



Evidence-Based Series 24-3 Version 2

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Referral of Suspected Prostate Cancer by Family Physicians and Other Primary Care Providers

The Prostate Cancer Referral Expert Panel

An assessment conducted in November 2022 deferred the review of Evidence-Based Series (EBS) 24-3 Version 2. This means that the document remains current until it is assessed again next year. The PEBC has a formal and standardized process to ensure the currency of each document ([PEBC Assessment & Review Protocol](#))

EBS 24-3 Version 2 is comprised of 4 sections. You can access the summary and full report here:

<https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/221>

Section 1: Guideline Recommendations (ENDORSED)

Section 2: Evidentiary Base

Section 3: Development Methods, Recommendations Development and External Review Process

Section 4: Document Assessment and Review

December 19, 2016

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Phone: 905-527-4322 ext. 42822 Fax: 905 526-6775 E-mail: ccopgi@mcmaster.ca

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Version 2 ENDORSED.

Guideline Report History

GUIDELINE VERSION	SYSTEMATIC REVIEW		PUBLICATIONS	NOTES AND KEY CHANGES
	Search Dates	Data		
Original version Oct. 2016	1999 – 2011	Full Report	Web publication	NA
Current Version 2 December 2016	2012 - 2016	New data found in section 4: Document Review Summary and Tool		2012 recommendations ENDORSED

Evidence-Based Series 24-3 Version 2: Section 1

**A Quality Initiative of the
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)
Referral of Suspected Prostate Cancer by Family Physicians
and Other Primary Care Providers**

*S. Young, P. Bansal, E. Vella, A. Finelli, C. Levitt, A. Loblaw,
and the Prostate Cancer Referral Expert Panel*

December 19, 2016

These guideline recommendations have been **ENDORSED**, which means that the recommendations are still current and relevant for decision making.

Please see **Section 4: Document Review Summary and Tool** for a summary of updated evidence published between 2012 and 2016, and for details on how this Clinical Practice Guideline was **ENDORSED**

GUIDELINE OBJECTIVE

How should patients presenting to family physicians and other primary care providers (PCPs) with signs and/or symptoms of prostate cancer, including incidental prostate specific antigen (PSA) test results, be managed? The following questions are the factors considered in answering the overall question:

RESEARCH QUESTIONS

1. What signs, symptoms, and other clinical features that present in primary care are predictive of prostate cancer?
2. What is the diagnostic accuracy of investigations commonly considered for patients presenting with signs and/or symptoms of prostate cancer?
3. What major, known risk factors increase the likelihood of prostate cancer in patients presenting with signs and/or symptoms of prostate cancer?
4. Which factors are associated with delayed referral? Which delay factors can be attributed to patients, and which factors can be attributed to providers or system-related factors? Does a delay in the time to consultation affect patient outcome?

TARGET POPULATION

Adult male patients presenting in primary care settings with signs, including incidental PSA results (defined as results not ordered by the attending FP or other primary care provider [PCP]), or symptoms suggestive of prostate cancer comprise the target population. This guideline does not provide recommendations for screening healthy patients or opportunistic PSA testing.

INTENDED USERS

This guideline is targeted to family physicians (FPs), general practitioners (GPs), emergency room physicians, other PCPs (nurse practitioners, registered nurses, and physician assistants), and urologists. For the purposes of this document, we have referred to FPs, GPs, emergency room physicians, and other PCPs as “FPs and other PCPs”. The guidelines are also intended for policymakers to help ensure that resources are in place so that target wait times are achieved. They are intended to coincide with the introduction of prostate cancer Diagnostic Assessment Programs (DAPS) in Ontario. DAPs provide a single point of referral, coordination of care using a clinical navigator, fast tracking of diagnostic tests, and a multidisciplinary team approach. They are an Ontario-wide strategic priority designed to improve patient access and outcomes, as outlined in the Ontario Cancer Plan, 2005-2011 and 2011-2014 (1).

Added in December 2019: Formal Cancer Care Ontario DAPs no longer exist in Ontario, but many hospitals provide ongoing multidisciplinary team approaches to diagnosing prostate cancer.

RECOMMENDATIONS

The following recommendations were adapted from the New Zealand Guidelines Group (NZGG) guideline “Suspected Cancer in Primary Care: Guidelines for Investigation, Referral and Reducing Ethnic Disparities” and the National Institute for Health and Clinical Excellence (NICE 2005), “Referral Guidelines for Suspected Cancer” (2,3). The recommendations below reflect the integration of the NZGG 2009 and NICE 2005 recommendations, an updated systematic review of the research evidence since the NZGG 2009 and the NICE 2005 guidelines, and consensus by the PEBC Prostate Cancer Referral Working Group (see Section 2: Appendix 1 for a list of members) (2,3). The recommended wait times for referral were based on consensus as opposed to strong evidence from well-conducted studies.

