

# **MSAC Application 1752**

## **Anal human papillomavirus and cytology testing in high-risk populations**

# Application for MBS eligible service or health technology

**MSAC Application Number:**

1752

**Application title:**

Anal human papillomavirus and cytology testing in high-risk populations

**Submitting organisation:**

The Royal College of Pathologists of Australasia

**Submitting organisation ABN:**

52000173231

## Application description

**Succinct description of the medical condition/s:**

Anal cancer, although relatively rare in Australia, has been rapidly rising in terms of incidence and mortality, with rates increasing over time in both men and women. Anal high-grade squamous intraepithelial lesions (HSIL) are the precursor of squamous cell carcinoma of the anus (SCCA) (Berry et al 2014). Like cervical cancer, human papillomavirus (HPV) infection, primarily HPV type 16, causes approximately 90 per cent of SCCA cases (Berenson et al 2022; Palefsky et al 2011). However, in people living with HIV, approximately 30% of SCCA is caused by non-HPV16 high-risk HPV types (Lin et al 2018). Also, due to the histological and biological similarities between cervical and anal cancer, HPV vaccination is expected to be the long-term solution to SCCA prevention; however, the full impact of vaccination programmes will not be felt for decades (Clifford et al 2021). Like cervical cancer, the treatment (most often by ablation) of HSIL significantly reduces anal cancer incidence.

**Succinct description of the service or health technology:**

This application proposes extending the existing cervical HPV testing and cytology MBS item numbers to include the anal canal, in populations at high-risk for HSIL and SCCA including all people living with human immunodeficiency virus (HIV) (both male and female), HIV-negative men who have sex with men (MSM), women diagnosed with HPV-related gynaecological precancerous lesions or cancer, and solid-organ (e.g. kidney) transplant recipients (Albuquerque 2020; Clifford et al 2021).

As with cervical cancer, anal HPV testing should be conducted first, with reflex anal cytology conducted on those patients testing positive for HPV. HPV testing and cytology should not be conducted at the same time. This application is seeking an amendment to the Cervical and Vaginal Screening MBS items 73070 to 73076 to include anal HPV and anal cytology.

## Application contact details

**Are you the applicant, or are you a consultant or lobbyist acting on behalf of the applicant?**

Applicant

**Are you applying on behalf of an organisation, or as an individual?**

Organisation

**Is the applicant organisation the organisation you are representing in the HPP today?**

Yes

## Application details

**Does the implementation of your service or health technology rely on a new listing on the Pharmaceutical Benefits Scheme (PBS) and/or the Prostheses List?**

No

**Is the application for a new service or health technology, or an amendment to an existing listed service or health technology?**

Amendment

**What is the nature of the amendment?**

An amendment to the medical condition under the existing item(s)

**Justification for amendment:**

An amendment to the way the service is clinically delivered under the existing item(s)

An amendment to the patient population under the existing item(s)

An amendment to cervical screening sample collection MBS items to include anal sample collection.

An amendment to the Cervical and Vaginal Screening MBS items to include anal HPV and anal cytology.

OR it may be simpler to say that these will be new MBS item numbers for a different patient population.

**Please select any relevant MBS items**

MBS item number	Selected reason type
2497	Expansion or amendment to existing item
2497	Expansion or amendment to existing item
2501	Expansion or amendment to existing item
2503	Expansion or amendment to existing item
2504	Expansion or amendment to existing item
2506	Expansion or amendment to existing item
2507	Expansion or amendment to existing item
2509	Expansion or amendment to existing item
2598	Expansion or amendment to existing item
2600	Expansion or amendment to existing item
2603	Expansion or amendment to existing item
2606	Expansion or amendment to existing item
2610	Expansion or amendment to existing item
2613	Expansion or amendment to existing item
2616	Expansion or amendment to existing item
73070	Expansion or amendment to existing item
73072	Expansion or amendment to existing item
73075	Expansion or amendment to existing item
73076	Expansion or amendment to existing item

**What is the type of service or health technology?**

Investigative

**Please select the type of investigative health technology:**

Histopathology and cytology

**PICO Set****Patients at increased risk of anal cancer****State the purpose(s) of the health technology for this PICO set and provide a rationale:****Purpose category:**

