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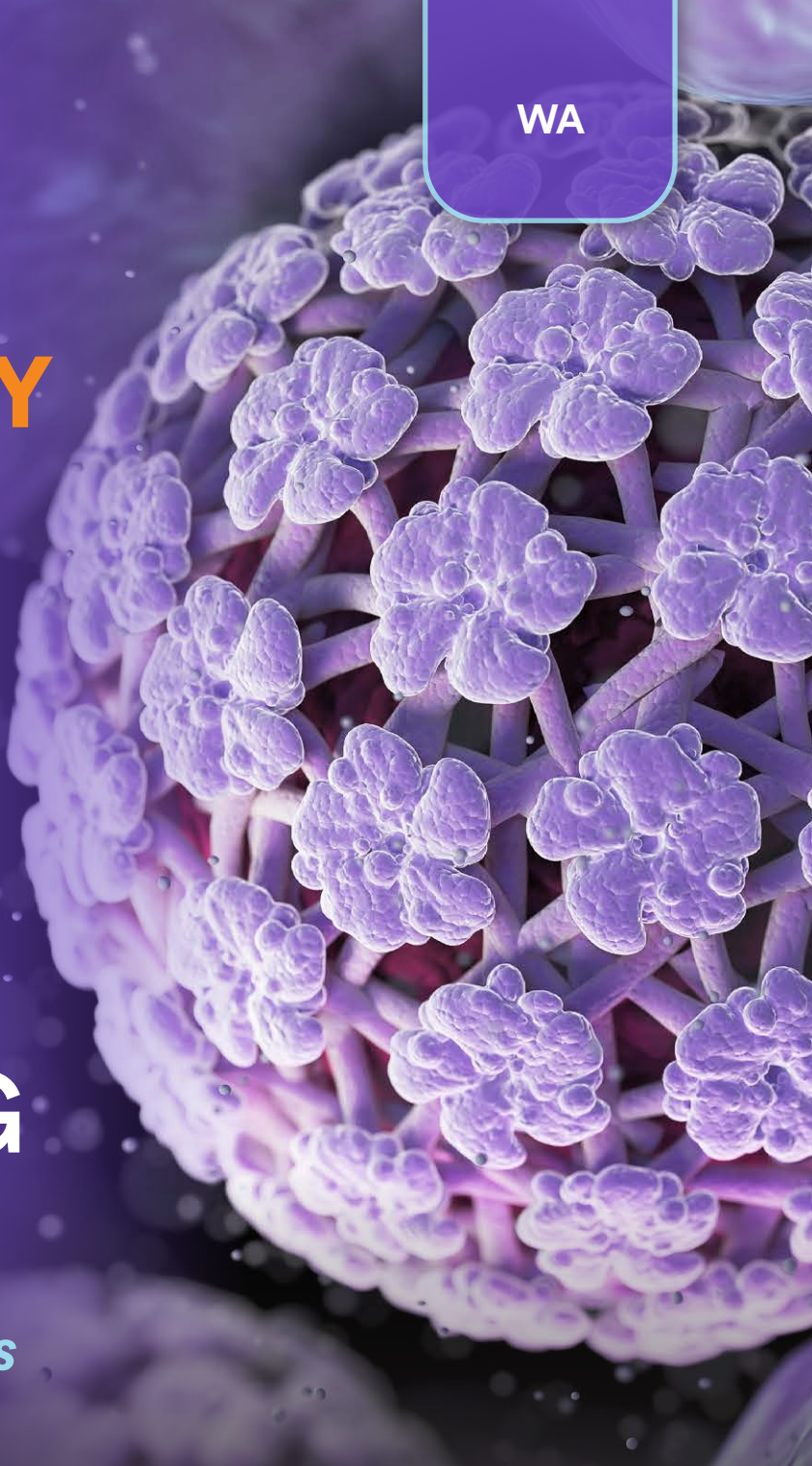

Navigating the NATIONAL CERVICAL SCREENING PROGRAM:

A clinical guide for GPs

By Dr Catherine Uzzell and Kerryn Jones, Head of Cytology (FASC, CCS)

The National Cervical Screening Program is more than just a screening program; the program encompasses all aspects of cervical health, including general population screening, management of detected cervical dysplasia and tumours, and investigation of signs and symptoms which may indicate cervical pathology. Each of these groups has specific guidelines for specimen collection, pathways for testing through the laboratory and recommendations based on the individual patient's screening and clinical history.