During the review process for this document in December 2016 when Version 2 of this guideline was ENDORSED, the Expert Panel noted that these wait time targets should be the goal, but may not always be possible.

Recommendation 1: Actions for Patients with Unexplained Symptoms of Metastatic Prostate Cancer
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<p>A man aged 40 years or older should have a digital rectal examination (DRE) and a PSA test if he has any unexplained symptoms suggestive of metastatic prostate cancer:</p>

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| <ul style="list-style-type: none"> • Suspicious lower back pain symptoms such as those associated with reproducible percussion tenderness • Severe bone pain • Weight loss, especially in the elderly |
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<p>Guidance for referral is as follows:</p>

- | |
|---|
| <ol style="list-style-type: none"> a. If the prostate is hard or irregular on DRE or PSA is 20 ng/ml or more, then patients should be referred urgently, which may include additional communication (e.g., telephone call, fax), and expect a consultation with a urologist or a prostate DAP within one week. b. If the PSA is between 10 and 20 ng/ml, then patients should be referred semi-urgently and expect a consultation with a urologist or a prostate DAP within two weeks. c. If the PSA is less than 10, then consider other metastatic cancers. If there is still a suspicion for prostate cancer, then patients should be referred non-urgently and expect a consultation with a urologist or a prostate DAP within four weeks. |
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Recommendation 2: Actions for Patients with Lower Urinary Tract Symptoms (LUTS)

For a man presenting with lower urinary tract symptoms (LUTS) (irritative and obstructive voiding symptoms), a DRE should be performed and a discussion about the benefits and risks of PSA testing should occur with the patient (refer to Individual Risk Assessment from the Canadian Partnership Against Cancer PSA toolkit) (4). Lower urinary tract infection should be excluded before PSA testing, especially in men presenting with LUTS. The PSA test should be postponed for at least one month after treatment for a proven urinary infection.

Guidance for referral is as follows:

- a. If the prostate is hard or irregular on DRE, a PSA test should be ordered, and the patient should be referred non-urgently and expect a consultation with a urologist or a prostate DAP within four weeks.
- b. If the prostate is hard or irregular on DRE and the [age-based PSA](#) is elevated but less than 10 ng/ml, then the patient should be referred non-urgently and expect a consultation with a urologist or a prostate DAP within four weeks.
- c. If the prostate is hard or irregular on DRE and the PSA is between 10 and 20 ng/ml, then the patient should be referred urgently, which may include additional communication (e.g., telephone call, fax), and expect a consultation with a urologist or a prostate DAP within one week.
- d. If the PSA is 20 ng/ml or more, then the patient should be referred urgently, which may include additional communication (e.g., telephone call, fax), and expect a consultation with a urologist or a prostate DAP within one week.
- e. If the prostate is normal on DRE and the PSA is between 10 and 20 ng/ml, then the patient should be referred semi-urgently and expect a consultation with a urologist or a prostate DAP within two weeks.
- f. If the prostate is normal on DRE and the [age-based PSA](#) is elevated but less than 10 ng/ml, then appropriate [nomograms](#)* should be used to determine the risk of high grade prostate cancer (5).
 - i. If the risk of high grade prostate cancer is less than 5%, then annual monitoring of PSA and DRE is recommended. This is based on the premise that repeated PSA testing is supported by the patient and FP or other PCP.
 - ii. If the risk of high-grade prostate cancer is between 5% and 20%, then discussion about other management options should occur with the patient. Based on patient preference, this could include referral to a urologist or a prostate DAP or annual or more frequent follow-up of PSA testing and DREs. This is based on the premise that repeated PSA testing is supported by the patient and FP or other PCP.
 - iii. If the risk of high-grade prostate cancer is greater than 20%, then the patient should be referred non-urgently and expect a consultation with a urologist or a prostate DAP within four weeks.