Targeted screening

**Purpose description:**

To test currently unaffected or asymptomatic individual(s) identified as at increased risk. For example: cascade screening

**Population****Describe the population in which the proposed health technology is intended to be used:**

Anal cancer, although relatively rare in Australia, has been rapidly rising in terms of incidence and mortality, with both rates increasing over time (Figure 1 to Figure 4). Although more often a cancer associated with gay and bisexual men, especially those who are human immunodeficiency virus (HIV)-positive, the incidence in Australian women is increasing (Lum et al 2020; Palefsky et al 2022). Women diagnosed with HPV-related gynaecological pre-cancerous lesions or cancer, as well as solid organ transplant recipients and patients with autoimmune diseases such as systemic lupus erythematosus, ulcerative colitis or Crohn's disease, are at higher-than-average risk of anal cancer (Clifford et al 2021).

The natural history of anal cancer is not as well characterised as that of cervical cancer; however, there are similarities. Persisting high-risk HPV infection can lead to the development of HSIL (categorised as AIN 2 and 3). Persisting infection with low-risk HPV genotypes can lead to the development of low grade squamous intraepithelial lesions (LSIL or AIN 1), which are not usually associated with progression to invasive malignancy (Lum et al 2020). HSIL are the precursor of squamous cell carcinoma of the anus (SCCA), which represent approximately 70-80% of all anal cancers (Berry et al 2014; Lum et al 2020). Like cervical cancer, human papillomavirus (HPV) infection, primarily HPV type 16 or 18, has a causal relationship in approximately 90 per cent of SCCA cases (Berenson et al 2022; Palefsky et al 2011). HIV co-infection markedly increases the risk of HPV-associated anal SCC, particularly in those individuals with low CD4 counts (Lum et al 2020).

Anal cancer is among the limited number of cancer types, including cervical and colon cancer, that are potentially preventable through treatment of known cancer precursors. Programs that identify HSIL early enable the early detection, prevention, and treatment of anal cancer. Due to the histological and biological similarities between SCC of the anus and cervix, and the causal association with infection with HPV, like cervical cancer, the treatment (most often by ablation) of HSIL significantly reduces the progression to anal cancer (Palefsky et al 2022). Patients treated for anal HSIL (primarily office-based electrocautery) have rates of progression to anal cancer approximately 60% lower than those who only undergo active monitoring without treatment (Palefsky et al 2022).

Like cervical cancer, gender-neutral HPV vaccination is expected to be the long-term primary prevention strategy to SCCA; however, the full impact of vaccination programmes will not be felt for decades (Clifford et al 2021).

The target populations for testing include:

- i) people living with HIV;
- ii) MSM;
- iii) women with other gynaecological HPV-associated lesions, including cancers;
- iv) solid organ transplant recipients.

As such, these populations are likely to be cared for in the health system by specialists and/or general practitioners. This high-risk population would normally undergo standard clinical care until they are symptomatic of an anal cancer. For example, a person living with HIV would have their CD4+ count, a transplant patient would have organ function tested

Those with defined abnormalities (such as HPV16/persisting non-16 high-risk HPV, cytology  $\geq$  pHSIL) will be referred on to specialised services, where the extent and nature of histologically-established HSIL can be characterised. People with HSIL deemed to be at high risk of progression to SCCA will be offered treatment. Both high-risk HPV testing and cytology can be used to assess response to treatment.

#### **Search and select the most applicable medical condition terminology (SNOMED CT):**

Primary malignant neoplasm

## **Intervention**

#### **Name of the proposed health technology:**

Anal sampling, followed by testing for HPV, capable of distinguishing between defined high- and low-risk HPV genotypes, and if clinically indicated, analysis for cytological changes.

## **Comparator**

**Nominate the appropriate comparator(s) for the proposed medical service (i.e. how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system). This includes identifying health care resources that are needed to be delivered at the same time as the comparator service:**

There is no direct comparator for this service.

