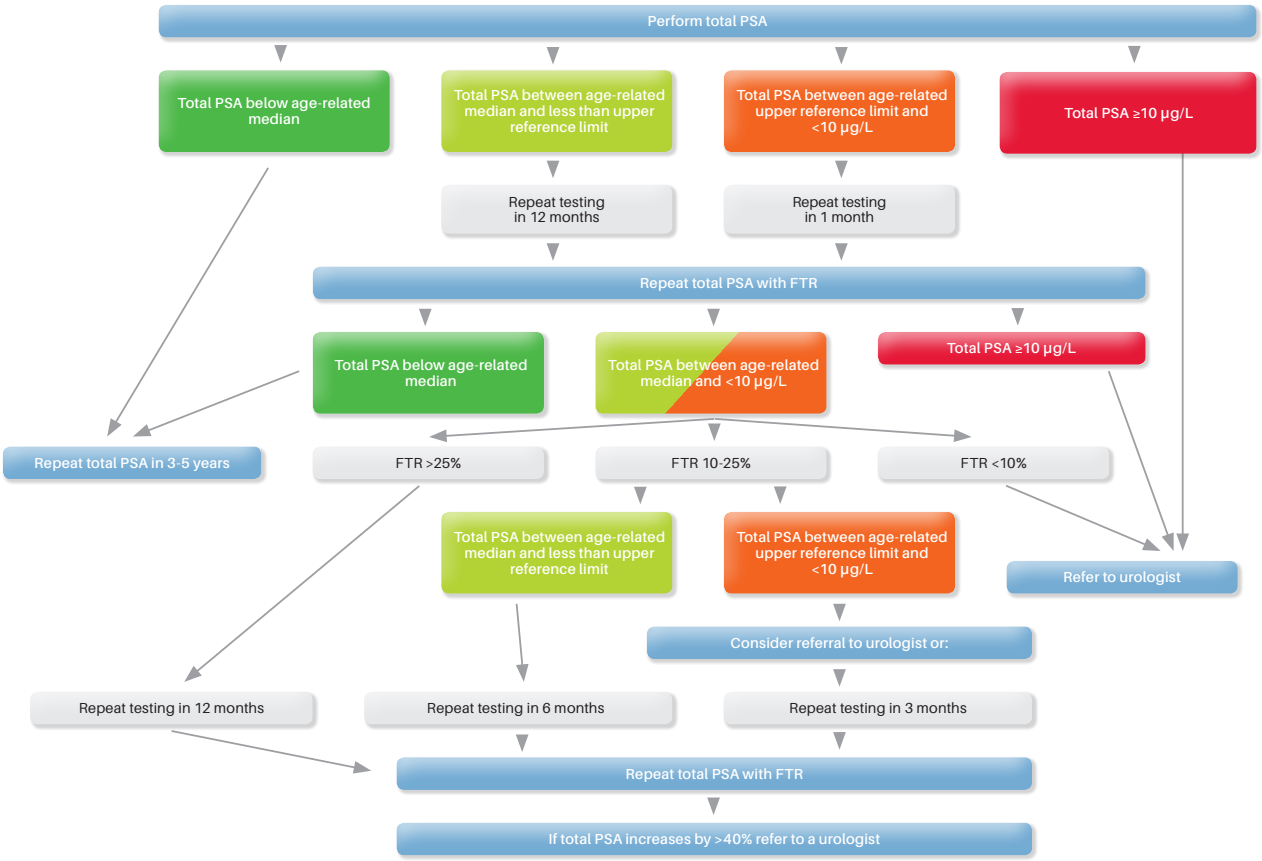
DOUGLASS HANLY MOIR PATHOLOGY

Quality is in our DNA

Assessment of prostate disease

Prostate carcinoma is the most commonly diagnosed cancer in Australian men, yet screening for early disease and the management of established disease both remain controversial. The pathology laboratory plays a key role at each point in this clinical pathway. PSA measurement (and phi estimation) allow early detection of established disease but also predict the risk of developing disease, while histological assessment of biopsy and resected tissue guides appropriate management and allows accurate prognosis.