In addition, special consideration and pathways exist for patients who may be immunocompromised, have had in utero exposure to diethylstilboesterol (DES) or who have other particular circumstances. The breadth of the program can be daunting for clinicians faced with understanding a patient's testing needs, providing the correct specimen for testing and interpreting the reasons for various recommendations given in the pathology report. Breaking down these specific groups often makes it easier to address the individual patient's needs.

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Screening Population

Overview

The National Cervical Screening Program (NCSP) recommends a liquid-based collection for HPV DNA testing with a five-yearly screening interval. Screening now commences at **25 years** of age (accepted from 24 years and 9 months), with an exit test up to the age of **74 years**. The age range is based on evidence that cervical cancer is rare in young patients; screening patients younger than 25 years of age has not altered the number of cervical cancer cases or deaths in this group. This measure also prevents the over-treatment of common cervical abnormalities in young patients, which usually resolve naturally. Additionally, HPV vaccination has already shown a significant reduction of these abnormalities amongst patients in this age bracket.

The patient will be sent an invitation to participate in the Program at 25 years and will be sent a reminder from the NCSP at the time of 5-year recall after a negative screening test (eligible > 4 years and 9 months since a negative screening result).

Collection Methods

The patient may have a traditional doctor-collected Liquid Based Cytology (LBC) cervical test where the cervix is sighted on speculum examination and the transformation zone of the cervix directly sampled, or may choose to have a self-collected vaginal sample (see Tables 3 and 4). Both samples will receive primary examination by molecular testing for High Risk (HPV 16 and HPV 18) and Intermediate Risk (non-16/18 HPV) Human papillomavirus (HPV) types.

Interpreting HPV-Negative Results

There is good evidence to support primary molecular HPV cervical testing in the screening population. Primary HPV testing has been shown to have a high negative predictive value; if a patient is negative for Intermediate or High Risk HPV types, there is a low risk of developing significant cervical pathology in the 5 year interval until the next cervical screening. This high negative predictive value underpins the recommendations for this group.

Patients with a negative test are deemed **LOW RISK** and can be safely screened after a 5-year interval.

As most patients in the screening population will test HPV-negative and require no further testing, a self-collected cervical test is an attractive, non-confronting screening option and has encouraged many individuals who would not otherwise participate in the Cervical Screening Program to undertake screening.

Management of HPV-Positive Results (Non 16/18 Types)

Patients who have HPV detected have a positive marker for potential cervical pathology and will require further investigation. Patients with non-16 non-18 HPV subtypes detected are considered to be at **INTERMEDIATE RISK** of significant cervical pathology and **require cytological examination of the cervix** to determine if cellular changes are present, and if so, the nature and degree of these changes.

Where an LBC-based collection was provided, this will be undertaken on the vial received, but patients who have had a primary self-collected vaginal sample will need to have a clinician-collected cervical LBC collection taken to facilitate cytological examination. The cytological findings will determine the recommendation; if no pathology (normal findings) or low-grade squamous intraepithelial lesion (LSIL)/possible LSIL is found, the patient will be recommended to have a repeat screening in 12 months. This repeat collection can also be done via self-collect testing. Evidence has shown that some of these HPV infections/LSILs will resolve and the patient requires only monitoring in the short term to ensure that their disease does not progress.

Where a high-grade squamous intraepithelial lesion (HSIL), endocervical or other neoplastic pathology is found or suspected, the patient is considered **HIGH RISK** and will be **recommended for colposcopy**. A patient who has not cleared their non-16 non-18 HPV after repeated surveillance (3rd annual repeat for patients under 50 years, 2nd annual repeat for patients 50 years and over) is also considered **HIGH RISK** despite the cytological findings and will be **recommended for colposcopic examination** to ensure significant cervical pathology is not being missed.