In the absence of the intervention, patients would receive routine clinical care, which would vary according to their risk profile. Men who have sex with men would be monitored under the care of their general practitioner, or a sexual health practitioner. Individuals may undergo testing for HIV antibodies or p24 antigen in addition to any routine health checks. Many individuals may opt to use point of care rapid HIV test self-testing; however, approved self-tests that are purchased by the end user are not eligible for an MBS rebate. At-risk individuals may have their CD4+ counts taken in order to identify those who would benefit from an early HIV diagnosis. People living with HIV would be monitored under the care of their general practitioner, or a sexual health practitioner. When on anti-retroviral therapy, HIV positive patients may undergo viral load testing or HIV genotyping. In addition, patients may have their CD4+ counts taken to monitor therapy effectiveness or disease progression. Organ transplant recipients may have regular quarterly clinical examinations with their transplant specialist, where routine blood tests are conducted including a full blood examination and biochemistry, lipid studies, viral screens (polyomaviruses, cytomegalovirus) and testing levels of

immunosuppressive agents. In addition, imaging, and clinical examination should be conducted including regular bone density scans (3 years), skin cancer checks (2 years), with kidney transplant patients undergoing regular renal function tests. Women with previous HPV-related lower genital tract cancer or cervical HSIL receive regular follow-up by their gynaecologist, surgeon or general practitioner. This includes cervical cytology, pelvic examination and HPV testing. People with previous anal cancer receive regular follow up by their surgeon, oncologist or radiation oncologist. This includes imaging and clinical examination.

## Outcomes

**Outcome description – please include information about whether a change in patient management, or prognosis, occurs as a result of the test information:**

Change in patient management.

Anal high-grade squamous intraepithelial lesions (HSIL) are the precursor of squamous cell carcinoma of the anus (SCCA) (Berry et al 2014).

Testing of asymptomatic patients may result in a change in patient management. It has been recently shown that, like cervical cancer, the treatment (most often by ablation) of HSIL significantly reduces anal cancer incidence (Palefsky et al 2022). If a positive HPV test is followed by positive cytology, indicating the presence of HSIL, it is recommended that (non-MBS funded) high-resolution anoscopy (similar to colposcopy in cervical cancer) is performed. This may then be followed by treatment such as (non-MBS funded) office-based electrocautery.

### Safety

- Harms associated with testing/not testing

### Clinical effectiveness

- Impact on clinical management
- Morbidity associated with anal carcinoma
- Mortality due to anal carcinoma
- Health-related quality of life
- Other patient-relevant outcomes

### Clinical validity

- Clinical sensitivity and specificity
- Positive and negative predictive values
- Prognostic value

### Healthcare resource use

- Number of events, and cost associated with anal carcinoma (e.g. hospitalisation; specialist visits; requirements for subsequent therapy; cost of testing)
- Cost-effectiveness of HPV testing and cytology
- Total Australian Government healthcare costs

## Proposed MBS items

### Proposed Item AAAAA

#### Category:

PROFESSIONAL ATTENDANCES

#### Proposed group:

GENERAL PRACTITIONER ATTENDANCES TO WHICH NO OTHER ITEM APPLIES

#### Item descriptor

Based on item number 2497 Category 1 – Professional attendances

AAAA

Professional attendance at consulting rooms by a treating physician:

(a) involving taking a short patient history and, if required, limited examination and management; and

(b) at which a specimen for an anal screening service is collected from the patient:

- i. if the patient has no history of biopsy-proven anal high-grade squamous intraepithelial lesions (HSIL) or cancer
- ii. is human immunodeficiency virus (HIV) negative
- iii. is at least 35 years of age; and
- iv. has not been provided with an anal screening service or an anal smear service in the last 5 years.

OR

(c) at which a specimen for an anal screening service is collected from the patient:

- i. if the patient has no history of biopsy-proven anal high-grade squamous intraepithelial lesions (HSIL) or cancer
- ii. is human immunodeficiency virus (HIV) positive
- iii. is at least 35 years of age; and
- iv. has not been provided with an anal screening service or an anal smear service in the last 3 years.