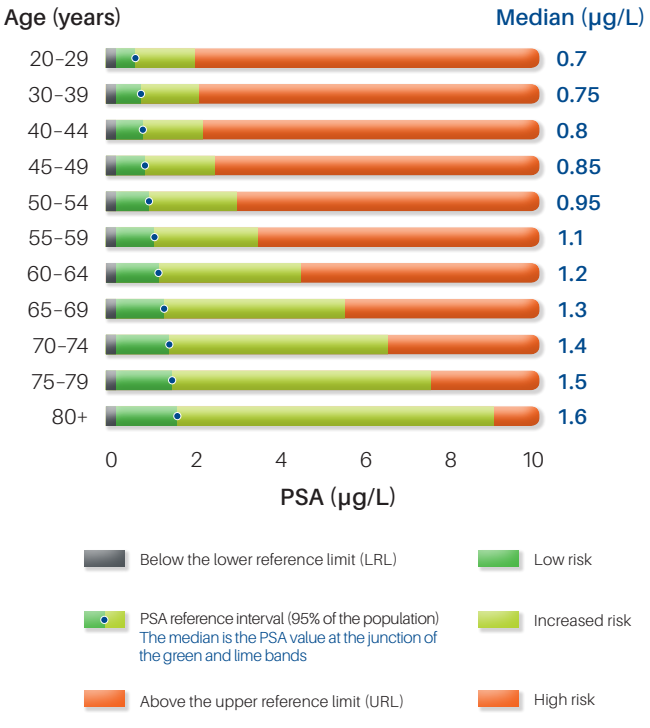
Prostate specific antigen (PSA)

This colour chart has been devised to assist with explaining results to patients.

Age-related PSA reference intervals are shown in dark green and lime, separated by the age-related median value (shown as a blue dot). Results below the median value and lower reference limit (LRL) are shown in green and indicate 'below average risk' of prostate cancer. Results between the median and the upper reference limit (URL), shown in lime, are associated with 'above average risk'. Results above the URL but less than 10 µg/L (shown in orange) are associated with 'increased risk' of prostate cancer. Results of 10 µg/L or above have 'significantly increased risk' of prostate cancer.

PSA reports include:

- The relevant age-specific reference interval for total PSA in five-year increments
- Median total PSA for age, where relevant
- If performed, the free PSA with age-related median
- Comments concerning follow-up



Medicare rebate and PSA

PSA test (total serum PSA) is rebated by Medicare

- One PSA test in a 12-month period if no history of prostate disease.
- For monitoring previously diagnosed prostate disease: no restrictions on total PSA ordering.

Free PSA test (free/total PSA ratio, FTR) is rebated by Medicare

- If total PSA is at, or above, the age-related median, but below the age-related method-specific upper reference limit: one episode FTR in a 12-month period.
- If total PSA is at, or above, the age-related method-specific upper reference limit, but below 10 µg/L: four episodes of FTR in a 12-month period.

A valid measurement of free PSA requires analysis without delay (within 24 hours). For measurement of free PSA on eligible patients on the same episode, please specify 'total PSA with free PSA if indicated' on the request form.

Medicare will NOT rebate free PSA (FTR) ordered in the following situations:*

- Total PSA result is below median for age (green and grey regions)
- PSA result is 10 µg/L or higher
- Number of free PSA tests already exceeded for a 12-month period.

*If free PSA is still required, the patient will be charged for the test.

What if my patient is a known prostate cancer patient?

Total PSA testing is unrestricted and can be ordered as considered clinically appropriate. Free PSA (FTR) is not indicated after prostate cancer has been diagnosed.

Prostate Health Index (phi)

An assay for a marker for prostate cancer is available — truncated proPSA (p2PSA). This molecule circulates as part of the free PSA fraction, and is present as a higher proportion of the free PSA fraction in patients with prostate cancer. Enhanced sensitivity and specificity for prostate cancer are found when proPSA is combined with free PSA and total PSA, as a calculation known as the Prostate Health Index (phi).

