncology service. An abnormal PSA result in the presence of any of these conditions may indicate that the man has advanced or metastatic prostate cancer.

For information on the level of urgency required in referring a man with a red flag present to a urology or radiation oncology service, see Note 6.

Table 2: Red flags that may indicate advanced or metastatic prostate cancer

Red flag	Description
Acute neurological symptoms (<i>ie, spinal cord compression</i>)	<p>Acute neurological symptoms consistent with spinal cord compression or cauda equina compression.</p> <p>The most common is spinal cord compression, which occurs in up to 12 percent of men with metastatic prostate cancer. Spinal cord compression is an emergency. It frequently presents as increasingly severe back pain and subsequent neurological symptoms including weakness, unsteadiness, numbness, urinary retention, urinary incontinence or faecal incontinence. Spinal cord compression less commonly presents as bladder or bowel incontinence or retention/constipation.</p> <p>Men who present with a clearly abnormal PSA and acute neurological symptoms should be immediately referred to a radiation oncology service or, where no radiation oncology service is available, to a urology service. Delays in referral and diagnosis may influence functional outcome. Early diagnosis and rapid treatment of spinal cord compression are crucial for neurological recovery.</p>
Renal failure	<p>Prostate cancer resulting in renal failure is usually evident as locally advanced disease on DRE. Symptoms of renal failure include tiredness, lack of energy, nausea, peripheral oedema and poor appetite.</p>
Bone pain	<p>Metastatic prostate cancer may initially present as new-onset, progressive and severe bone pain, often with local tenderness. Men with a clearly abnormal PSA and bone pain should be discussed with a urologist and considered for prostate biopsy and androgen deprivation therapy. If the bone pain is severe, admission to hospital should also be considered for symptom control.</p>
Macroscopic haematuria (<i>without urinary tract infection</i>)	<p>Haematuria is rarely associated with prostate cancer but, when it is, it is usually a late sign of locally advanced disease. DRE is often grossly abnormal. Patients with haematuria and a markedly raised PSA level (in the absence of infection) should be discussed with a urologist.</p>

Note 5: Follow-up options after a normal PSA and DRE

5.1. Follow-up options for men with a family history of prostate cancer

As noted in section 1.2 a man is defined as having a family history of prostate cancer if he has at least one first-degree relative (father or brother) who was diagnosed with prostate cancer. Although there is no strong evidence to support how often to test men with a family history of prostate cancer, best practice suggests that these men should be offered a PSA test and DRE every 12 months from the age of 40–70 years.

5.2. Follow-up options for men without a family history of prostate cancer

To date, there has been no clear evidence to indicate that regularly testing men without a family history of prostate cancer will reduce their risk of prostate cancer mortality. These men, particularly those aged over 70 years, can therefore be reassured further prostate cancer testing is not likely to be of any benefit. However some men will want further testing regardless. If a man with a normal PSA and DRE, or a single abnormal PSA, requests further testing, he should be offered repeat PSA tests and DREs every two to four years, depending on his personal preference (Catalona et al 2011; Basch et al 2012). If his situation changes, use the algorithm on page 3 to guide the decision on whether to refer him to a urology service.

Note 6: Referral to a specialist service

Table 3 identifies how urgently men should be seen by a urology or radiation oncology service, depending on their particular signs and symptoms. These referral criteria aim to ensure that priority is given to:

- men who have progressive or new onset symptoms that may indicate metastatic or advanced prostate cancer (see note 4 for more detail on which acute neurological, renal, bone pain and haematuria symptoms are considered red flags)
- men who are likely to have more advanced localised prostate cancer and who would benefit from early assessment and treatment.

For more information on PSA testing and DRE, see Notes 2 and 3.

Table 3: Criteria for referral to a urology or radiation oncology service

Type of referral	Criteria
Immediate referral (<i>should be seen within 24 hours</i>)	<ul style="list-style-type: none"> PSA is ≥ 10 $\mu\text{g/L}$ AND severe back pain AND acute neurological symptoms consistent with spinal cord compression or cauda equina compression (<i>Note: Where available, refer to a radiation oncology service in the first instance by phone consult with on-call radiation oncologist</i>)
Urgent referral (<i>should be seen within 14 days</i>)	<ul style="list-style-type: none"> PSA is ≥ 10 $\mu\text{g/L}$ AND renal failure is present (<i>Note: Phone consult with an on-call urologist is recommended</i>) PSA is ≥ 10 $\mu\text{g/L}$ AND bone pain (new onset, progressive and severe) is present (<i>Note: Phone consult with an on-call urologist is recommended</i>) PSA is ≥ 10 $\mu\text{g/L}$ AND macroscopic haematuria is present (<i>Note: Phone consult with an on-call urologist is recommended</i>) PSA is ≥ 10 $\mu\text{g/L}$ AND prostate feels hard and/or irregular on DRE
Routine referral (<i>should be seen within 6–8 weeks</i>)	<ul style="list-style-type: none"> PSA is between 4 and 10 $\mu\text{g/L}$ AND macroscopic haematuria is present (in the absence of infection) PSA is < 10 $\mu\text{g/L}$ AND prostate feels hard and/or irregular on DRE Two clearly abnormal PSA results 6–12 weeks apart (see <i>Table 1 on page 8 for definitions of a clearly abnormal PSA</i>)

The Government's Faster Cancer Treatment (FCT) programme⁵ aims to reduce waiting times for appointments, tests and treatment and standardise care pathways for all patients wherever they live. The rationale for implementing the FCT programme is that prompt treatment is more likely to ensure better outcomes for cancer patients. Men who meet any of the criteria set out in Table 3 are considered to have a 'high suspicion of cancer'. However, only men who require immediate or urgent referral to a urology or radiation oncology service should be included in the cohort for the FCT 62 day health target.

⁵ For more information on the Faster Cancer Treatment health target, visit: www.health.govt.nz/new-zealand-health-system/health-targets/about-health-targets/health-targets-faster-cancer-treatment

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