OR

(d) at which a specimen for an anal screening service is collected from the patient;

- i. if the patient has a history of biopsy-proven anal high-grade squamous intraepithelial lesions (HSIL) or cancer and
- ii. has not been provided with an anal screening service or an anal smear service in the last year

Fee: \$17.90 Benefit: 100% = \$17.90

#### Proposed MBS fee:

\$17.90

#### Indicate the overall cost per patient of providing the proposed health technology:

\$17.90

**Please specify any anticipated out of pocket costs:**

\$0.00

**Provide details and explain:**

An amendment to cervical screening sample collection MBS items to include anal sample collection.

MBS item numbers: 2497, 2501, 2504, 2507, 2598, 2600, 2603, 2606 in addition to item numbers 2503,

2506, 2509, 2610, 2613, 2616, when a cervical screen is done outside of a general practice.

**Proposed Item BBBBB**

**Category:**

PATHOLOGY SERVICES

**Proposed group:**

CYTOLOGY

**Item descriptor:**

Based on item number 73070 Category P6 – Cytology

BBBB

A test, including partial genotyping, for oncogenic human papillomavirus that may be associated with anal pre cancer or cancer:

(a) performed on a liquid based anal specimen; and

(b) for an asymptomatic patient who is at least 35 years and has satisfied the conditions of sample collection using MBS item AAAA

Fee: \$35.00 Benefit: 75% = \$26.25 85% = \$29.75

**Proposed MBS fee:**

\$35.00

**Indicate the overall cost per patient of providing the proposed health technology:**

\$35.00

**Please specify any anticipated out of pocket costs:**

\$0.00

**Provide details and explain:**

An amendment to cervical screening sample collection MBS items

MBS item numbers: 73070, 73071, 73072, 73073, 73074, 73075

A test, including partial genotyping, for oncogenic human papillomavirus that may be associated with cervical pre-cancer or cancer

**Proposed Item CCCCC****Category:**

PATHOLOGY SERVICES

**Proposed group:**

CYTOLOGY

**Item descriptor:**

Based on item number 73072 Category P6 – Cytology

CCCC

A test, including partial genotyping, for oncogenic human papillomavirus, performed on a liquid based anal specimen:

(a) for the investigation of a patient in a specific population that appears to have a higher risk of anal pre-cancer or cancer; or

(b) for the follow-up management of a patient with a previously detected oncogenic human papillomavirus infection or anal pre-cancer or cancer; or

(c) for the investigation of a patient with symptoms suggestive of anal cancer.

Fee: \$35.00 Benefit: 75% = \$26.25 85% = \$29.75

**Proposed MBS fee:**

\$35.00

**Indicate the overall cost per patient of providing the proposed health technology:**

\$35.00

**Please specify any anticipated out of pocket costs:**

\$0.00

**Provide details and explain:**

An amendment to cervical screening sample collection MBS items

MBS item numbers: 73070, 73071, 73072, 73073, 73074, 73075

A test, including partial genotyping, for oncogenic human papillomavirus that may be associated with cervical pre-cancer or cancer

**Proposed Item DDDDD****Category:**

PATHOLOGY SERVICES

**Proposed group:**

CYTOLOGY

**Item descriptor:**

Based on item number 73075 Category P6 – Cytology

DDDD

A test, including partial genotyping, for oncogenic human papillomavirus, if:

(a) the test is a repeat of a test to which item BBBB, CCCC or this item applies; and

(b) the specimen collected for the previous test is unsatisfactory

Fee: \$35.00 Benefit: 75% = \$26.25 85% = \$29.75

**Proposed MBS fee:**

\$35.00

**Indicate the overall cost per patient of providing the proposed health technology:**

\$35.00

**Please specify any anticipated out of pocket costs:**

\$0.00

**Provide details and explain:**

An amendment to cervical screening sample collection MBS items

MBS item numbers: 73070, 73071, 73072, 73073, 73074, 73075

A test, including partial genotyping, for oncogenic human papillomavirus that may be associated with cervical pre-cancer or cancer

**Proposed Item EEEEE**

**Category:**

PATHOLOGY SERVICES

**Proposed group:**

CYTOLOGY

**Item descriptor:**

Based on item number 73076 Category P6 – Cytology

EEEE

Cytology of a liquid based anal specimen, where the stained cells are examined microscopically or by automated image analysis by or on behalf of a pathologist, if:

(a) the cytology is associated with the detection of oncogenic human papillomavirus infection by:

(i) a test to which item BBBB applies; or

(ii) a test to which item CCCC applies for a patient mentioned in paragraph (a) or (b) of that item; or

(b) the cytology is associated with a test to which item CCCC applies for a patient mentioned in paragraph (c) of that item; or

(c) the test is a repeat of a test to which this item applies, if the specimen collected for the previous test is unsatisfactory

Fee: \$46.00 Benefit: 75% = \$34.50 85% = \$39.10

**Proposed MBS fee:**

\$46.00

**Indicate the overall cost per patient of providing the proposed health technology:**

\$46.00

**Please specify any anticipated out of pocket costs:**

\$0.00

**Provide details and explain:**

An amendment to cervical screening sample collection MBS items

MBS item number: 73076 Cytology of a liquid based cervical or vaginal vault specimen, where the stained cells are examined microscopically or by automated image analysis by or on behalf of a pathologist

**How is the technology/service funded at present? (For example: research funding; State-based funding; self-funded by patients; no funding or payments):**

There are currently no MBS item numbers for anal HPV testing or cytology. At-risk patients are either managed in private settings (self funded) or in state-based sexual health clinics until symptomatic of an anal cancer

## Claims

**In terms of health outcomes (comparative benefits and harms), is the proposed technology claimed to be superior, non-inferior or inferior to the comparator(s)?**

Superior

**Please state what the overall claim is, and provide a rationale:**

Anal cancer is among the limited number of cancers, including cervical and colon cancer that are potentially preventable through treatment of known cancer precursors. Identifying HSIL early enables the early detection, prevention and treatment of anal cancer. Patients treated for anal HSIL (primarily office-based electrocautery) have rates of progression to anal cancer approximately 60% lower than those only undergo active monitoring without treatment (Palefsky et al 2022).

## Estimated utilisation

**Estimate the prevalence and/or incidence of the proposed population:**

Although there are good data on the prevalence and rate of anal cancer in Australia (Figure 1 and Figure 3), these figures do not give an indication of the number of individuals at risk of developing HSIL or anal cancer. Certain population groups are known to have higher than average anal cancer risk including people living with HIV (PLHIV), men who have sex with men (MSM), women diagnosed with human papillomavirus (HPV)-related gynaecological precancerous lesions or cancer, solid organ transplant recipients (SOTRs) and patients with autoimmune diseases. Figure 7 describes the level of risk for each of these groups, with PLHIV, especially those ages >45 years, being at greatest risk (Clifford et al 2021).

In Australia the number of HIV notifications with a first ever diagnosis declined markedly in 2021 to 552, compared to 1,068 notifications in 2012. This decrease was likely due to COVID-19 public health measures placed on travel and movement, social activity, and lack of access to HIV testing. It may reasonably be expected that the number of HIV notifications will increase post-COVID. MSM are the major HIV risk exposure group in Australia, accounting for 378 (68%) HIV notifications in 2021, with heterosexual sex reported for 148 (27%) notifications, and injection drug use for 9 (less than 2%) notifications (King et al 2022).

In 2021, the proportion of all people in Australia who are living with HIV (HIV prevalence), was estimated to be 0.14% of the population, equating to 29,460 people, and of these, 21,530 were MSM. It has been estimated that one third of MSM are HIV positive, therefore the total 'prevalent' MSM population would be estimated to be 64,590 (including HIV positive and HIV negative men) (King et al 2022).

There were 591 new cases of anal cancer reported in Australian in 2021, with approximately 60 per cent having a 5-year survival. Patients with a previous case of anal cancer are likely to be HPV positive, and would therefore undergo cytology testing every 2-years.

Women with previous anogenital HPV cancer, including cancer of the vulva and vagina, but excluding anal cancer, are also considered a high-risk group. Cancers of the vulva and vagina are rare, with an estimated number of incident cases in Australia of 456 and 95 in 2020, respectively, with an age-standardised incident rate of 1.83 and 0.38, respectively (Bruni et al 2021). It has been estimated that there will be 952 new cases of cervical cancer diagnosed in 2022.