Management of High Risk HPV 16 and 18

A patient who tests **positive for HPV 16 or HPV 18** will be **immediately recommended for colposcopic examination** due to the **HIGH RISK** nature of these infections and association with both squamous and endocervical high grade lesions and tumours. Where an LBC collection has been performed, the cytology will be examined but this will not inform the need for colposcopic examination. Patients who have their HPV 16 or 18 infections discovered on self-collect testing are recommended to go directly to colposcopic examination. These patients do not require an LBC collection to be done by their general practitioner, as it will be performed by the gynaecologist, usually at the time of colposcopy. Patients who continue to test positive for HPV 16 or 18 will be recommended for colposcopic examination with each positive test.

Role of the National Cervical Screening Registry

Pathology providers of cervical screening have access and provide information to the National Cervical Screening Registry which tracks individual patient screening history and management. This history informs our recommendations, and patients may be recommended for colposcopic examination if they are underscreened and have persisting HPV infection/LSIL according to their screening history, or have had a previous significant result which has not been followed up. General Practitioners are also able to request access to a participant's screening history by accessing the Healthcare Provider Portal via PRODA.

> *"A self-collected cervical test is an attractive, non-confronting screening option and has encouraged many individuals who would not otherwise participate."*

It should be noted that individuals can opt out of the Registry collecting their information. In cases where a history is not available, the pathology provider will determine the recommendation based on the information available to them; this may include any clinical history provided, HPV status and/or LBC findings, and any other previous tests held by that provider.

Screening in Pregnancy

Screening should be continued as scheduled during pregnancy. Self-collection is considered safe. If a clinician-collected specimen is taken, a broom-type brush should be used.

Screening Populations with Specific Recommendations

Some patients have conditions with known increased risk factors for HPV infection and cervical disease (see Table 1).

Immune Deficiency

This group includes patients with congenital (primary) and acquired (HIV+) immune deficiency, solid organ transplant recipients, patients treated by immunosuppressant therapy for auto-immune disease, and bone marrow transplant recipients being treated for graft vs host disease. These patients should be considered for screening every 3 years rather than the usual 5-year screening interval.

In Utero Exposure to Diethylstilboesterol

Diethystilboesterol was given to some pregnant patients up until the early 1970s when it was discovered that in utero exposure was associated with an increased risk of clear cell carcinoma of the cervix and vagina. This rare tumour is not HPV-associated, so patients exposed in utero require a clinician-collected LBC screening test so co-testing with cytology can be performed. Self-collect testing is not suitable for these patients.

Screening After Hysterectomy

Screening will depend on prior screening history and the presence or absence of cervical pathology at the time of hysterectomy. If no screening history or test of cure for HSIL has been previously completed and no pathology is found at hysterectomy, no further screening is required. Patients with known HSIL should complete their Test of Cure. Patients with HSIL or LSIL found at hysterectomy, or no screening history, should have annual HPV tests until two consecutive negative tests. Patients with endocervical adenocarcinoma in situ should commence annual vaginal vault co-testing. Patients who have had a subtotal hysterectomy with an intact cervix should follow the routine cervical screening program.

Table 1. Populations with specific recommendations for screening.

Patient Group	Examples/Conditions *(Include details on Pathology Test request form)*	Recommended Screening Interval	Collection Method
Immune deficient patients	• Congenital (primary) immune deficiency • Acquired immune deficiency (including HIV+) • Solid organ transplant recipients • Patients on immunosuppressant therapy for autoimmune disease • Bone marrow transplant recipients treated for graft versus host disease	3 years	Self-collect
In utero exposure to Diethylstilbestrol (DES)	• Increased risk of clear cell carcinoma of the cervix and vagina • Tumour is not HPV associated	3 years	Clinician-collected LBC for co-testing (HPV + Cytology). Self-collect testing not suitable.