The phi is reported as a single value (or index) and is interpreted according to the table, which gives a probability of prostate cancer according to phi.

phi	0–24	25–34	35–54	55+
Probability of prostate cancer (95%CI*)	11% (6.5–15.8%)	18.1% (13.7–22.6%)	32.7% (27.3–38.0%)	52.1% (42–62.1%)

*Confidence Interval

A study showed that men with higher phi values had a higher risk of prostate cancer (study population n, 892 with serum PSA 2–10 µg/L). A man with phi greater than 55 had a 52% probability of positive prostate biopsy, whereas a man with phi less than 25 had an 11% probability of prostate cancer.

What is the benefit of the phi result?

Phi has been found to be more accurate than PSA and free PSA (FTR).[1]

The study indicated a phi result can give confidence about whether to proceed to prostate biopsy.

PSA	~55% diagnostic accuracy for prostate cancer†
Free/total PSA ratio	~65% diagnostic accuracy for prostate cancer
phi	~75% diagnostic accuracy for prostate cancer

† Based on Area Under Curve analysis of Receiver Operator Characteristic Curves

Because the proPSA is expressed in malignant cells, the phi can preferentially detect more aggressive cancers which are likely to grow and spread more rapidly.

Phi is minimally influenced by the age of an individual (hence no problem with reference intervals).

[1] Catalona W, et al. A multi-center study of [-2] pro-prostate specific antigen (PSA) combined with PSA and free PSA for prostate cancer detection in the 2.0 to 10.0 ng/mL PSA range. *J Urol.* 2011; 185(5):1650-1655

When is phi indicated?

The phi is likely to be most useful in men where the total PSA lies between 2 and 10 µg/L.[1] Determining the cancer risk in this range can be difficult, as up to 25% of new prostate cancer patients have a total PSA <4 µg/L and 60–70% of men with a PSA value >4 µg/L have a benign biopsy result. Because of this uncertainty, a prostate biopsy is often considered necessary to establish the diagnosis.

It is envisaged that this test may assist in reducing the number of unnecessary biopsies in these patients. The role of phi in other clinical situations, such as follow-up of radical prostectomy, has yet to be established. The phi test is currently not rebated by Medicare and patients will receive an account for $100.^

^Correct at time of printing

For further information on PSA and phi testing, or to discuss an individual patient, please contact our Chemical Pathologists on (02) 9855 5312.

Prostate Prognostic Grade Groups

The Grade Group is a recently adopted categorisation derived from the ISUP Modified Gleason Score, and allocates the patient into one of five prognostic categories or groups, with the lowest number indicating a very good prognostic tumour, and higher numbers indicating a poorer prognosis.

Grade Groups are designed to indicate to the patient the true range of low-grade to high-grade carcinoma and simplify the prognostic steps.

- **Needle biopsy specimens** – the Grade Group is derived from the score of the core biopsy/location with the highest ISUP Modified Gleason Score, NOT the composite score.
- **Radical prostatectomy specimens** – the Grade Group is derived from the index carcinoma within the prostate, NOT the composite carcinoma score. The index area of carcinoma ('index carcinoma') is defined for this purpose as that area of carcinoma in the prostate that has the highest clinical significance based upon grade, volume or stage, or any combination of the three.

The five Grade Groups and their corresponding ISUP Modified Gleason Scores are:

Prostate Prognostic Grade Groups	
Grade 1	Gleason Score ≤6
Grade 2	Gleason Score 3+4=7
Grade 3	Gleason Score 4+3=7
Grade 4	Gleason Score =8
Grade 5	Gleason Score ≥9

Prostate Grade Group (Modified Gleason)

Needle Core Grading

Primary pattern plus highest pattern

e.g. 3+4+5 → 3+5
4+3+5 → 4+5

- Grade Group from core with highest grade

Radical Prostatectomy Grading

Primary pattern plus secondary pattern plus comment on tertiary pattern.

e.g. 3+4+5 → 3+4=7 plus tertiary 5

- Grade Group from index carcinoma

Gleason Pattern of Variants

Ductal	= Pattern 4 (or 5 if necrosis)
Signet ring	= Pattern 4
Mucinous	= Subtract mucin and then grade. Many will be pattern 3
Small cell	= Not graded
Sarcomatoid	= Not graded
Post-therapy	= Not graded
Purely intraductal	= Not graded

For additional information regarding histopathology and Grade Groups, please contact our Anatomical Pathology Department on (02) 9855 5150.

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