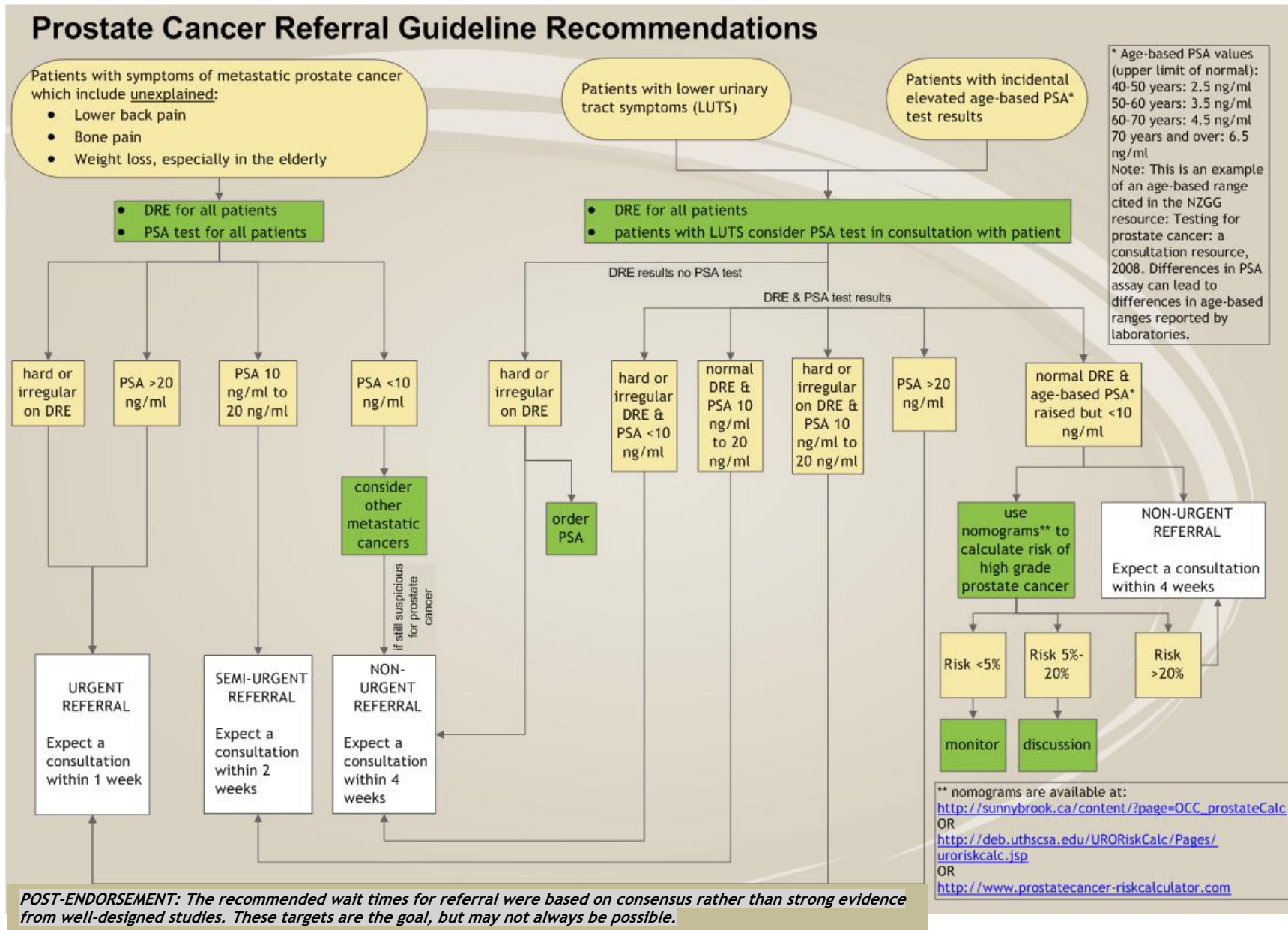
*If a nomogram is not used, then the patient should be referred non-urgently and expect a consultation with a urologist or a prostate DAP within four weeks.

Recommendation 3: Actions for Patients with Incidental PSA

For incidental elevated [age-based PSA](#) findings, a DRE should be performed for all patients. Rule out other reasons for elevated PSA values (e.g. age-related hypertrophy [benign prostatic hypertrophy; BPH], infection, inflammation, prostatitis, recent sexual activity,

etc.). Repeat PSA test if unsure. The recommendations b) through f) for LUTS (see Recommendation 2: above) should be followed.

ALGORITHM



KEY EVIDENCE AND JUSTIFICATION

All recommended wait times were based on consensus of the Working Group. The Canadian Association of Radiation Oncology recommended a wait time from referral to consultation with a radiation oncologist of no longer than 10 working days (6). This was taken into consideration when developing the wait times in this guideline.