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Management Population

The aim of the Cervical Screening Program is to recognise HSIL and treat these lesions before they develop into invasive squamous cell carcinoma (SCC), and additionally to detect neoplasia of the endocervical glands. In patients with ongoing evidence of HPV infection and/or LSIL, continued surveillance is required to detect progression to HSIL and development of endocervical lesions, as previously described.

Test of Cure (TOC)

Patients who have been treated for HSIL (CIN 2/3) are required to undergo a Test of Cure (TOC) to confirm successful treatment (see Table 2). Test of Cure requires HPV testing to be performed annually until two consecutive negative results are achieved and can be performed as clinician-collected or self-collected samples. Again, if HPV is detected, the recommendation and need for cytological examination or colposcopic examination will depend on the type of HPV detected +/- the cytological findings.

Adenocarcinoma in Situ (AIS)

Patients who have been treated for adenocarcinoma in situ (AIS) with histologically confirmed clear margins should commence annual co-testing with a clinician-collected LBC sample. If 5 consecutive co-tests are negative, the patient can be extended to co-tests every 3 years until 25 years of negative surveillance has been achieved. If any abnormal result is found on co-testing, the patient will be recommended for colposcopic examination.

Invasive Cervical Cancer

Patients who had hysterectomy for cervical SCC or invasive adenocarcinoma of the endocervix should have their ongoing management informed by their treating gynaecologist or oncologist.

Investigations of Signs and Symptoms

Patients who present with gynaecological signs and symptoms which may be indicative of cervical pathology are not considered part of the screening population; they require investigation and exclusion of cervical disease. **Self-collected specimens are NOT appropriate in these patients** as they require cytological examination in addition to their HPV status (co-testing). Cytological examination may also detect endometrial abnormalities in some cases.

Patients presenting with the following symptoms require clinician collected LBC and investigation:

- Post-menopausal bleeding
- Unexplained intermenstrual bleeding
- Persistent post-coital bleeding
- Unexplained abnormal vaginal discharge

The request form should clearly state that the patient is symptomatic so the required testing is performed and appropriate recommendation is given. It should be noted that a negative cervical test does not exclude significant gynaecological pathology and further investigation and/or gynaecological referral should be considered.

When is Co-Testing Required and Covered by the MBS?

- For symptomatic patients
- For patient's undergoing surveillance after complete excision of adenocarcinoma in situ (AIS)
- Patients with a history of DES exposure

Table 2. Test of Cure (TOC) – Patient Surveillance

Patient Group	Details
Who requires TOC?	• Patients treated for HSIL (CIN 2/3) are required to undergo a Test of Cure.
Purpose of TOC	• To confirm successful treatment following HSIL (CIN 2/3).
Testing Requirements	• HPV testing annually until two consecutive negative results are achieved.
Collection Methods	• Clinician-collected (LBC) • Self-collected (swab)
If HPV is detected	• Further management depends on HPV type detected.

Table 3. Clinician-collected versus self-collected samples for cervical screening tests.

	Clinician-collected cervical sample	Self-collected vaginal sample
Is co-testing possible?	Yes	No
Indicated for • Those who are eligible and due or overdue for cervical screening, including during pregnancy • Other points in the pathway where only a HPV test is required, including Test of Cure after HSIL treatment • People who have had a total hysterectomy with history of HSIL	Yes	Yes
• Those undergoing surveillance after completely excised AIS	Yes	No
• People who have signs and symptoms suggestive of cervical cancer • People who have postcoital or intermenstrual bleeding, post-menopausal bleeding, or unexplained persistent vaginal discharge • People who were exposed to DES in utero	Yes	No

Table 4. Collection method and device.

Collection Method and Device	Site of collection	Test Performed	Population
Self-collect Swab (FLOQSwab - Copan 552C) 	Vagina	HPV	Screening (not symptomatic patients)
Clinician-collected LBC 	Cervix, Vault	HPV +/- LBC	Management and symptomatic patients

For further information, please visit the Cervical Screening page on our website at clinicallabs.com.au/doctor/cervical-screening or scan the QR code.