Solid organ transplant recipients, most commonly kidney transplant but could include liver, intestines, heart, lung and pancreas, are also considered to be at risk of anal cancer. In Australia in 2021 a total of 1,371 solid organs were transplanted, the majority of which were kidneys (n=668) and the 5-year survival rate for solid organ transplants is approximately 83% (ANZOD Registry 2019; ANZOD Registry 2022). As a rough estimate of organ transplant recipients who may require monitoring for risk of anal cancer, in 2019 the number of individuals living with a functioning kidney transplant in Australia was 12,815 (Wyld et al 2021). As kidney transplants represent approximately 50 per cent of all solid organ transplants, the number of patients requiring testing may be 26,000.

**Provide the percentage uptake of the proposed health technology by the proposed population:**

**Year 1 estimated uptake(%):**

See attached Table 1 Estimated uptake of HPV and cytology testing in Australia 2023-2026

**Year 2 estimated uptake(%):**

See attached Table 1 Estimated uptake of HPV and cytology testing in Australia 2023-2026

**Year 3 estimated uptake(%):**

See attached Table 1 Estimated uptake of HPV and cytology testing in Australia 2023-2026

**Year 3 estimated uptake(%):**

See attached Table 1 Estimated uptake of HPV and cytology testing in Australia 2023-2026

**Estimate the number of patients who will utilise the proposed technology for the first full year:**

See attached Table 1 Estimated uptake of HPV and cytology testing in Australia 2023-2026

**Will the technology be needed more than once per patient?**

Yes, multiple times

**Over what duration will the health technology or service be provided for a patient?**

See below

**Optionally, provide details:**

For some at-risk individuals, testing would only need to commence after 35 years of age, with frequency of testing as described (Patients considered to be at high-risk, including those with a history of biopsy-proven HSIL/cancer anywhere in the anogenital region, should be tested for HPV annually. For HIV negative and HIV positive individuals testing should be conducted every 5-years and 3-years, respectively. Solid organ transplant recipients should be tested every 2-years). For other at-risk individuals, such as women with previous anogenital HPV cancer, testing may begin at any age and would continue for life.

**What frequency will the health technology or service be required by the patient over the duration? (range, preferably on an annual basis):**

See below

**Optionally, provide details:**

Patients considered to be at high-risk, including those with a history of biopsy-proven HSIL/cancer anywhere in the anogenital region, should be tested for HPV annually. For HIV negative and HIV

positive individuals testing should be conducted every 5-years and 3-years, respectively. Solid organ transplant recipients should be tested every 2-years.

## Consultation

**List all appropriate professional bodies / organisations representing the group(s) of health professionals who provide the health technology/service:**

- Australian Pathology
- Public Pathology Australia
- The Royal College Of Pathologists Of Australasia

**List all appropriate professional bodies / organisations representing the group(s) of health professionals who request the health technology/service:**

- Royal Australasian College of Physicians, Sexual Health Chapter
- Royal Australian College of General Practitioners (RACGP)

**List all appropriate professional bodies / organisations representing the group(s) of health professionals that may be impacted by the health technology/service:**

- Australian Pathology
- Public Pathology Australia
- The Royal College Of Pathologists Of Australasia

**List the patient and consumer advocacy organisations or individuals relevant to the proposed health technology:**

- ACON
- Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM)
- Mardi Gras
- National Association of People with HIV Australia (NAPWHA)
- Positive Life NSW

**List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed service or health technology:**

-

## Regulatory information

**Would the proposed health technology involve the use of a medical device, in-vitro diagnostic test, radioactive tracer or any other type of therapeutic good?**

Yes

**Has it been listed or registered or included in the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)?**

No

**Is the therapeutic good classified by the TGA as either a Class III or Active Implantable Medical Device (AIMD) against the TGA regulatory scheme for devices?**

Class III

**Is the therapeutic good to be used in the service exempt from the regulatory requirements of the Therapeutic Goods Act 1989?**

No

**Is the therapeutic good classified by the TGA as for Research Use Only (RUO)?**

No