The primary care literature evidence examining the diagnostic accuracy of tests for prostate cancer was very weak. Two studies suggested that DREs performed by FPs may be useful in identifying patients who should be referred (7,8), and four studies suggested that PSA values were good predictors of prostate cancer with PPVs ranging from 34.3% to 47% (7,9-11). The working group chose to endorse the recommendations from NICE 2005 and NZGG 2009 to recommend a DRE and PSA test for all patients with symptoms of metastatic prostate cancer (2,3). NICE 2005 recommended performing a DRE and PSA test for all men with LUTS and NZGG 2009 recommended these tests only for older men with LUTS (2,3). The working group chose to recommend a DRE for all men with LUTS and a PSA test for selected patients with LUTS, following discussion and treatment. The limited evidence from the systematic review suggested that men with LUTS may not be at any higher risk for prostate cancer or have a poorer prognosis than asymptomatic men would be (9,12). The Canadian Urological Association's benign prostatic hyperplasia guideline for men presenting with LUTS recommended a DRE for all men and a PSA test for selected patients (13). The working group chose to be consistent with this guideline.

Recommendation 1. Actions for Patients with Symptoms of Metastatic Prostate Cancer

The NZGG 2009 guideline recommendation that patients with symptoms of metastatic prostate cancer should have a DRE and PSA was endorsed (3). An age threshold of 40 years was included at the suggestion of the Expert Panel and due to the few cases of prostate cancer in men under 40 years in Canada (14). The working group did not think it necessary for a man with erectile dysfunction to undergo a DRE and PSA test and therefore excluded it as a symptom of metastatic prostate cancer. This is consistent with the NZGG 2009 guideline but in contrast to the NICE 2005 guideline (2,3). The working group also excluded unexplained hematuria as a symptom of metastatic prostate cancer because although it can be associated with advanced prostate cancer, the Working Group believed the vast majority of men with gross hematuria usually have a different underlying cause such as benign prostatic hyperplasia, bladder or renal cancer, stones or infections. The working group believed hematuria requires urologic assessment but is not part of a prostate cancer care algorithm.

a-c. The cut-off values of 10 and 20 ng/ml were taken from the D'Amico classification system for categorizing patients at low risk (cT1-cT2a, Gleason <7 and PSA ≤10 ng/ml), intermediate risk (cT2b, Gleason = 7 or [PSA >10 and ≤20 ng/ml]) or high risk (cT2c or PSA >20 ng/ml or Gleason >7) for prostate cancer (15,16). Although this was not developed in the primary care population, the working group chose to include this classification system because it is widely used to classify risk of prostate cancer and using these thresholds provides guidance for family physicians in determining their course of action.

Recommendation 2. Actions for Patients with Lower Urinary Tract Symptoms (LUTS)

The recommendation that a man with LUTS should have a DRE and a discussion about PSA testing was consistent with the Canadian Urological Association's guideline for benign prostatic hyperplasia (13). The working group referred to the individual risk assessment developed by the Canadian Partnership Against Cancer as a guide to who should be given a PSA test (4). This document describes the benefits and harms of PSA testing. The working group also endorsed the recommendations to exclude urinary infection before PSA testing and

to postpone PSA testing for at least one month after treatment from the NICE 2005 and NZGG 2009 guidelines (2,3).

- a. This recommendation was endorsed from the NICE 2005 guideline (2).
- b. The age-based PSA values were endorsed from the NZGG 2009 guidelines (3).
- c-e. Please refer to a-c in the previous section under Recommendation 1: Actions for Patients with Symptoms of Metastatic Prostate Cancer.
- f. i. A cut-off risk value of 5% was chosen because in Ontario, Canada, the hospital admission rate for urological complications within 30 days of TRUS-guided biopsy was found to be 4.1% in 2005 (17). The working group decided to use 5% as a cut-off to separate patients into a higher risk category because for these patients the risk of high-grade prostate cancer would be higher than the risk of complications from TRUS-guided biopsy.
 ii-iii. The prostate risk calculator developed at Sunnybrook Hospital, Toronto, Ontario, Canada, showed a net benefit (the relative value of false-positive versus false-negative results) when a risk of 15% for aggressive prostate cancer was chosen as a threshold to agree to a biopsy (18). Based on the consensus of the working group a conservative cut-off risk value of 20% was chosen.

Recommendation 3. Actions for Patients with Incidental PSA

Although this guideline excludes patients in a screening program, the working group thought that FPs and other PCPs need guidance on how to manage patients with incidental PSA test results, a frequently encountered occurrence in practice. Opportunistic screening has been excluded because it is beyond the scope of this guideline.