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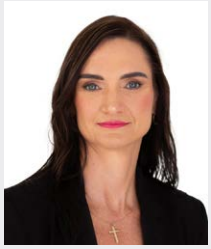

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Will the Real Assessment of Vitamin B12 Deficiency Please Stand Up?

By Associate Professor Chris Barnes

The MBS changes introduced in 2025 have prompted necessary reflection on how vitamin B12 deficiency is best assessed in clinical practice. Our laboratory previously published an article outlining the potential advantages of Active B12 testing and its role in detecting early deficiency. With the MBS review in June 2025, it is timely to revisit that position, acknowledge the limitations of holoTC, and consider alternative strategies that prioritise the detection of functional B12 deficiency. Functional vitamin B12 deficiency refers to impaired intracellular cobalamin activity despite normal or borderline serum B12 or holo-transcobalamin levels (Active B12), leading to accumulation of the metabolic intermediates methylmalonic acid (MMA) and homocysteine. In the context of the 2025 MBS changes, this biochemical phenotype may be appropriately detected through reflex testing.

Revisiting the complexity of B12 deficiency

Vitamin B12 deficiency remains challenging because no single test can accurately diagnose or exclude deficiency in ***all*** clinical settings. Total serum B12 lacks sensitivity, and clinically meaningful (functional) deficiency can occur even when levels fall within the laboratory reference range.[1] This is particularly relevant in older adults, where cognitive decline, neuropathy, anaemia, and frailty may develop subtly and be mistaken for ageing.[2]

Risk factors for the development of vitamin B12 deficiency are common and often cumulative, including:

- Long-term proton pump inhibitor or H2-blocker therapy
- Metformin use
- Pernicious anaemia or autoimmune gastritis
- Older age, gastric atrophy and reduced intrinsic factor production[3]

Active B12: useful but far from perfect

Although Active B12 reflects the biologically available fraction of cobalamin, several practical and biological limitations should be acknowledged.

- Both serum vitamin B12 and holo-transcobalamin testing are characterised by a wide diagnostic “grey zone” that frequently necessitates confirmatory investigations and are significantly influenced by binding-protein biology.
- Active B12 measures cobalamin bound to transcobalamin II, the carrier protein responsible for cellular delivery, rather than serving as a direct marker of intracellular B12 activity.

Vitamin B12 deficiency remains challenging because no single test can accurately diagnose or exclude deficiency in all clinical settings.

- Transcobalamin II concentrations and receptor function are influenced by inflammation, liver and renal disease, ageing and genetic variation, such that holo-transcobalamin may appear normal or elevated despite impaired cellular utilisation, with documented cases demonstrating markedly elevated methylmalonic acid and homocysteine in the presence of normal serum and Active B12 levels.

A functional, clinically aligned pathway: reflex HCY testing

As methylmalonic acid is technically available under the MBS but requires specialised mass-spectrometry platforms and is not routinely accessible in many laboratories, and in response to the recent MBS changes aimed at improving identification of clinically significant (functional) vitamin B12 deficiency, our laboratory will implement reflex homocysteine (HCY) testing for all serum vitamin B12 results below 360 pmol/L, reframing this interval as “borderline” rather than “low-normal.”

This approach ensures that individuals at risk of early or functional deficiency, particularly older patients, receive additional biochemical clarification without the need for a separate test request or delays associated with referral MMA testing.

However, meaningful interpretation of HCY is essential:

- Mild elevations (16–20 µmol/L) are often non-specific and may reflect renal function, folate or B6 deficiency, or pre-analytical factors
- HCY >20 µmol/L correlates more strongly with clinically significant B12 deficiency and aligns with historic Active B12–based detection thresholds [1,6]

Reports will now include the updated interpretive comment:

“HCY is above the laboratory reference range, but values below 20 µmol/L are often non-specific and may not indicate clinically significant B12 deficiency. Levels >20 µmol/L are more consistent with vitamin B12 deficiency.”

Where does this leave GPs?