The working group believed that if an incidental PSA test was abnormal, then standard practise would be to perform a DRE. A hard or irregular prostate on DRE may increase the urgency of referral.

Cases with enlarged, smooth prostates were excluded because it was beyond the scope of this guideline since it was not considered to be a sign of prostate cancer. Also, although a rising PSA level could be considered a sign of prostate cancer, the working group believed the guideline was sufficiently thorough to include most possible scenarios for prostate cancer using the absolute PSA values. Furthermore, there were no studies examining the factors associated with delayed referral that could directly inform these recommendations.

FUTURE RESEARCH

Further studies are required that specifically investigate the diagnostic performance of signs, symptoms, or tests for prostate cancer in the primary care setting.

GLOSSARY

Age-based PSA

Age-based PSA values (upper limit of normal):

40-50 years: 2.5 ng/ml

50-60 years: 3.5 ng/ml

60-70 years: 4.5 ng/ml

70 years and over: 6.5 ng/ml

Note: This is an example of an age-based range cited in the NZGG resource:

Testing for prostate cancer: a consultation resource, 2008 (19). Differences in PSA assay can lead to differences in age-based ranges reported by laboratories.

Nomograms

Prostate Risk Calculator developed by Nam et al 2011 is available here: http://sunnybrook.ca/content/?page=OCC_prostateCalc (5). The prostate risk calculator includes the free:total PSA ratio, which is the ratio of free PSA, unbound to serum proteins, to total PSA. This ratio is decreased in men with prostate cancer (20). The free:total PSA ratio in some cases may be charged a laboratory fee to the patient. If this ratio is not determined, then a value of 0.1 can be entered into the risk calculator.

The Prostate Cancer Prevention Trial Prostate Cancer Risk Calculator developed by Thompson et al 2006 using data from the Prostate Cancer Prevention Trial is available here: <http://deb.uthscsa.edu/URORiskCalc/Pages/uroriskcalc.jsp> (21)

The Prostate Cancer Risk Calculator developed by the Prostate Cancer Research Foundation, Rotterdam, in partnership with the European Randomized Study of Screening for Prostate Cancer is available here: <http://www.prostatecancer-riskcalculator.com/assess-your-risk-of-prostate-cancer> (22)

Case Examples

1. *Symptoms of metastatic prostate cancer*

A healthy 70 year old vigorous gentleman, on no medications, who ran marathons yearly in the spring presented to a FP. He lived in Florida in the winter and usually was seen only once yearly in the spring. He came home to Canada earlier than usual as he had urinary retention in Florida, was catheterized but was having tremendous lower back pain. This thin, muscular man had never complained about lower back pain before. On examination, a firm fixed pelvic mass was noted. DRE noted a firm, irregular, fixed, and enlarged prostate. The urologist saw him within two days. A presumptive diagnosis of prostate cancer with bone metastasis was made. The PSA was 20ng/ml. Although diagnosis of prostate cancer was likely, the patient refused a biopsy and further diagnostic tests. His pain was quite severe and he was admitted to a palliative care unit for pain control and died within three weeks.

2. *LUTS*

A healthy 72 year old man with some symptoms of urinary retention and urgency presented to a FP. His older brother was diagnosed with prostate cancer at age 76. Urine analysis was negative and DRE found a smooth, normal prostate. The FP and patient discussed having a PSA test but the patient refused and asked to see a urologist to discuss the LUTS and his family history and was seen two months later. After a discussion with the urologist, the patient agreed to have a PSA and the result was 4.9ng/ml. The urologist explained to the patient that the result was within normal limits for his age. The patient elected to be followed with serial PSAs and DREs by his

family physician. No treatments were initiated for the patient's symptoms of some urinary retention and urgency which seemed to resolve spontaneously. Since the first visit with the urologist, the PSA has been monitored every three months and has not increased beyond 6.8ng/ml in two years.

3. ***Incidental PSA***

A healthy 49 year old banker had a PSA test as part of a comprehensive medical examination offered through his insurance company. The physical examination was normal but the PSA was elevated for his age. He presented to his family doctor with a PSA of 3.5ng/ml and no other symptoms. The family doctor on DRE found a smooth, normal prostate. The family doctor evaluated the patient's risk for prostate cancer at 10-20% using the Prostate Risk Cancer nomogram and the patient elected to repeat the PSA and DRE in a few months. However, after further consideration at home, the patient called and asked to be referred to a urologist for a consultation.

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Updating

All PEBC documents are maintained and updated as described in the PEBC Document Assessment and Review Protocol at <http://www.cancercare.on.ca/>.

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Contact Information

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