The inevitable question is: what is the real measure of B12 deficiency?

In practice, there is no single biochemical marker that answers this confidently. Clinical context, risk factors, and functional testing provide the most reliable pathway forward.

Our updated approach aims to:

- Avoid missed deficiency in high-risk groups
- Reduce over-calling of non-specific biochemical abnormalities
- Provide clearer, more clinically aligned interpretive comments
- Support GPs in making confident, evidence-based decisions in assessing patients at risk of vitamin B12 deficiency

> *Our laboratory will now implement reflex homocysteine (HCY) testing for all serum B12 results below 360 pmol/L, reframing this interval as "borderline" rather than "low-normal."*

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Associate Professor Chris Barnes joined Clinical Labs in 2016 and is the National Director of Clinical Pathology. Prior to this, he worked as a consultant haematopathologist with Healthscope Pathology from 2009. Chris is a dual-trained clinical and laboratory haematologist, having trained at the Royal Children's Hospital and the Royal Melbourne Hospital. He also undertook training at The Hospital for Sick Children in Toronto, Canada. He holds a part-time public hospital appointment at the Royal Children's Hospital, where he serves as the Director of the Henry Ekert Haemophilia Treatment Centre. Chris has extensive clinical research interests and is the principal investigator on eight separate clinical trials based at the Murdoch Children's Research Institute. He has held numerous leadership positions, including Chair of the Medical Staff Association at the Royal Children's Hospital and Chair of the Australian Haemophilia Directors Association. He is currently the Chair of the Australian Bleeding Disorders Registry with the National Blood Authority and a Director of Melbourne Haematology and Melbourne Paediatric Specialists. Chris' focus within Clinical Labs is the national supervision and management of clinical pathology disciplines, including haematology, biochemistry, microbiology and immunopathology.

Supporting Contemporary Cardiac Care: Focus on high-sensitivity troponin testing

By Dr David Deam

Australian Clinical Labs will shortly withdraw CK-MB from its routine test repertoire. Contemporary practice now relies on cardiac troponin I or T as the recommended laboratory markers for myocardial infarction, reflecting their superior sensitivity and specificity.

Hospital admission and management decisions should not be delayed while awaiting laboratory results. Testing complements clinical assessment and ECG findings, particularly when ECG changes are non-specific or left bundle branch block is present.

High-sensitivity troponin assays typically become abnormal within 1–3 hours of symptom onset and may remain elevated for 7–10 days. Serial testing is recommended to demonstrate a rise or fall in concentration, with myocardial infarction defined by dynamic troponin change and at least one value above the 99th percentile in the appropriate clinical context.

GPs should continue to request high-sensitivity troponin for suspected acute coronary syndromes and contact the laboratory for advice in unusual cases or when CK-MB is being requested.

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REMINDER

High-Risk Result Notifications via SMS

Clinical Labs has recently enhanced our communication protocol for high-risk results to improve timeliness and reliability. Based on clinician feedback, urgent results will now be notified to referrers instantly via SMS, directly to their mobile device.

Each SMS will alert you that a high-risk result is available and can be accessed securely via our eResults at results.clinicallabs.com.au/login. This allows you to review the result at a time that is convenient, without interruption.

Simply log in to eResults by clicking the link provided in the SMS and enter your username and password. To register for eResults, scan the QR code or visit the link below to get started.

On receipt of the SMS, we ask that you reply 'Y' to confirm you have received the notification. This replaces the need for a manual acknowledgment and ensures our team is aware the result has reached you. If the SMS cannot be delivered, our standard escalation process will apply.

As outlined by the Medical Board of Australia's Good Medical Practice guidelines, clinicians have a professional responsibility to ensure they are available for the receipt and communication of clinically significant and high-risk results. Ensuring timely access helps protect both patient safety and practitioners from the risk of delayed or missed result notification.

This update reflects our commitment to timely communication and patient safety, and we're confident it will make managing urgent results simpler and more efficient for you and your practice.

Register for eResults today at clinicallabs.com.au/eresults-registration or by scanning the QR code.

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